RARE DISEASES

[Abstract:0123]

A RARE CAUSE OF ENCEPHALOPATHY: DIAGNOSIS OF UREA CYCLE DISORDER IN AN ADULT

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A 26-year-old woman started with nausea and vomiting. 48 hours later, she experienced a decline in general condition with weakness and bradypsychia, without other symptoms. She was on a regular diet, with limited meat consumption, and had no significant medical history except for eradicated H. pylori infection and vitamin B12 deficiency. Both the patient and her mother mentioned a similar episode 5 years before, that resolved without the need for medical attention. Initial examinations showed stable vital signs, normal organ functions, and unremarkable neurological signs. However, due to deteriorating consciousness level, ammonia level was tested and found to be 340 µmol/L. Brain CT scan and abdominal ultrasound showed no abnormalities. An electroencephalogram showed mild global slowing. Amino acid profile showed elevated glutamine and decreased citrulline in plasma and elevated orotate in urine, consistent with ornithine transcarbamylase (OTC) deficiency, an urea cycle disorder (UCD). In addition to the low-protein diet initiated upon admission, chelation treatment was initiated with carglumic acid and subsequently with phenylbutyrate, resulting in a gradual decrease of ammonia level and clinical improvement.

The patient is currently under follow-up in outpatient care, gradually increasing protein intake to reach levels recommended for a healthy population, without chelating agents, maintaining ammonia and amino acid levels within normal range. Urea cycle disorders are a group of metabolic diseases caused by alterations in any of the enzymes involved in the urea cycle. Although they are mainly diagnosed in childhood, they should be considered in patients with hyperammonemia, which is their main characteristic.

Keywords: *urea cycle disorder, encephalopathy, rare disease*

[Abstract:0125]

USEFULNESS OF BEVACIZUMAB IN CHRONIC DIGESTIVE BLEEDING IN PATIENTS WITH HEREDITARY HEMORRHAGIC TELANGIECTASIA

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Hereditary haemorrhagic telangiectasia (HHT) is a rare autosomal dominant hereditary disease primarily caused by mutations in the ENG and ACVRL1 genes, affecting angiogenesis regulation and resulting in telangiectases and vascular malformations (VM). Common manifestations include epistaxis, digestive bleeding, and visceral vascular malformations (VM). Severe cases may require multiple transfusions, affecting quality of life and mortality. Bevacizumab, an anti-angiogenic drug, has been used as a treatment for these severe cases. We present our experience with bevacizumab in HHT patients.

Clinical Observations: We present four patients with HHT treated with bevacizumab due to digestive bleeding requiring iron therapy and/or frequent red blood cell transfusions. The mean age was 61.1 years; 2 were women. Genetic studies were performed in three of them, detecting mutations in ENG gene in 2 cases and ACVRL1 in one. Two patients also had hepatic VM. Pulmonary VM were not detected. All patients underwent endoscopic studies prior to treatment, where lesions amenable to electrocoagulation were treated, and had undergone a therapeutic trial with octreotide without success. Bevacizumab treatment led to reduced bleeding, increased haemoglobin levels, and decreased transfusion requirements in all our patients. Figure 1 shows the evolution in the most representative patient in our series.

Conclusions: Our four patients managed to restore adequate haemoglobin levels without the need for new transfusions, with evident results since the first month. Adverse effects were considered mild. Therefore, we recommend considering bevacizumab in patients requiring frequent transfusions due to bleeding that does not respond to other therapies.

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Keywords: *hereditary haemorrhagic telangiectasia, bevacizumab, rare disease*

Patient Nº	Age (years)	Gender	Mutation	Hb pre (g/dL)	Hb post (g/dL)	Average transfusions per month in the last year pre-treatment	Average transfusions per month in the last year post-treatment
1	70	Male	ACVRL1	9.1	13.3	2.6	0.1
2	64	Woman	ENG	9.8	14.1	0.7	0
3	51	Woman	Unknown	9.9	12.8	0.5	0
4	61	Male	ENG	7.3	14.7	6.8	0

Table 1. *Summary of patient characteristics and mean haemoglobin concentration and units of red blood cell concentrates transfused in the 12 months before and after bevacizumab treatment.*

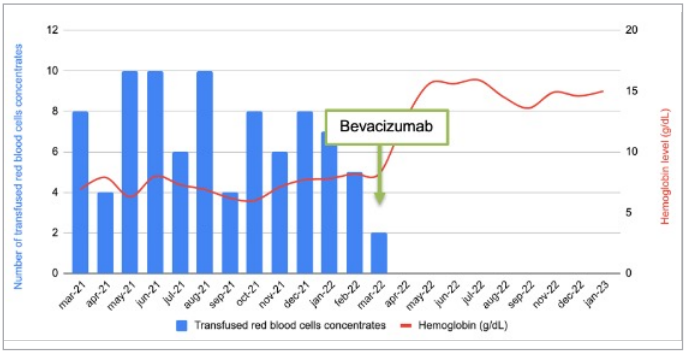

Figure 1. *Evolution of haemoglobin levels and the need for red blood cell concentrates in one of the patients before and after Bevacizumab.*

[Abstract:0132]

HARD CORD BENEATH THE CHEST WALL: MONDOR'S DISEASE

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A 27-year-old woman presented to the outpatient clinic with 8 days of left chest wall pain. Her past medical history included a single episode of left intercostal neuralgia one year prior to presentation, and no suggestive triggers such as previous trauma, surgery, infection, excessive exercise, or prolonged pressure. Family history was unremarkable and the patient did not smoke or drink alcohol and denied any allergies. Physical examination revealed a hard cord, slightly raised and tender to palpation, extending from left sub mammary region to upper abdominal area. She reported Numerical Rating Scale (NRS) pain of 6 out of 10. Her body temperature was 35.9°C, and other vital signs and laboratory testing were normal including erythrocyte sedimentation rate, C-reactive protein, coagulation panel, and WBC. Chest wall ultrasound revealed a superficial cord, tubular and anechoic, measuring 1.15 cm at its widest diameter. The cord length is 15 cm extended from the left breast to the upper abdomen. Doppler imaging demonstrated normal blood flow surrounding the cord, with no blood flow within. Based on the characteristics of the lesion, we diagnosed her with Mondor's disease. She was prescribed NSAIDs twice a day for approximately 3 weeks. Her pain gradually improved over the course of about 3 weeks and the cord disappeared after approximately two months. She remains symptom-free. It has been predominantly reported that Mondor's disease is caused by thrombophlebitis of the superficial veins.

Keywords: *Mondor's disease, thrombophlebitis, hard cord*

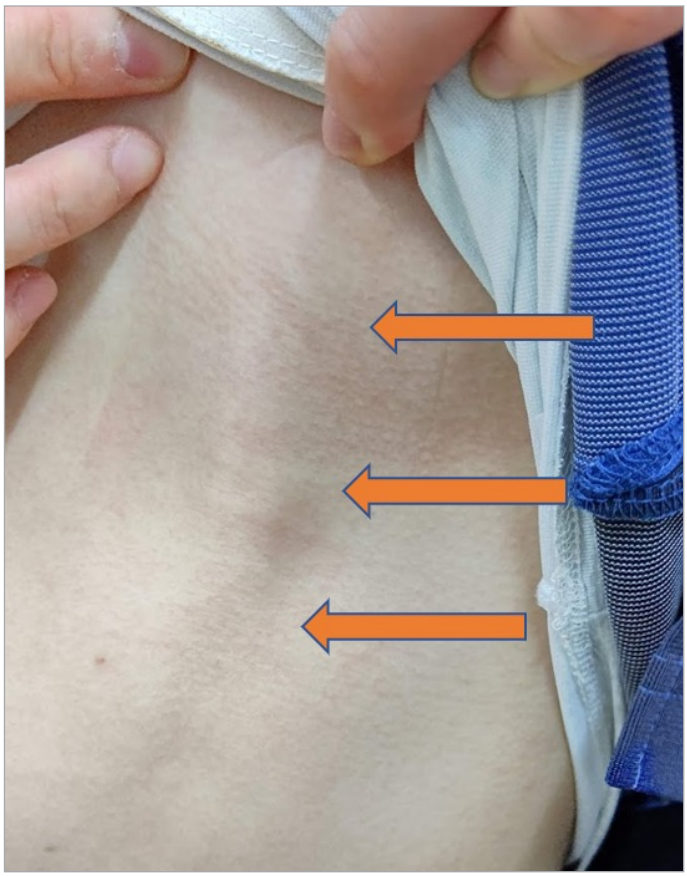

Figure 1. *This was a hard cord in left submammary to abdominal with orange arrows which is characterized of Mondor's disease.*

[Abstract:0141]

HEREDITARY HEMORRHAGIC TELANGIECTASIA: ASSOCIATION BETWEEN EXTRANASAL TELANGIECTASIAS AND PULMONARY ARTERIOVENOUS MALFORMATIONS

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Background and Aims: Hereditary haemorrhagic telangiectasia (HHT) is an autosomal dominant disease characterised by development of mucocutaneous telangiectasias and arteriovenous malformations (AVMs) in internal organs. The aim of this study was to assess the association between the location

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of extranasal mucocutaneous telangiectasia and the development of pulmonary AVMs.

Methods: A cross-sectional study was conducted on patients diagnosed with HHT according to Curacao criteria or genetics, who presented AVMs in internal organs, including pulmonary, hepatic, gastrointestinal, and cerebral locations. Mucocutaneous telangiectasias were assessed and reported by clinicians. Clinicians evaluated and recorded mucocutaneous telangiectasias. Comparisons using Student's-t test. Logistic regression models were used to derive odds ratios (OR) with 95% confidence intervals (CI). Significance was set at p<0.05.

Results: We included n=41 HHT patients who had AVMs in internal organs, of which 21/41 (51.2%) were women. Epistaxis was present in 92.7% (38/41), while extranasal mucocutaneous telangiectasias were present in 78.0% (32/41). The most prevalent AVM was pulmonary (68.3%; 28/41), followed by hepatic (36.6%; 15/41), cerebral (31.7%; 13/41) and gastrointestinal (24.4%; 10/41). Patients with telangiectasias on fingers had a significantly reduced risk of developing pulmonary AVMs compared to those without finger telangiectasias (42.9% vs. 76.9%, OR [95%CI]: 0.225 [0.051 - 0.999]; p =0.042). Similarly, the presence of extrafacial telangiectasias tended to be associated with a lower prevalence of pulmonary AVMs (57.1% vs. 84.6%, OR [95%CI]: 0.242 [0.045 - 1.304]; p=0.084).

Conclusions: The presence of extranasal telangiectasias appears to be associated with the presence of pulmonary arteriovenous malformations.

Keywords: *HHT, AVM, telangiectasias*

[Abstract:0142]

ASSOCIATION BETWEEN SEVERITY OF EPISTAXIS AND LOCATION OF EXTRANASAL TELANGIECTASIAS IN PATIENTS WITH HEREDITARY HEMORRHAGIC TELANGIECTASIA

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Background and Aims: Hereditary haemorrhagic telangiectasia (HHT) is an autosomal dominant disease mainly characterised by epistaxis. We aimed to evaluate the association between severity of epistaxis and location of mucocutaneous telangiectasia.

Methods: We conducted a cross-sectional study involving HHT patients diagnosed according to Curacao criteria or genetics, who had AVMs in internal organs (e.g., pulmonary, hepatic, gastrointestinal, and cerebral). The severity of epistaxis was assessed using the Epistaxis Severity Score (ESS). Mucocutaneous telangiectasias were assessed and reported by clinicians. Variables presented as frequencies (%) and compared using Student's-t test, with a significance level of p<0.05.

Results: N=41 HHT patients with AVMs in internal organs were included, of which 21/41 (51.2%) were women. A total of 38/41 (92.7%) had epistaxis, with a mean ESS of 2,49 ± 1,79. Extranasal mucocutaneous telangiectasias were present in 32/41 (78.0%) patients, including 23/41 (65.1%) on tongue and 5/41 (12.2%) on face. A greater severity of nosebleeds tended to be associated with the presence of telangiectasias on the tongue (2.91 ± 1.80 vs. 1.96 ± 1.66; p=0.089) and face (3.53 ± 1.62 vs. 2.24 ± 1.76; p=0.068).

Conclusions: From these findings, it can be suggested that the location of extranasal mucocutaneous telangiectasias may be associated with the severity of bleeding in patients with HHT.

Keywords: *HHT, epistaxis, telangiectasias*

[Abstract:0143]

ASSOCIATION BETWEEN EXTRANASAL TELANGIECTASIAS AND THE PRESENCE OF CEREBRAL ARTERIOVENOUS MALFORMATIONS IN HEREDITARY HEMORRHAGIC TELANGIECTASIA

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Background and Aims: Hereditary haemorrhagic telangiectasia (HHT) is an autosomal dominant disease characterised mainly by epistaxis. We aimed to evaluate the association between the location of extranasal mucocutaneous telangiectasia and the presence of cerebral arteriovenous malformations (AVMs).

Methods: We conducted a cross-sectional study of patients diagnosed with HHT, according to Curacao criteria or genetics, who had AVMs in internal organs (pulmonary, hepatic, gastrointestinal, and cerebral). Mucocutaneous telangiectasias were assessed and reported by clinicians. Variables presented as frequencies (%). Comparisons using Student's-t test. Odds ratios (OR) with 95% confidence interval (CI) derived from logistic regression models. Significance p<0.05.

Results: A total of n=41 HHT patients with AVMs in internal organs were included, of which 21 (51.2%) were women. Epistaxis was present in 38/41 (92.7%) of patients and extranasal mucocutaneous telangiectasias were present in 32/41 (78.0%). Pulmonary was the most frequent location for AVMs (28/41; 68.3%), followed by hepatic (15/41; 36.6%), cerebral (13/41; 31.7%) and gastrointestinal (10/41; 24.4%) locations. Patients with lip telangiectasias had a higher risk for presenting cerebral AVMs (92.3% vs. 57.1%; OR [95% CI]: 9.00 [1.03 - 79.06]; p=0.024).

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No significant associations were observed between location of telangiectasias and other AVMs.

Conclusions: Location of extranasal telangiectasias appear to be associated with the presence of cerebral AVMs.

Keywords: *HHT, cerebral arteriovenous malformations, telangiectasias*

[Abstract:0152]

GOOD SYNDROME, DIARRHEA AS CLINIC PRESENTATION OF THYMOMA

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77-year-old woman with diarrhoea, up to 11 bowel movement per day, and weight loss, 9 kg in two months. Medical history of hypertension. Normal physical examination. Routine blood test showed diminished A, G and M Immunoglobulins, and normal: renal, hepatic function, hemogram, acute phase reactants, thyroid hormones, ions and tumour markers. Celiac disease and Helicobacter pylori were discarded and multiple stool cultures were negative.

Colonoscopy could not be correctly done because of a fixed-handle, reason why virtual colonoscopy was done, with only diverticular presence. That was why she was treated as diverticular colitis without improvement. Finally, a Thorax CT was done to complete constitutional syndrome study, finding a solid mass, about 7 cm of diameter, on superior mediastinum. Was biopsied by thoracoscopy, final diagnosis was thymoma. Surgery was practiced and diarrhea improved, not disappearing at all, few weeks later.

Good´s syndrome is an infrequent disorder associated with humoral immunodeficiency and thymoma. Patients can present chronic diarrhoea, frequently associated with gastrointestinal pathogens or bacterial overgrowth. Usually, thymoma is diagnosticated before immunodeficiency. Relationship between the aetiology of immunodeficiency and thymoma is unknown. It is considered as a common variable immunodeficiency in adults. 10% of patients with hypogammaglobulinemia in adult age present a thymoma, and 5% of patients with thymoma present hypogammaglobulinemia. Is also unknown how hypogammaglobulinemia is involucrate on diarrhoea, which could be infectious or not. Treatment is thymoma surgery and immunoglobulins administration.

Keywords: *Good syndrome, thymoma, chronic diarrhoea*

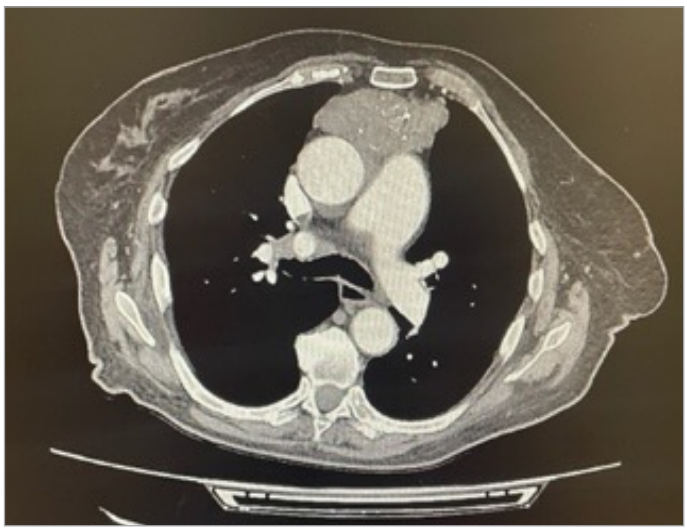

Figure 1. *Upper mediastinal thymoma.*

[Abstract:0177]

SUPERIOR MESENTERIC ARTERY SYNDROME: A CASE REPORT

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Superior mesenteric artery syndrome also known as arterio mesenteric artery syndrome, cast syndrome, Willkie syndrome is a rare clinical condition which occurs as a result of compression of third part of duedonum between aorta and superior mesenteric artery. It is a serious condition that requires prompt diagnosis and treatment to prevent long-term complications.

Symptoms can be nonspecific as unexplained weight loss, nausea and vomiting, abdominal distension. Symptoms may have acute onset or progressive course. The diagnosis of SMA syndrome has always been a challenge because there is no single specific test available. Laboratory values may show nonspecific changes due to weight loss and electrolyte imbalances, or they may even be normal. SMA syndrome can be managed conservatively or with surgery. In this case report 22-year-old female patient who has dyspeptic symptoms for seven years, lost 14 kilograms in twelve months and complaints of nausea vomiting that increased in last 2 weeks is presented.

Keywords: *superior mesenteric artery syndrome, wilkie syndrome, cast syndrome*

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[Abstract:0185]

HEREDITARY HEMORRHAGIC TELANGIECTASIA: A SERIES OF 20 CASES AND A LITERATURE REVIEW

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Purpose: Hereditary haemorrhagic telangiectasia (HHT) is an autosomal dominant minority disease characterised by the presence of arteriovenous malformations (AVM). In this paper we have studied the clinical manifestations and treatments received in a sample of 20 patients.

Methods: Retrospective observational study using a sample of 20 patients diagnosed with HHT between 2017 and 2023. A database was created with information on the clinical manifestations, tests performed and treatment received by these patients.

Findings: Our sample included 12 women and 8 men. Sixty percent of the patients had mutation in the *ACVRL1/ALK1* gene, 30% in ENG and 10% in SMAD4. All met 3 or 4 of the Curacao criteria, with epistaxis being the most frequent finding. To assess the presence of AVM, all patients underwent echocardiography, cranial MRI, abdominal ultrasound and, when necessary, angio-CT of the pulmonary arteries, where 8 patients had liver lesions, 7 pulmonary, 6 gastrointestinal and 6 in the central nervous system. Treatment was decided on the basis of clinical involvement: 60% of patients received oral iron, 40% intravenous iron, 25% red cell concentrate transfusion and 1 patient received bevazizumab. In addition, 4 patients required pulmonary artery embolization.

Conclusions: HHT is an autosomal dominant minority disease that requires a correct diagnostic work-up to assess first-degree relatives and the presence of vascular complications.

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Keywords: *hereditary haemorrhagic telangiectasia, arteriovenous malformations, Curacao criteria*

[Abstract:0210]

THE IMPORTANCE OF MULTIDISCIPLINARY COLLABORATION IN INTERNAL MEDICINE: A MULTIDISCIPLINARY APPROACH IN RARE DISEASES

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Summary: Adult-onset Still's disease (AOSD) is a rare inflammatory systemic disease, characterised by elevated acute phase reactants, particularly serum ferritin. In anecdotical cases, AOSD may be associated with trombocitopenic thrombotic purpura (TTP). We describe a clinical case with a complex multidisciplinary approach in internal medicine.

Case Presentation: Female patient, 44 years, diagnosed with AOSD during pregnancy in January 2022. She was initially treated with prednisone. Delivery in July 2022 without complications, as steroid-sparing treatment methotrexate 15 mg/week was prescribed. In December 2022 she was admitted in our ward for asthenia, arthritis and fever recurrence (up to 40°C). Blood tests showed HB 8,5, PLT <10,000, aptoglobin < 10. ESR was 115 mm/h and serum ferritin 7450. ADAMTS-13 levels < limit of our laboratory, and anti-ADAMTS-13 positivity. A TTP associated with AOSD reactivation was diagnosed. The clinical course was aggravated by epilepsy with loss of consciousness with a brain MR showing oedema in temporal lobes. She was initially treated with plasma exchange and caplacizumab (a von-Willebrand factor antagonist) without improvement. After two days a treatment focused against AOSD was started (methylprednisolone 500 mg for 3 days) and anakinra (an IL-1 receptor antagonist) with rapid reduction of fever and rise of haemoglobin and platelet values. The patient was discharged after two weeks in clinical remission.

Conclusions: the internal medicine doctor is pivotal in the management of patients also with acute rare disease, coordinating different specialists, complex drugs interactions and complications of the treatments.

Keywords: *rare disease, inflammation, Still's disease*

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[Abstract:0227]

CADASIL SYNDROME: A MISSED DIAGNOSIS FOR 18 YEARS

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Case Description: A 69 year-old female presented with gradually worsening confusion over the last three weeks. Past medical history consisted of ischemic stroke at the age of 51 without any causative underlying condition, with subsequent diagnosis of epilepsy, dementia, and bipolar disorder. She was afebrile, without neck stiffness or focal neurological deficits, with raised inflammation markers.

Clinical Hypothesis: Based on clinical presentation, our initial assumption was either a stroke or a CNS infection.

Diagnostic Pathways: Infection workup, including CSF analysis, was negative. Brain CT showed cerebral microangiopathy and atrophy. Upon reviewing family history, her mother died from stroke at an early age, hinting towards an inherited disorder. Brain MRI showed bilateral multiple lacunar lesions and cerebral microbleeds with hemosidirin deposition, raising suspicion of CADASIL syndrome. A skin biopsy was performed and examined under electron microscope, showing pathognomonic granular osmiophilic material at the surface of vascular smooth muscle cells and pericytes, confirming diagnosis.

Discussion and Learning Points: CADASIL syndrome is an autosomal dominant disorder caused by pathogenic variants in NOTCH3 gene, resulting in nonatherosclerotic angiopathy involving small arteries, primarily in the brain. Onset occurs in adulthood, manifested as ischemic stroke at early age, migraines, seizures, cognitive impairment and psychiatric disturbances. Diagnosis is made by genetic testing of $NOTCH_3$ gene or skin biopsy showing deposits of granular osmiophilic material. Even though there is no specific treatment, it is important to be alert to CADASIL cases, so that genetic counselling is offered to asymptomatic family members and secondary stroke prevention measures are taken.

Keywords: *CADASIL syndrome, ischemic stroke, dementia*

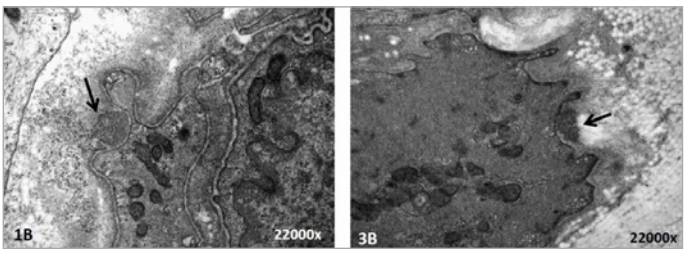

Figure 1. *Skin biopsy examined under electron microscope showing deposition of pathognomonic granular osmiophilic material at the surface of 1B) pericytes, 3B) vascular smooth muscle cells.*

[Abstract:0232]

TUBEROUS SCLEROSIS WITH REFRACTORY EPILEPTIC SEIZURES

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18-year-old woman with history of tuberous sclerosis complex (16q13.3 deletion, contiguous gene Syndrome, involving TSC2 and PKD1 gene), polycystic kidney disease with renal angiomyolipomas, and Lennox-Gastaut Syndrome with secondary drug-resistant epileptic encephalopathy, presenting three types of seizures: facial movements, daily tonic seizures, and more sporadically generalized tonic-clonic seizures. Currently treated with valproic acid, zonisamide, clobazam, cannabidiol and everolimus. Dependent for all basic activities of daily living, she has had seizures since she was 13 months-old, having up to 40 episodes a day during childhood.

In the last video-electroencephalogram, traces of epileptic encephalopathy can be seen. Likewise, in the last brain MRI multiple cortico-subcortical tubercles were seen in both cerebral hemispheres and subpendymal nodules, findings in the context of tuberous sclerosis, without changes compared to previous MRIs.

Multiple combinations of drugs have been used during the patient's life, without achieving seizure control. Starting ketogenic diet was proposed, which was not feasible due to the patient's associated behavioural disorder.

Cannabidiol was started in 2021, noticing some initial improvement, although she began later with longer crises. Subsequently, everolimus was started, achieving prodrome control. Withdrawal of everolimus was considered due to hypertriglyceridemia, although it was decided to maintain it given its additional benefit with regard to renal cysts.

She has also been evaluated by Neurosurgery, considering vagus nerve stimulation, which was not carried out due to the SARS-CoV-2 pandemic.

She is currently being treated with valproic acid, zonisamide, clobazam, cannabidiol and everolimuas, as well as midazolam if necessary in case of crisis.

Keywords: *tuberous sclerosis, epilepsy, phakomatoses, everolimus, cannabidiol*

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[Abstract:0241]

PAROXYSMAL ABDOMINAL PAIN AND MINIMAL ASCITES: WHEN THE CHILD SAVES HIS MOTHER

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Familial Mediterranean fever is an autosomal recessive autoinflammatory disease characterized by recurrence of episodes of fever and abdominal and joint pain and ascites. Hereditary angioedema (HAE) is an autosomal dominant genetic disease manifested by oedema and paroxysmal pain. We report the case of a family with a diagnosis of FMF corrected after several years towards angioneurotic oedema.

MM, 46, married and mother of 5 living children with a history of appendectomy at the age of 26, has presented paroxysmal abdominal pain associated with arthralgia and has minimal ascites. in a feverish context. The diagnosis mentioned is FMF and colchicine seemed to improve his condition.

Her second child born in 2005 as well as her daughter born in 2011 presented similar symptoms from a young age with mainly paroxysmal abdominal pain associated with peritoneal effusion on ultrasound.

In March 2022, the son was urgently evacuated following generalized oedema. In-depth analysis of the three files revealed the notion of paroxysmal hand oedema in the mother, generalized oedema in the boy at the age of 5 and urticaria in the girl during childhood. The weight dosage of C1 antigen inhibitor was collapsed. the same assessment was carried out on the mother with the same result. The diagnosis of hereditary angioedema (HAE) type 1 was made after 21 years of diagnostic wandering.

The mode of entry into hereditary angioedema (HAE) is sometimes misleading; FMF can pose a differential diagnosis problem in the face of abdominal pain and ascites in a family context.

Keywords: hereditary angioedema, familial mediterranean fever, abdominal pain, ascites, oedema

[Abstract:0242]

PHENYLKETONURIA: BENEFIT OF EARLY TREATMENT. ABOUT A CASE AND REVIEW OF THE LITERATURE

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Phenylketonuria (PKU) is a genetic disease linked to phenylalanine hydroxylase (PAH) deficiency. The deficiency leads to an increase in phenylalanine which is toxic to the brain. PKU represents the forms requiring treatment (Phe level without treatment or diet >360 µmol/L [>6 mg/dL]).

Case Presentation: Patient T is 36 years old, followed since birth for phenylketonuria detected on the 5th day of life following the discovery of the pathology in her older brother and sister.

His brother and sister have a severe delay in psychomotor development. Following the diagnosis, very rigorous nutritional and psychological monitoring was provided throughout this period by a well-trained multidisciplinary team. The patient presented normal intellectual development with perfect school attendance. She currently holds a university degree and holds a senior position in an airline. The clinical examination is generally normal, except for a slight decrease in unilateral hearing acuity and chronic constipation.

Conclusions: Our patient's case gives hope to families of phenylketonuria and confirms the importance of neonatal screening of children. It seems essential to generalize screening among children suffering from delayed psychomotor development or autistic traits in order to protect their siblings. Phenylketonuria is a curable disease thanks to neonatal diagnosis, early treatment and therapeutic progress.

Keywords: phenylketonuria, neonatal diagnosis, early treatment, psychomotor development

[Abstract:0250]

THE SHARP SWORD OF GENERALIZED INFLAMMATION: FERRITIN

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Purpose: In the intensive care unit (ICU) patients, increased levels of ferritin have been associated with increased mortality in increased inflammatory conditions including hemophagocytic syndrome (HPS). We aimed to determine the temporal changes of ferritin on prognosis and mortality in patients with HPS.

Methods: We conducted a retrospective cohort study between January 2013 and June 2022. 143 patients diagnosed with HPS according to HLH-2004 diagnostic criteria in the Ege University Hospital Internal Medicine ICU were included. Patients with a known history of malignancy were excluded. Demographic characteristics, comorbidities, temporal variations of laboratory data, including ferritin were collected. The difference between the ICU admission and outcome (death/discharge) values were reported as delta (Δ). Univariate Logistic Regression analysis for mortality predictors and ROC analysis for cut-off value was performed.

Results: We determined Δ ferritin [Odds Ratio (OR):1.00, p 0.005], maximum (max) H-score (OR: 1.012, p 0.001) and maximum ferritin levels (OR: 1.00, p 0.006) as mortality predictors (Figure 1). In the ROC analysis, the cut-off value of

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max ferritin in the presence of mortality was determined as 3000 µg/L with 89% sensitivity, 52% specificity and AUC: 74.3% (Figure 2).

Conclusions: In clinical conditions with hyperinflammation such as HPS, close monitoring of serum ferritin levels rather than baseline ferritin seems more valuable. Temporal changes during follow-up, an increasing ferritin level should alert the clinician to take precautions for immediate treatment.

Keywords: ferritin, inflammation, hemophagocytic syndrome

	Odds Ratio	95% CI	p
Age	1.042	1.05-4.08	<0.001
Δ Ferritin (x10^3 mcg/L)	1.000	1.00-1.00	0.005*
Maximum H –Score	1.012	1.004-1.009	0.001*
Δ Albumin (g/dL)	0.25	0.13-0.50	<0.001*
Δ NLR	1.04	1.01-1.07	0.004*
Δ MPV (fL)	1.78	1.32-2.42	<0.001*
Δ Lenfosit (x10^3/µL)	0.99	0.99-1.00	0.001*
Δ CRP (mg/dL)	1.05	1.02-1.09	<0.001*
Maximum Ferritin (x10^3 mcg/L)	1.00	1.00-1.00	0.006*

Table 1. *Mortality Predictors.*

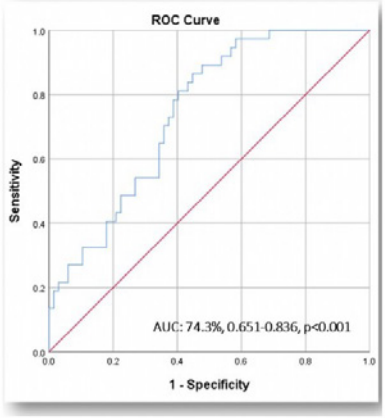

Figure 1. *ROC analysis for ferritin.*

[Abstract:0257]

BIRT-HOGG-DUBÉ SYNDROME: WHEN A HIGH LEVEL OF SUSPICION IS REQUIRED

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Introduction: An uncommon pathology for which a high level of suspicion is necessary.

Case Presentation: We present a 73-year-old woman with a medical history of pleuritis, spontaneous pneumothorax, Parkinson's disease, and bilateral renal carcinoma. At the age of 52, and oncocytoma was found in her left kidney as well as a chromophobe carcinoma in the right so partial nephrectomies were required. Besides the surgery, new bilateral nodules appeared two years later. During Urology´s follow-ups numerous pulmonary nodules were described so she was referred to Internal Medicine. She denied any respiratory symptoms and only 2-4 mm papules with smoot and shiny surface on the nape and nasal wing highlighted. Blood tests were performed without abnormalities and a whole-body CT scan revealed countless pulmonary cysts.

Final diagnose was Birt-Hogg-Dubé Syndrome with all its manifestations: fibrofolliculomas, pulmonary cysts, and renal tumours. Genetic study found a pathogenic variant in the FLCN gene. Her children also carried the mutation but were asymptomatic. No specific treatment is available excluding outpatient follow-up. Recently underwent a partial nephrectomy on her right kidney due to a rapidly growing solid nodule, confirmed as chromophobe renal carcinoma.

Conclusions: Birt-Hogg-Dubé Syndrome (BHD) is an autosomal dominant disorder characterized by the presence of fibrofolliculomas, pulmonary cysts and an increased risk of renal carcinomas. It involves germline mutations in the tumour suppressor gene FLCN. Differential diagnosis includes tuberous sclerosis complex. The importance of an accurate diagnosis is critical, not only for the patient but also for their family members, due to its hereditary nature.

Keywords: Renal carcinoma, Pulmonary cyst, Fibrofolliculoma

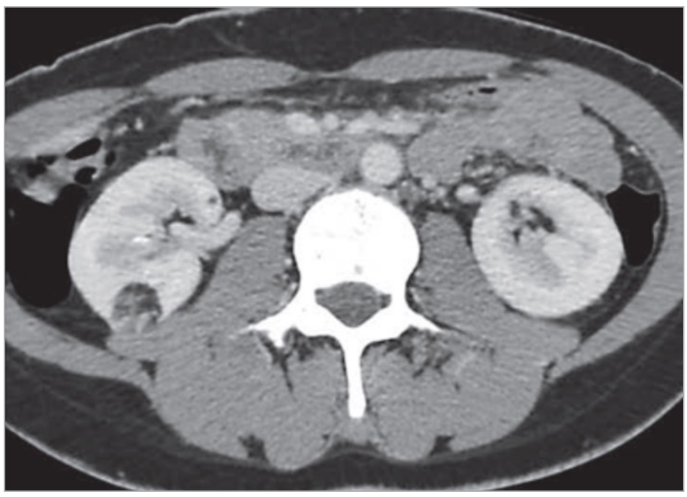

Figure 1. *Solid nodule in the right kidney suggesting renal carcinoma.*

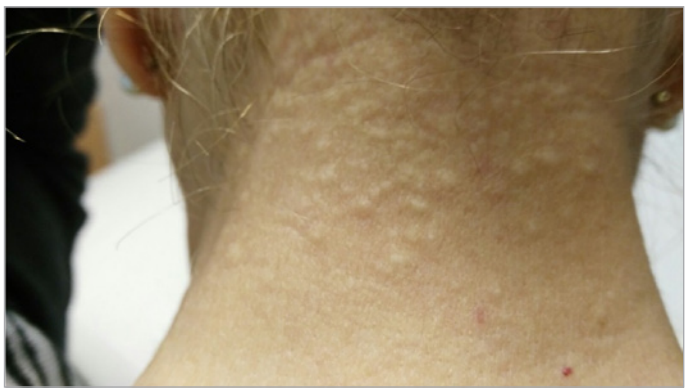

Figure 2. *Milimetric papules with smoot and shiny surface on the nape suggesting fibrofolliculomas.*

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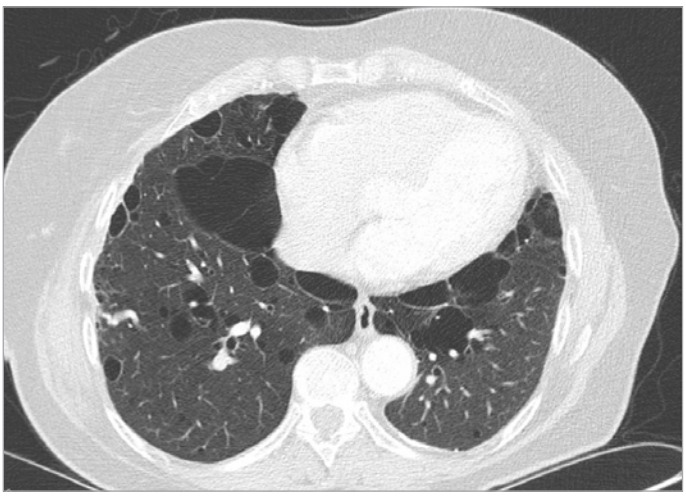

Figure 3. Bilateral pulmonary cysts.

[Abstract:0291]

ROSAI-DORFMAN DISEASE: PRESENTATION OF A CASE

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A 17-year-old man presented with a 4-day stomach pain and cyclic fever for 1 month. He was admitted to hospital for further studies. The patient has a similar episode 5 years before without diagnosis even though a bone marrow biopsy was performed. The patient took no medication or illicit drugs and had no known drug allergies. On examination, his temperature was 38.9ºC and heart rate 105 beats per minute. There were no rash or palpable lymphadenopathies. A mild pain in his epigastrium with an absence of critical signs was reported by the patient. A high level of beta 2-microglobulin was shown on laboratory tests. Therefore, diagnostic tests were performed.

An abdominal computed tomography scan shown retroperitoneal lymphadenopathies. These pathological findings prompted the performing of a positron emission tomography with 18F-fluorodeoxyglucose which showed an alarming rate of uptake on lymphadenopathies both above and below the diaphragm, in the bone marrow and the skin. A core needle biopsy of an inguinal accessible lymph node was performed. A histological examination showed sinus histiocytosis and emperipolesis, a crucial finding for diagnosing Rosai-Dorfman disease. Rosai-Dorfman disease is a non-Langerhans histiocytic benign disease of unknown aetiology. Since its first case in 1969, only about 1000 cases have been reported worldwide. Rosai-Dorfman disease is an ignored entity on differential diagnosis of fevers of unknown origin of which, nearly 50% remain with no diagnosis. Over the next 8 months, the patient remained totally asymptomatic with no recurrences only being prescribed symptomatic treatment.

Keywords: Rosai-Dorfman, lymphadenopathies, fever of unknown origin

[Abstract:0298]

FROM PLEURITIC PAIN TO GENETIC CONFIRMATION: A COMPLEX CASE OF INFLAMMASOPATHY

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Case Description: A 48-year-old male presented to the Emergency Department (ED) with pleuritic thoracic pain and fever, maintaining hemodynamic stability and an auricular temperature of 38.5ºC. He reported a history of recurrent episodes of severe abdominal pain associated with fever, lacking a definitive diagnosis. Five years prior, he began experiencing recurring fever, sometimes accompanied by polyarthralgia and thoracic pain. In the ED, the patient exhibited a pericardial rub, and the electrocardiogram (EKG) showed sinus rhythm without repolarization pattern alterations. Bloodwork revealed normal troponin and CK levels, mild leukocytosis (total leukocyte count 11.6x10^9/L), and a notable increase in C-reactive protein (CRP) (21.3 mg/dL). Diagnosis of pericarditis prompted treatment with nonsteroidal anti-inflammatory drugs and colchicine, leading to admission to the Internal Medicine ward for further investigation.
Diagnostic Pathways and Clinical Hypothesis: Transthoracic echocardiography showed no significant functional or anatomical alterations. Additional studies for infectious or inflammatory intestinal diseases revealed no abnormalities. A positive antinuclear cytoplasmic antibody (1:320) with a dense fine-speckled pattern was detected, with no other positive antibodies towards autoimmune causes. Due to a high clinical suspicion of an inflammasopathy, genetic testing was conducted.
Conclusions: The patient achieved symptomatic remission, with a significant reduction in inflammatory markers, and was discharged on long-term colchicine treatment. Genetic testing confirmed a pathologic mutation for Mediterranean familial fever. Due to chronic colchicine treatment intolerance, he began anakinra treatment, showing excellent long-term symptomatic control.

Keywords: inflammasopathy, pleuritic pain, pericarditis, Mediterranean familial fever, anakinra

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[Abstract:0310]

GOODPASTURE SYNDROME. A CASE REPORT

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We report the case of a 58-year-old female patient with a personal history cigarette smoking, morbid obesity, arterial hypertension, diabetes mellitus, dyslipidaemia, right nephrectomy for renal carcinoma and episodes of respiratory failure without a clear etiological filiation. She was admitted to the Internal Medicine ward with hemoptysis, kidney failure, nephrotic-range proteinuria that had developed in the previous three months. Anti-glomerular basement membrane antibodies were positive, leading to Goodpasture syndrome diagnosis. She was transferred to the Nephrology department and was treated with plasmapheresis, steroids and cyclophosphamide, with a good clinical evolution.

Goodpasture syndrome is a rare glomerular disease with an incidence of 0.5-1 cases per million people/year. It is caused by autoantibodies against type IV collagen, a constituent of the glomerular basement membrane.

Clinical presentation may range from an isolated rapidly progressive glomerulonephritis to a renopulmonary syndrome, associated with massive hemoptysis. Diagnosis is based on serological tests for the detection of antibodies, although these may be negative in up to 10 % of cases. In this context a renal biopsy is required to establish the diagnosis. High-resolution chest CT scans are used to assess alveolar haemorrhage.

Treatment is based on plasmapheresis and immunosuppression (corticosteroids plus cyclophosphamide). In refractory disease rituximab may be useful. Mortality is close to 90 % without treatment but decreases to 8.5 % were plasmapheresis and immunosuppression are used.

Reference:

Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int. 2021; 100(4S): S1-S276.

Keywords: *goodpasture, renopulmonary, hemoptysis, kidney failure, plasmapheresis, glomerular basement membrane*

[Abstract:0367]

AN UNUSUAL CAUSE OF ACUTE HYPERCAPNIC RESPIRATORY FAILURE: HYPER IGE SYNDROME

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Hyper IgE syndrome (HIES), also recognized as Job syndrome, represents an exceptionally uncommon primary immunodeficiency disorder marked by recurrent skin and lung infections, heightened serum IgE levels, and eosinophilia. The potential emergence of acute hypercapnic respiratory failure, stemming from recurrent pulmonary infections and bronchiectasis, poses a severe life-threatening complication associated with HIES. This case report aims to delineate the clinical and treatment attributes of a patient with HIES, elucidating its rare role as a cause of acute hypercapnic respiratory failure. A 23-year-old female, with a medical history of Job syndrome and recurrent pulmonary infections, was admitted to the intensive care unit due to septic shock and acute hypercapnic respiratory failure (Figure 1). The patient underwent intubation owing to the acute respiratory failure, coupled with the initiation of vasopressor therapy and broad-spectrum antibiotics. Unfortunately, the patient experienced *Pseudomonas aeruginosa* bacteraemia that proved unresponsive to appropriate antibiotics, ultimately leading to death from multiorgan failure on the 30th day of intensive care unit admission. Overall, HIES is an uncommon yet grave disorder that profoundly impacts both the quality of life and lifespan of affected individuals. Currently, no specific curative treatment exists for HIES. Complications arising from pulmonary infections remain the predominant causes of death. Timely diagnosis and expeditious infection management are imperative to avert complications and enhance outcomes for patients grappling with HIES.

Keywords: *respiratory failure, job syndrome, pulmonary complications*

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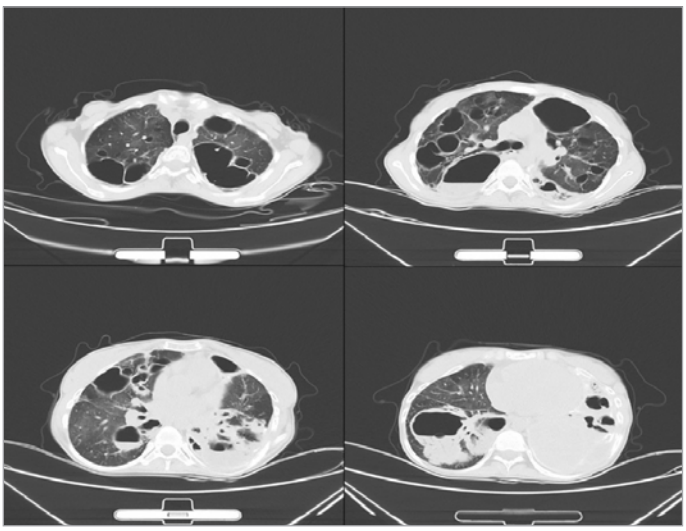

Figure 1. Axial CT scan of the thorax showing bilateral large pneumatoceles with air fluid level and thin-walled cystic lung changes.

[Abstract:0370]

THE RECESSIVE PATH TO TRANSPLANTATION: AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE DIAGNOSED IN ADULTHOOD

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Autosomal recessive polycystic kidney disease (ARPKD) is a severe monogenic disorder that occurs due to mutations in the *PKHD1* gene. The disorder usually manifests in infancy, with a high mortality rate in the first year of life. Patients who survive the neonatal period present with a broad spectrum of symptoms involving kidneys, liver and pancreas. We report a case of ARPKD patient who is diagnosed at the age of 42 with recurrent cholangitis, congenital hepatic fibrosis, renal cysts and stage 4 renal disease.

Keywords: *autosomal polycystic kidney disease, Caroli disease, transplantation*

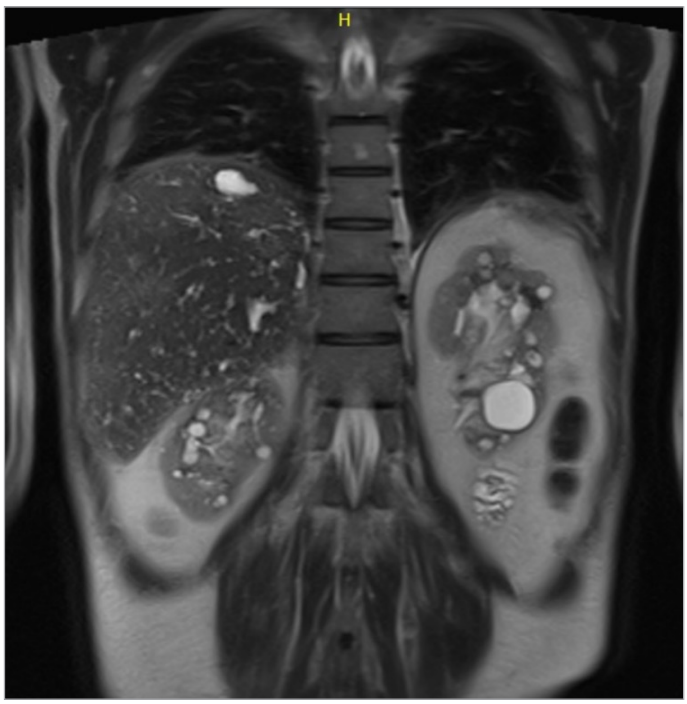

***Figure 1.** MRCP coronal section: Renal cysts and hepatic fibrosis.*

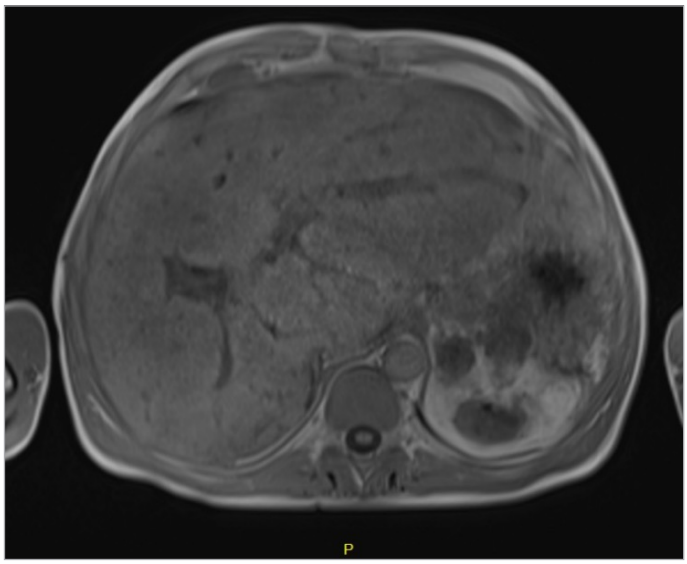

***Figure 2.** MRCP transvers section: Renal cysts and hepatic fibrosis.*

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[Abstract:0372]

RAPID ESTABLISHMENT OF CIRRHOSIS IN ALSTORM SYNDROME

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Alstrom syndrome is a rare autosomal recessive genetic disorder characterized by cone-rod dystrophy, hearing loss, childhood truncal obesity, type 2 diabetes, hypertriglyceridemia, cardiomyopathy, and progressive pulmonary, hepatic and renal dysfunction. Liver pathology has been reported to be slowly progressive, although end-stage liver failure is not uncommon. In this case report, we address Alstrom syndrome as a rare cause of liver cirrhosis at a young age.

A 23-year-old male patient presented to the emergency department with fatigue and abdominal distension. He was under follow-up for Alstrom syndrome since his childhood. Diabetes mellitus and hyperlipidemia for about 10 years and visual impairment and hearing loss that developed much earlier were recorded as the established features of the syndrome. His physical examination was remarkable for generalized pallor and abdominal distension. Blood tests were not remarkable except for anaemia of chronic disease nature. Transaminase levels were within normal range. Ultrasonography showed free fluid in the abdomen and a granular appearance of the liver. Serum-ascites albumin gradient was below 1.1 g/dL. Elective esophagogastroduodenoscopy revealed grade-3 oesophageal varices. Viral hepatitis was excluded and cardiac evaluation was normal.

Cirrhosis is predictable in Alstorm syndrome because it involves characteristic features of the metabolic syndrome. However, the present patient was relatively young and he had not yet been diagnosed with liver involvement of the syndrome, including fatty liver disease. The current report is a unique example of not only early but also rapidly established cirrhosis in Alstorm syndrome.

Keywords: alstrom syndrome, liver cirrhosis, metabolic syndrome

[Abstract:0382]

CLINICAL PRESENTATION, COURSE, AND PROGNOSIS OF PATIENTS WITH MIXED CONNECTIVE TISSUE DISEASE: A MULTICENTER RETROSPECTIVE COHORT

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[9] Department of Internal Medicine and clinical immunology, North-West National Refe-rence Center for Rare Systemic Autoimmune Diseases iques et Auto-Immunes Rares du Nord-Ouest, Hôpital Claude Huriez, Université de Lille, France

Objectives: The objective of this study is to better characterize the features and outcomes of a large population of patients with mixed connective tissue disease (MCTD).

Methods: We performed an observational retrospective multicentre cohort study in France. Patients who fulfilled at least one diagnostic criteria set for MCTD and none of the criteria for other differentiated connective tissue disease (dCTD) were included.

Results: Three hundred and thirty patients (88% females, median [interquartile range] age of 35 years [26-45]) at diagnosis were included. The diagnostic criteria of Sharp or Kasukawa were met by 97.3% and 93.3% of patients, respectively. None of the patients met other classification criteria without fulfilling Sharp or Kasukawa criteria. After a median follow-up of 8 [3-14] years, 149 (45.2%) patients achieved remission, 92 (27.9%) had interstitial lung disease (ILD), 25 (7.6%) had pulmonary hypertension and 18 (5.6%) died. Eighty-five (25.8%) patients progressed to a dCTD, mainly systemic lupus erythematosus (15.8%) or systemic sclerosis (SSc) (10.6%). Median duration between diagnosis and progression to a dCTD was 5 [2-11] years. The identification at MCTD diagnosis of an abnormal pattern on nailfold capillaroscopy

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(OR=2.44, 95%CI [1.11-5.58]) and parotid swelling (OR=3.86, 95%CI [1.31-11.4]) were associated with progression to a dCTD. Patients who did not progress to a dCTD were more likely to achieve remission at the last follow-up (51.8 vs 25.9%).

Conclusions: This study shows that MCTD is a distinct entity that can be classified using Kasukawa and/or Sharp criteria, and that only 25.8% patients progress to a dCTD during follow-up.

Keywords: *mixed connective tissue disease, Sharp syndrome, anti-U1RNP, connective tissue disease, systemic sclerosis, Sjogren's syndrome*

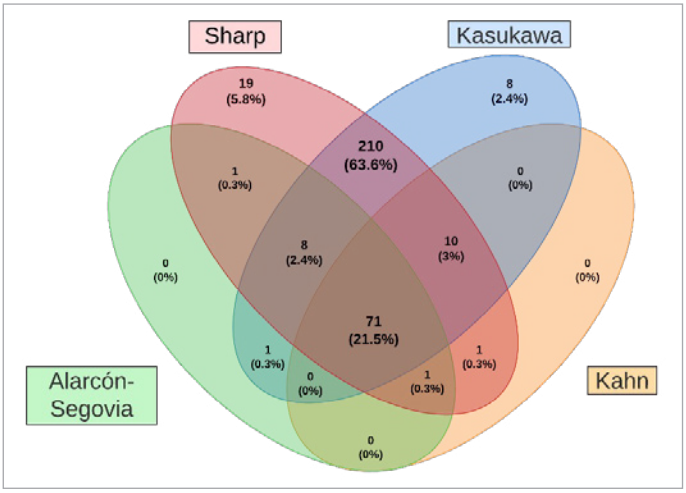

Figure 1. *Numbers (percentages) of patients fulfilling diagnosis criteria for mixed connective tissue disease.*

[Abstract:0429]

UNRAVELLING A DIAGNOSTIC ENIGMA: NAVIGATING AN INTRICATE CASE OF SPONTANEOUS CEREBROSPINAL FLUID (CSF) RHINORRHEA

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Purpose: CSF rhinorrhoea is a rare medical condition characterized by the drainage of CSF through the nasal cavity. CSF leakage can be attributed to numerous different causes, mostly traumatic or iatrogenic, but it can also be spontaneous. Due to its rarity, CSF rhinorrhoea is often a diagnostic trap and can be misdiagnosed and mistreated as rhinosinusitis or allergic rhinitis. This can result in severe complications, which could potentially have life-threatening consequences if not accurately identified and managed.

Methods: In this case report, a 53-year-old woman presented at the emergency department with symptoms of headache, fever, nasal discharge from her left nostril when leaning forward, and mild neck stiffness. Based on the patient's clinical presentation and physical examination findings, there was a high suspicion of central nervous system infection and cerebrospinal fluid leakage.

Findings: A lumbar puncture confirmed the diagnosis of meningitis, while imaging with computed tomography (CT) scan and magnetic resonance imaging (MRI) revealed a fistula between the posterior wall of sphenoid sinus and the subarachnoid space. Additional findings included an empty sella turcica, suggesting a potential underlying cause for this condition and an incidental meningioma near the area of leakage. The patient received empiric intravenous antibiotic therapy and was discharged after ten days. She was referred to the neurosurgical department for surgical repair of the CSF leak and removal of the meningioma, in line with appropriate treatment guidelines.

Conclusions: This study highlights the importance of promptly identifying and investigating potential causes of CSF leakage to provide appropriate medical management.

Keywords: *CSF rhinorrhoea, empty sella turcica, sphenoid sinus fistula*

[Abstract:0469]

RESISTANT ANAEMIA DUE TO COPPER DEFICIENCY: THINK OUT OF THE BOX

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Department of Medicine and Research Laboratory of Internal Medicine, National Expertise Center of Greece in Autoimmune Liver Diseases European Reference Network on Hepatological Diseases (ERN-Rare Liver), General University Hospital of Larissa, Larissa, Greece

Purpose: Chronic malabsorption syndrome affects any system, with numerous clinical and laboratory presentations including resistant anaemia. Iron, vitamin B12 and folic acid are hematopoietic factors we usually evaluate. Are these enough?

Methods and Findings: An 80-year-old male with history of resection of the 2/3 of the jejunum and ileum due to colon ischemia was admitted to our Department for investigation of refractory anaemia, lower limbs' oedema, and fatigue. Laboratory tests showed normocytic normochromic anaemia with increased absolute reticulocyte count, increased prothrombin time, hypocalcemia, low albumin and hypogammaglobulinemia. Considering that the patient has not responded to administration of iron, B12 and folic acid our differential diagnosis was expanded to investigate for other causes of refractory anaemia.

Bowel malignancy, celiac disease, pernicious anaemia and nephrotic syndrome were ruled out. Ferritin, B12, folic acid and soluble transferrin receptors were within normal limits. Peripheral blood smear revealed normal findings, while bone marrow biopsy was not pathognomic of myelodysplastic syndrome. The differential diagnosis headed to other factors, whose deficiency may lead to refractory anaemia. Copper is one of these factors.

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Both, serum ceruloplasmin and serum copper levels were low. Replacement therapy started with chelated copper at a dose of 5mg daily resulting to increase of the hemoglobulin levels without side effects.

Conclusions: Copper deficiency should be considered in cases of refractory anaemia in patients with malabsorption syndrome, especially when all the other hematopoietic factors are normal. Diagnosis relies in laboratory findings. Replacement therapy is effective, without side effects.

Keywords: *anaemia, malabsorption syndrome, copper*

[Abstract:0507]

MAN WITH CONGENITAL HAND ANOMALY: NOT EVERY RARE DISEASE IS A SERIOUS ILLNESS

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We present the case of a 33-year-old male with no relevant medical history. His mother and brother have congenital anomalies in their hands and feet. He was referred by his family doctor due to congenital anomalies in his right hand, similar to those described in his relatives.

During the physical examination, the absence of the second and third fingers of the right hand was noted (Figure 1). Despite this, the patient demonstrated proper thumb opposition and reported no limitations in his daily life.

Considering ectrodactyly in the right hand with a possible autosomal dominant (AD) inheritance pattern, further investigation was carried out through an X-ray (Figure 2). It revealed the absence of the second metacarpal, fusion of the third and fourth metacarpals, and the absence of the phalanges of the second and third fingers. A molecular study was requested for sequencing the TP63 gene, revealing a likely pathogenic variant C.563_561del in heterozygosity.

Ectrodactyly is a rare condition typically inherited in an autosomal dominant manner. It is characterized by limb deformities, which may include partial or total absence of fingers, syndactyly, and "lobster or crab claw" deformities. It can occur in isolation or be associated with various syndromes. Treatment options, such as physiotherapy, orthopedic/prosthetic interventions, or surgery, depend on functional limitations, but in this patient, no intervention was necessary. Further testing was performed on his mother, who carried the same genetic variant, and genetic counselling was provided.

Keywords: *ectrodactyly, rare diseases, hand*

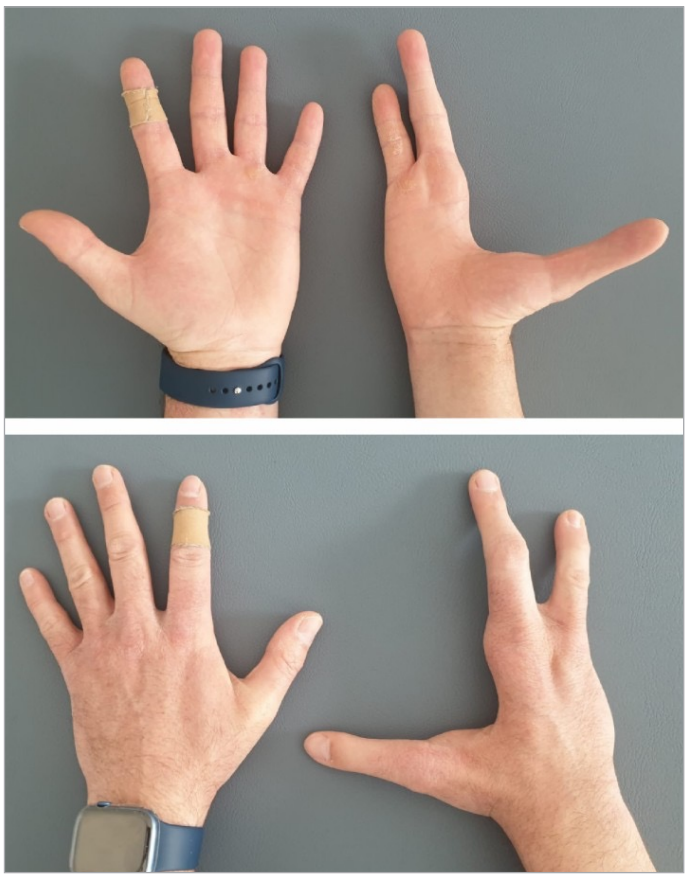

Figure 1. *Appearance of both hands of the patient.*

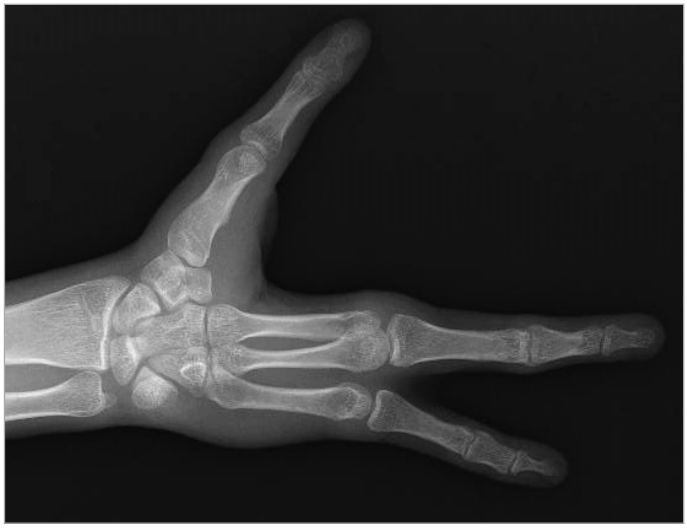

Figure 2. *X-ray of the patient's right hand.*

[Abstract:0527]

CHARACTERIZATION OF FABRY PATIENTS IN MACAU

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Introduction: Fabry disease is an X-linked recessive lysosomal storage disorder caused by reduced activity of alpha-galactosidase

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A, resulting in the accumulation of glycosphingolipids, particularly globotriaosylceramide (Gb 3), and globotriaosylsphingosine (Lyso-Gb 3) in various cells. This accumulation leads to the diverse manifestations of the disease. Diagnosis confirmation in male patients relies on detecting alpha-Gal A leukocyte activity, while genetic testing is necessary for female patients due to potential residual enzymatic activity. Available Fabry-specific therapies encompass enzyme replacement therapy (ERT) involving intravenous agalsidase-alfa or agalsidase-beta administered every two weeks, as well as oral chaperone therapy with Migalastat.

Methods: For 4 index patients with Fabry disease, family trees were built and genetic testing was arranged to family members.

Results: The pathogenic GLA variant associated with Fabry disease was detected in these initial cases. Conducting family testing through genotyping led to the identification of 9 Fabry disease cases among the 18 family members at risk who were tested. Among those patients, eight of them were eligible to start enzyme replacement therapy with agalsidase-beta. Two males were classified as classical cases with xerostomia, anhydrosis, acroparesthesias, tinnitus, angiokeratomas and renal involvement. All the others manifested with cardiomyopathy. Among the female patients, two of them have brain and eye involvement besides cardiac involvement.

Conclusions: Though family screening, family members were identified who might benefit from earlier intervention. Raising awareness about the importance of early detection and treatment of Fabry disease is crucial to prevent permanent tissue damage and organ failure.

Keywords: *fabry disease, lyso-GB3, alpha-galactosidase deficiency, cardiomyopathy*

[Abstract:0530]

GASTROINTESTINAL BLEEDING AS AN INITIAL MANIFESTATION OF AL AMYLOIDOSIS

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Background: Systemic amyloidosis is group of disorders characterized by the accumulation of insoluble proteins in tissues. So far, more than 30 "amyloidogenic" proteins have been identified in humans. The most common form of systemic amyloidosis is light chain amyloidosis, which results from the accumulation of misfolded immunoglobulins. It affects any organ in the body and often presents with a range of nonspecific symptoms making the identification and diagnosis of this entity a challenge.

Case Presentation: We, present a case of 77-years-old female, history of ischemic heart disease who presented with recurrent upper abdominal discomfort and vomiting for half a year. Therefore, she was admitted several times and discharged with diagnosis of angina and chronic gastritis. Later she developed bloody diarrhoea and was admitted again. Endoscopic exams showed duodenal and sigmoid erosion. Biopsy revealed amyloid deposits in both gastric antrum and sigmoid. Monoclonal band was identified in protein electrophoresis and clonal plasmacytosis was detected in bone marrow biopsy. Echocardiogram revealed GLS decreased and "cherry-on-top" pattern consistent with cardiac amyloidosis. Finally she was diagnosed with AL amyloidosis with cardiac and gastrointestinal tract involvement. haematology Specialist proposed chemotherapy but she deceased before starting treatment.

Conclusions: Amyloidosis is a rare disease that can involve multi-system with various presentations. Gastrointestinal bleeding is a rare initial manifestation of amyloidosis. Early diagnosis and treatment prior to the development of end-organ damage remains essential to improving mortality. Therefore, we would like to increase awareness of this condition as clinicians should become familiar with this disease.

Keywords: *gastrointestinal bleeding, cardiomyopathy, AL amyloidosis*

[Abstract:0544]

MYALGIAS AND COVID-19 INFECTION. BEYOND WHAT WOULD BE EXPECTED

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We present a 35-male with no medical history who was admitted in the Emergency Department due to myalgias and cold symptoms of three days evolution. On physical examination generalized weakness and intense pain with movement was observed, mainly on the lower limbs. An urgent analysis was requested with the following results: creatine-kinase of 110454 U/L and creatinine of 5.74 mg/dL. Also positive polymerase chain reaction (PCR) of COVID-19 was received too. He was admitted with the diagnosis of rhabdomyolisis and acute renal failure. In a directed medical-history interview about previous episodes of myalgias in the context of intercurrent infectious diseases or similar, the patient referred several episodes over the years but no as long as the current one.

Due to this background a complete analysis was requested with

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determination of inflammatory markers, rheumatoid-factor, anti-nuclear antibodies, extractable nuclear antibodies (including myopathy-related antibodies), anti-neutrophil cytoplasmic antibodies, anti-cyclic citrullinated peptide and complement, which were all negative.

At this point, we requested a muscular biopsy to complete the studies. Anatomopathological study showed an increase of lipids at the muscle level and an excess of type-1 fibers (up to 80%), which could be related to myopathy associated with RIR1 mutation. With these findings, autoimmune/necrotizing myositis and dystrophies were ruled out. We requested genetic studies, detecting a pathogenic variant in the CPT2:c.1148T>A;p.(Phe383Tyr) gene. Pathogenic variants in this gene have been associated with carnitine-palmitoyltransferase-II deficiency, an inherited metabolic disease that affects the oxidation of fatty acids. The myopathic form of this rare entity is autosomal recessive inheritance.

Keywords: *rhabdomyolisis, COVID-19, congenital myopathy, carnitine palmitoyltransferase-II deficiency*

[Abstract:0550]

EVALUATION OF A SCREENING METHOD FOR VEXAS SYNDROME BASED ON THE BORDEAUX UNIVERSITY HOSPITAL'S BIOMEDICAL DATA WAREHOUSE

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Introduction: VEXAS syndrome is an acquired monogenic auto-inflammatory disease linked to a mutation in the UBA1 gene discovered in 2020. This disease, which has a poor prognosis in the absence of treatment, combines systemic auto-inflammatory disorders, particularly of the skin and joints, with dysmyelopoiesis. Early diagnosis using molecular biology is important, as certain therapies, such as bone marrow allografts, are curative.

Objectives: Interrogate the Bordeaux University Hospital's clinical data warehouse (CDW) via the i2b2 platform to detect VEXAS syndrome in at least one patient not tested for the UBA1 mutation despite a compatible clinical history according to our eligibility criteria.

Methods: Thirty thousand two hundred and ninety-seven files were selected from the CDW of the Bordeaux University Hospital via the i2b2 platform, enabling the extraction of files of interest by recognition of criteria previously defined from the literature. These 30,297 files were prioritized according to their number of criteria. The first 240 files were reviewed on the SmartCRF application to determine those actually eligible for UBA1 mutation testing, after elimination of differential diagnoses.

Results: Of the 240 files reviewed, 9 were those of VEXAS patients already diagnosed, and 49 were selected as eligible for UBA1 mutation testing. Only 15 patients could be tested on preserved genetic material, and 2 had a UBA1 mutation.

Conclusions: The use of the i2b2 platform and SmartCRF to screen for VEXAS syndrome appears promising, but still has certain limitations.

Keywords: *VEXAS, UBA1, auto-inflammatory, diagnosis, screening, health data warehouse*

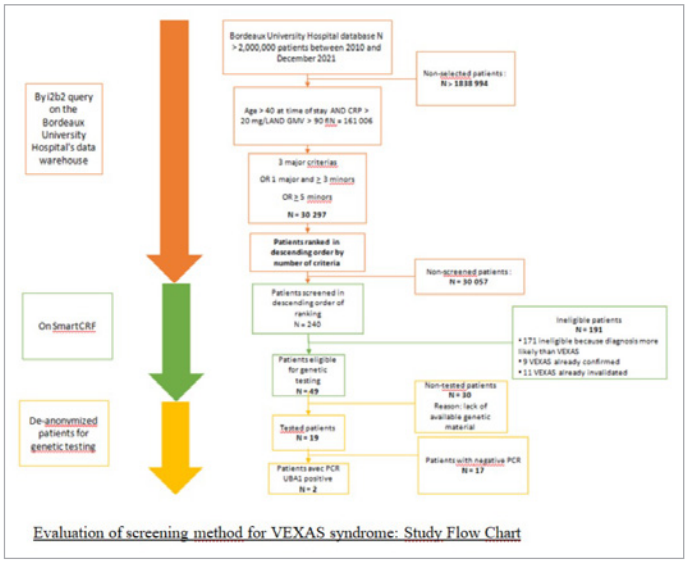

Figure 1. *Evaluation of screening method for VEXAS syndrome: Study Flow Chart.*

[Abstract:0556]

TRACHEOBRONCHOPATHIA OSTEOCHONDROPLASTICA AND GRANULOMATOSIS WITH POLYANGIITIS: A NOVEL ASSOCIATION?

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Introduction: Tracheobronchopathia osteochondroplastica (TOP) is a rare disorder characterized by the development of multiple osseous and cartilaginous nodules beneath the mucosa of the trachea and main bronchi. The association with granulomatosis with polyangiitis (GPA) has never been described in the literature.

Case Presentation: A 70-year-old female admitted for investigation of prolonged fever associated with inflammatory arthralgia, dry cough and exertional dyspnoea in NYHA functional class 2.

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Clinical examination revealed fine bilateral pulmonary crackles. Biological tests showed a Biological Inflammatory Syndrome with ESR of 140 and CRP of 236. The 24-hour proteinuria was 2 g with moderate renal failure. The chest X-ray (Figure 1) revealed diffuse calcifications along the tracheal borders with an interstitial syndrome. Imaging of the thoracic region revealed diffuse calcification of the tracheobronchial wall with diffuse interstitial pneumopathy. In the abdominal region, there was enhancement of the ureteral walls and two renal pelvises along with increased density of perivesical fat. Exhaustive infectious and neoplastic investigations yielded negative results, and anti-myeloperoxidase ANCA type was positive. The diagnosis of GPA was established, involving pulmonary, renal, and ureteral manifestations, along with concurrent TOP

The patient was treated with corticosteroids at a dose of 1 mg/kg/day with gradual tapering, coupled with monthly courses of cyclophosphamide, showing a favourable clinical and biological outcome.

Conclusions: TOP is a rare condition affecting the central airways. Its origin remains unknown. To our knowledge, an association with ANCA-associated vasculitis has never been reported. Given the rarity of this association, it is crucial to continue documenting these entities to better understand the pathophysiological mechanism.

Keywords: *Tracheobronchopathia osteochondroplastica, granulomatosis with polyangiitis, rare*

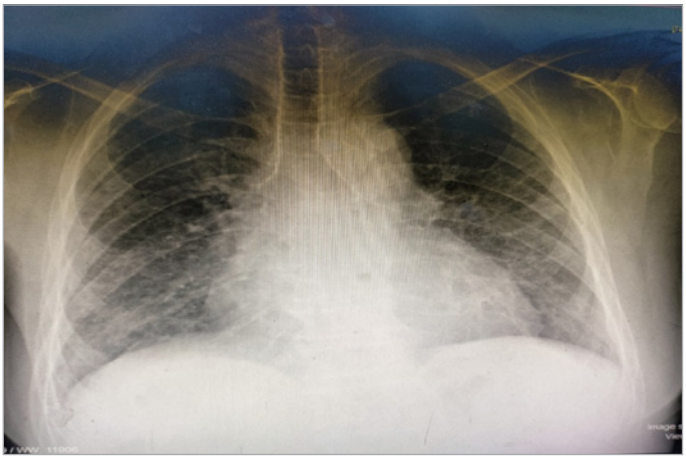

Figure 1. *Chest X-ray.*

[Abstract:0565]

ATAXIA IN A PATIENT WITH ADDISON'S DISEASE

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A 37-year-old male, with history of primary adrenal insufficiency diagnosed at 9-year-old, presented to the Emergency department with urinary retention, associated with gait ataxia and preferential imbalance to the right. His family also referred to mood disorders some years ago. Neurologic examination revealed mild lower limb paraparesis with sensitive disturbances and generalized hyperreflexia. His initial laboratory exam and work-up for autoimmune and infectious diseases were unremarkable. After one-year, cognitive symptoms were characterized with rapid evolution to a profound demented state.

The MRI of the brain revealed hyperintense lesions in the deep white matter, splenium, corpus callosum and corticospinal projection fibres. The MRI of the spinal cord showed slight atrophy. Such imaging features, associated with the clinic and the history of Adisson's disease, were consistent with pathognomic description of X-linked adrenoleukodystrophy (ALD). The analysis of very long chain fatty acids (VLCFA) showed elevation of C24, C26, C24/C22 ratio and C26/C22 ratio. Exome sequencing was performed revealing a heterozygous variant in ABCD1, c.1682A>T.

ALD is a genetic peroxisomal disorder resulting from a mutation in ABCD1 gene, that plays a significant role in the VLCFAs transport system. Four main subtypes have been described: neonatal, childhood cerebral form, adrenomyeloneuropathy and adrenal insufficiency. Leukodystrophies commonly manifest in childhood, while adrenomyeloneuropathy has a more prominent role in adults. We report an atypical cerebral late-onset case, in which the clinical course was insidious and diagnosis delayed. The prognosis is unfavourable, and timely diagnosis influences patient outcomes as gene therapy may be effective in patients with early-stage-ALD.

Keywords: *ataxia, addison's disease, X-linked adrenoleukodystrophy*

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[Abstract:0614]

MARBLE EAR AND PERSISTENT DYSPNEA

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Keutel Syndrome (KS), a rare genetic disorder, is characterized by extensive cartilage calcification, brachytelephalangia, pulmonary stenosis, midline anomalies, punctate epiphyses in infancy, hearing impairment, and recurrent respiratory infections, often mimicking asthma. We report the case of a 23-year-old female with a history of asthma-like symptoms since childhood, who presented with dyspnea and wheezing. Initial treatments targeting asthma proved ineffective. Diagnostic investigations, including a sinus CT scan, pulmonary function test, and fiberoptic bronchoscopy, indicated tracheal stenosis and revealed calcifications in the respiratory tract. Histopathological analysis of biopsy samples showed squamous metaplasia and calcifications beneath the surface epithelium, alongside a mild to moderate lymphoplasmacytic inflammatory reaction. A transthoracic echocardiogram indicated Stage 1 diastolic dysfunction. The patient's ear cartilage appeared firm and inflexible upon physical examination. The diagnosis of Keutel Syndrome was confirmed through genetic analysis, which identified a homozygous c.43delG mutation in exon 1 of the MGP gene. This case represents the 43rd documented instance of Keutel Syndrome in scientific literature and the fifth associated with the c.43delG mutation. Our findings underscore the importance of considering KS in differential diagnosis for patients presenting with resistant asthma-like symptoms and calcifications in cartilaginous structures.

Keywords: *Keutel syndrome, tracheal stenosis, dyspnea, asthma*

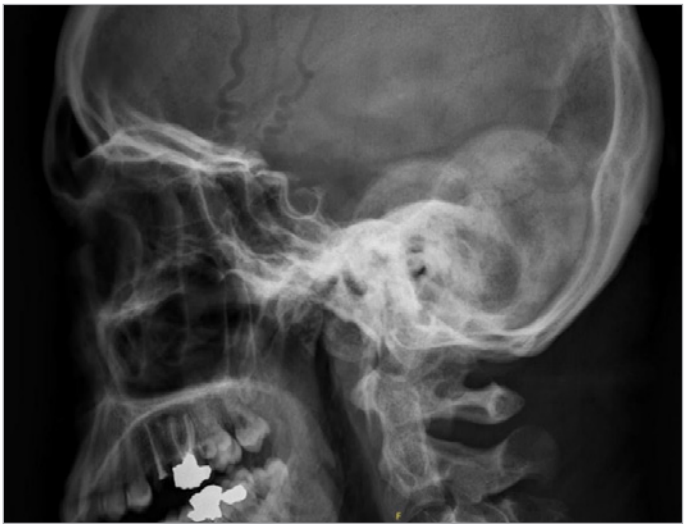

Figure 1. *The ear cartilages are pronouncedly visible in the head X-ray.*

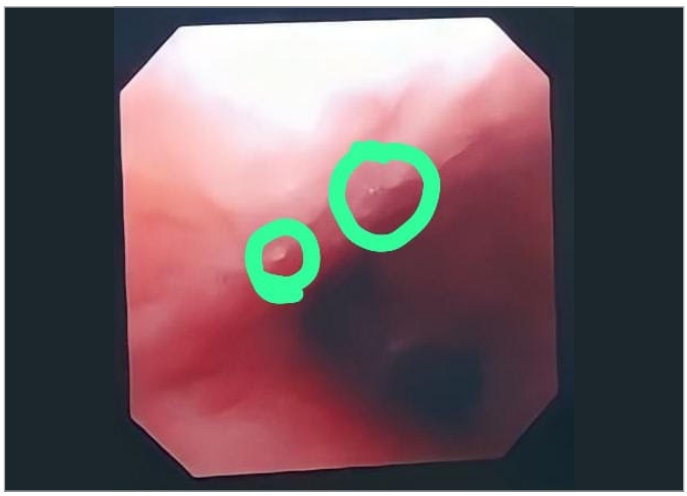

Figure 2. *Calcified focus observed during fiberoptic bronchoscopy. The area marked with a green circle indicates calcification foci.*

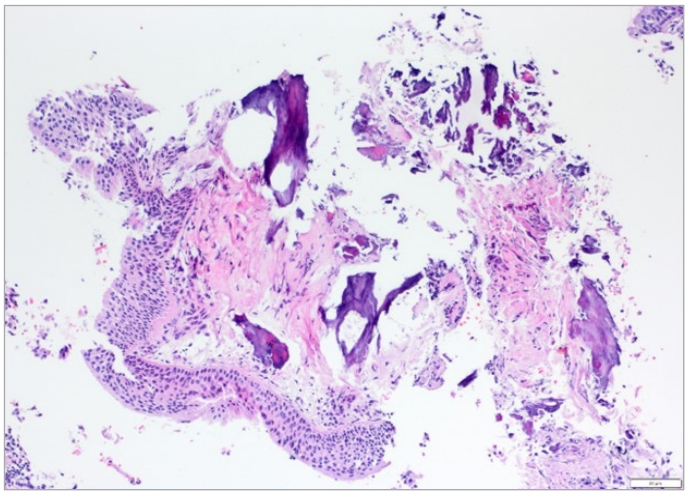

Figure 3. *Biopsy specimen obtained from the bronchial mucosa of the patient.*

[Abstract:0661]

KIKUCHI- FUJIMOTO DISEASE- A DIAGNOSTIC CHALLENGE

Krystallenia Logioti, Anastasios Makris, Christina Taxiarchou, Nikolaos Kosmas, Maria Bompoli, Maria Chini

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Purpose: We present two cases of Kikuchi-Fujimoto disease, a rare benign entity of unknown cause, occasionally associated with autoimmune conditions. It is mostly described in young females of Asian origin and it has an heterogeneous clinical phenotype.

Case Presentation: Case 1: A 17-year-old female from Asia, with a recent hospitalization for aseptic meningitis without identifiable cause, presented with fever and headache. On physical examination, supraclavicular and bilateral axillary lymphadenopathy were found. Laboratory tests revealed leukopenia and increased inflammatory markers. Infectious disease and immunological work-up were negative and no further pathology was evident from imaging. After an initial spontaneous remission of her symptomatology,

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she relapsed with additional arthralgias, facial angioedema, aphthous stomatitis and an acneiform rash. A lymph node biopsy revealed histiocytic necrotizing lymphadenitis, without evidence of lymphoproliferative disease. Due to persisting symptoms, systemic corticosteroids were administered with a favourable response. Case 2: A 23-year-old female presented with acute fever, cervical lymphadenopathy and a maculopapular rash of trunk and extremities. Laboratory tests revealed pancytopenia and increased inflammatory markers. Hepatosplenomegaly was evident from imaging. A search for infectious diseases was unrevealing. Immunological work-up showed positive ANA (1:640), anti-Ro, anti-La, prominent polyclonal hypergammaglobulinemia and low C4 complement. A lymph node biopsy revealed histiocytic necrotizing lymphadenitis, consistent with Kikuchi disease. Due to symptom relapse following initial remission, corticosteroids were administered with subsequent improvement.

Conclusions: The above cases illustrate the clinical spectrum of Kikuchi disease and highlight the diagnostic challenges that accompany this entity, which should be included in the differential diagnosis of cervical lymphadenopathy.

Keywords: *Kikuchi Fujimoto, necrotizing lymphadenitis, cervical lymphadenopathy*

[Abstract:0668]

TITLE: LONG-TERM FOLLOW-UP OF HYPEREOSINOPHILIC SYNDROME PATIENTS TREATED WITH MEPOLIZUMAB: A NATIONWIDE REAL-LIFE STUDY OF 59 PATIENTS

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Background: Mepolizumab, a humanized monoclonal antibody directed against IL-5, has proven efficacious for the treatment of FIP1L1/PDGFRA (F/P)-negative hypereosinophilic syndrome (HES). However, both its efficacy and safety profiles on the long term are unknown.

Methods: All F/P-negative HES patient treated with mepolizumab in France from 2003 to 2022 were included. For each study visit, we retrospectively collected the following data: drug doses (and spacing), HES-disease status, absolute eosinophil counts and doses of oral corticosteroids (OCS).

Results and Discussion: Data were available for 64 patients. Five patients were excluded because of misdiagnoses. After a median follow-up of 4.5 [2.5-12.3] years, 11 patients (19%) relapsed, among whom five were related to prior mepolizumab spacing to more than four weeks between injections (Figure). Most of the patients were in clinical remission (n=55, 93%) and/or haematological remission (n=56, 95%) at last follow-up, including 38 (64%) OCS-free patients. When focusing on the 21 (36%) patients with more than eight years of follow-up (median 14.4 [12.2-17.3] years), outcomes tended to be the same as those of the overall population. At last follow-up, more than 70% of patients were able to space mepolizumab's infusions for more than four weeks. Four patients were able to discontinue mepolizumab without relapse. There was no new safety signal due to a treatment-related adverse event.

Conclusions: Mepolizumab remains highly efficacious in the long, enabling sustained disease remission despite tapering of OCS and spacing of injections. Very few cases of mepolizumab failure were identified, among which the leading cause was HES misdiagnosis.

Keywords: *Mepolizumab, hypereosinophilic syndrome, eosinophils, IL5*

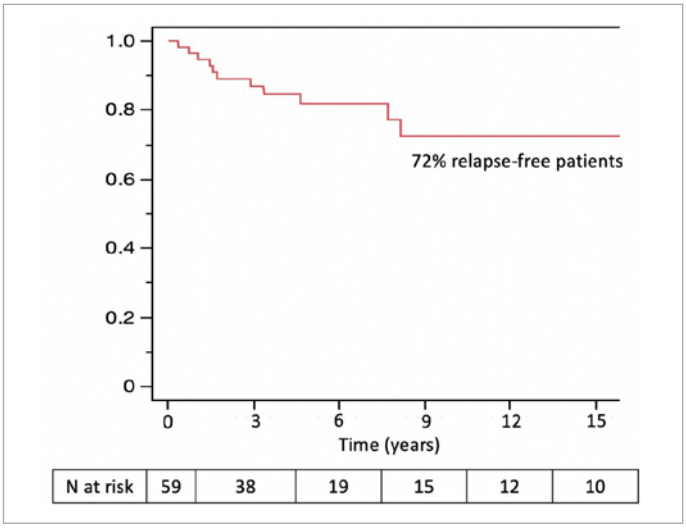

Figure 1.

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[Abstract:0673]

OUTCOMES OF SUBCUTANEOUS IMMUNOGLOBULIN DOSE REDUCTION STRATEGY IN PRIMARY IMMUNE DEFICIENCIES AMID GLOBAL SHORTAGE

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Objective: This work aimed to investigate the clinical and analytical impacts of a standardized subcutaneous immunoglobulin (SCIg) dose reduction regimen in patients with humoral primary immune deficiencies (PID). This investigation was prompted by the global immunoglobulin shortage during the COVID-19 pandemic.

Materials and Methods: In our institution, patients with PID under SCIg treatment for ≥6 months, with IgG trough levels ≥ 700 mg/dl, and no significant infections in the last 6 months were homogeneously dose-adjusted by 15 mg/Kg/week for each 150 mg/dl their trough levels were above 700 mg/dl, or 900 mg/dl in cases with enteropathy, bronchiectasis, GLILD, or immunosuppressants. Clinical and analytical parameters were retrospectively recorded and analysed at baseline, and at 6 and 12-month follow-up.

Results: The study included 31 patients. The most common diagnosis was common variable immunodeficiency (CVID) (n=17). Mean IgG-through levels were significantly reduced after dose-adjustment but the mean in all periods was over 900 mg/dL (p<0.01). There were no differences in the incidence of severe infections such as pneumonia and other lower respiratory tract infections, major bacterial infections, opportunistic infections, skin and soft tissue infections or severe gastrointestinal infections. Furthermore, no recurrent infections (≥3/6 months) were observed after adjustment.

Conclusions: The Ig dose adjustment led to a significant decrease in IgG levels, but always over supratherapeutic values, without an increase in severe or recurrent infections; meaning this standardized dose reduction could be a promising strategy to optimize the use of a scarce blood product which is vital for patients with humoral immunodeficiencies.

Keywords: *common variable immune deficiency (CVID), subcutaneous immunoglobulin (SCIg), COVID-19 pandemic, primary immune deficiencies (PID)*

VARIABLE	FREQUENCY (N=31)	PERCENTAGE (%)
SEX		
Male	15	48.4%
Female	16	51.6%
DIAGNOSIS		
Common Variable Immune Deficiency (CVID)	17	54.8%
Selective IgG subtype deficit	3	9.7%
Other primary immune deficiencies (PID)	11	35.5%
TYPE OF SUBCUTANEOUS Ig (SCIg)		
Conventional SCIg formulation	19	61.3%
Hyaluronidase facilitated SCIg	12	38.7%

Table 1. *Characteristics of patients.*

VARIABLE	6 MONTHS PRE-DOSE ADJUSTEMENT Average (SD)	6 MONTHS POST-DOSE ADJUSTEMENT Average (SD)	6 TO 12 MONTHS POST-DOSE ADJUSTEMENT Average (SD)	p VALUE
Nº of severe bacterial infections	0 (0)	0.04 (0.21)	0.04 (0.21)	p=0.264
Nº of minor infections (≥3 in 6 months = recurrent infection)	0.15 (0.42)	0.43 (0.81)	0.5 (0.72)	p<0.05
Trough IgG levels (mg/dL)	1128.52 (257.62)	948.67 (268.52)	1007.26 (301.51)	p<0.001

Table 2. *Results.*

There were no differences in the incidence of severe infections such as pneumonia and other lower respiratory tract infections, major bacterial infections, opportunistic infections, skin and soft tissue infections or severe gastrointestinal infections. Furthermore, there was an increase in the number of minor infections after adjustment at the expense of upper respiratory tract and genitourinary infections (p<0,05), however no recurrent minor infections (≥3/6 months) were observed. Mean IgG-through levels were significantly reduced approximately 4% at 6 months and up to 17% at 12 months after dose-adjustment but the mean in all periods was over 900 mg/dL (p<0.01).

[Abstract:0687]

LIFE-THREATENING MEASLES PNEUMONITIS IN ADULT PATIENT

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While measles is commonly considered a mild viral illness occurring in childhood, it can affect individuals of any age, leading to serious respiratory or neurological complications in adults. In this case report, we aim to discuss the clinical and treatment attributes of an adult patient with severe measles pneumonitis. A 33-year-old male patient admitted to the emergency department with complaints of a persistent sore throat, fatigue, shortness of breath, a week-long cough, fever, and the presence of mouth sores. Upon admission to the emergency department, the patient had mild respiratory distress, and thoracic CT revealed bilateral

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miliary centrilobular infiltrations in both lungs (Figure 1). He was admitted to the general ward with a preliminary diagnosis of miliary tuberculosis and pneumonia. Antituberculosis treatment was initiated. The patient, experiencing persistent respiratory distress despite conventional oxygen therapy, was intubated and subsequently admitted to our intensive care unit. The patient underwent bronchoscopy, revealing no endobronchial lesions in the bilateral bronchial system. Moreover, bronchoalveolar lavage for both mycobacteria PCR and *Pneumocystis jirovecii* PCR yielded negative results. The patient's antituberculosis treatment was discontinued. The patient tested positive for measles IgM, leading to a diagnosis of measles pneumonitis. Subsequently, high-dose vitamin A supplementation and corticosteroid therapy were initiated. The patient was successfully extubated on the third day of ICU admission, and was transferred to the infectious diseases department on the sixth day following admission to the ICU. Severe measles-related pneumonitis in adults might be more prevalent than previously recognized, regardless of the patient's immune status.

Keywords: *measles, complication, pneumonia, acute respiratory failure*

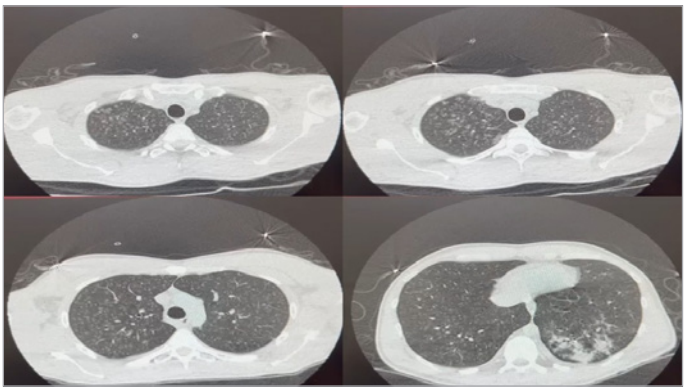

Figure 1. *The axial section of the thoracic CT scan for the patient reveals widespread miliary centrilobular infiltrations in both lungs, along with consolidation observed in the lower lobe of the left lung.*

[Abstract:0721]

A RARE CASE PRESENTATION: MELAS SYNDROME PRESENTED WITH CACHEXIA AND EPILEPSY

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Kanuni Sultan Suleyman Training and Research Hospital, Department of Internal Medicine, Istanbul, Turkey

Introduction: MELAS syndrome is a rare mitochondrial disorder characterized by encephalomyopathy, lactic acidosis, and stroke-like attacks. The most prevalent mutation associated with MELAS syndrome is the m.3243A>G mutation. We diagnosed MELAS syndrome in a patient presenting with cachexia, myopathy, status epilepticus, and lactic acidosis.

Case Presentation: A 32-year-old male with no chronic illnesses was brought to the emergency department with status epilepticus. His medical history revealed progressively worsening hearing loss over four years, along with complaints of fatigue, weight loss, and recurrent headaches. Family history indicated cachexia in his mother and sister. The body mass index was 17. Physical examination revealed decreased muscle strength in the upper and lower extremities. Blood gas analysis showed a pH of 6.76 (normal range: 7.35-7.45), HCO_3 of 10.6 mmol/L (normal range: 21-29), and lactate of 20.2 mmol/L (normal range: 0.5-4). Celiac disease tests were negative, and other laboratory tests showed no abnormalities. Whole-body imaging revealed no pathology. Endoscopy results were normal, and sensorineural hearing loss was present. Considering cachexia, lactic acidosis, recurrent headaches, myopathy, hearing loss, and epilepsy attacks, MELAS syndrome was suspected. Genetic analysis confirmed the presence of the most common mitochondrial mutation in MELAS syndrome, m.3243A>G.

Conclusions: Our case exhibited the characteristic features of MELAS syndrome, including encephalomyopathy, lactic acidosis, and stroke-like symptoms, along with weight loss and hearing impairment. In cases with multisystemic involvement, especially those with a family history of lactic acidosis, clinicians should consider MELAS syndrome in the differential diagnosis and conduct genetic mutation analysis if necessary.

Keywords: *mitochondrial diseases, MELAS, rare disease*

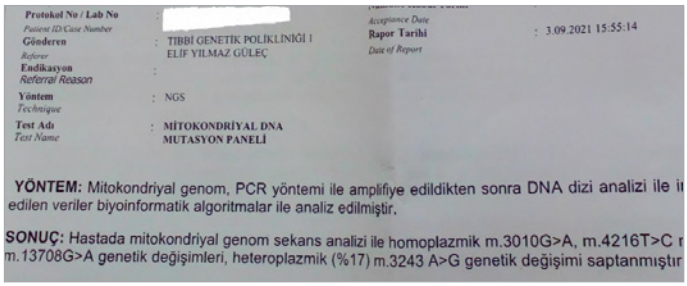
Protokol No / Lab No
Gönderen : TIBBİ GENETİK POLİKLİNİĞİ 1
ELİF YILMAZ GÜLEÇ
Rapor Tarihi : 3.09.2021 15:55:14
Endikasyon
Yöntem : NGS
Test Adı : MİTOKONDRİYAL DNA MUTASYON PANELİ
YÖNTEM: Mitokondriyal genom, PCR yöntemi ile amplifiye edildikten sonra DNA dizi analizi ile i
edilen veriler biyoinformatik algoritmalar ile analiz edilmiştir.
SONUÇ: Hastada mitokondriyal genom sekans analizi ile homoplazmik m.3010G>A, m.4216T>C r
m.13708G>A genetik değişimleri, heteroplazmik (%17) m.3243 A>G genetik değişimi saptanmıştır

Figure 1. *Patient's genetic analysis report.*
As a result of genetic analysis, the most common m3243A>G mutation compatible with MELAS was detected. *References: 1-Ayman W.El-Hattaba Adekunle, M.Adesinab,Jeremy Jonesc,Fernando Scaglia. MELAS syndrome: Clinical manifestations, pathogenesis, and treatment options. https://doi.org/10.1016/j.ymgme.2015.06.004 2-Panades-de Oliveira L, Montoya J, Emperador S, et al. A novel mutation in the mitochondrial MT-ND5 gene in a family with MELAS. The relevance of genetic analysis on targeted tissues.Mitochondrion 2020; 50: 14-8. 3-Y Falfoul, A Hassair, A Chebil, N Chaker, L El Matri.MELAS syndrome: Clinical manifestations, pathogenesis, and treatment options. Documented case of MELAS syndrome. DOI: 10.1016/j.jfo.2019.08.016.*

 DOI: 10.12890/2024_V11Sup1

[Abstract:0792]

NEW AND RARE DIAGNOSIS IN AN OLD PATIENT WITH TWO YEARS RELAPSING FEVER AND MEGALOBLASTIC ANAEMIA

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Purpose: Presenting a case with high relapsing fever, fatigue, inflammatory eye disease, intermittent palpable purpura, who doesn't fulfil any criteria for any specific autoinflammatory disease. VEXAS syndrome is a not very rare, recently discovered, autoinflammatory disorder that might explain different autoinflammatory symptoms.

Methods: A 76-year-old man was followed for a period of almost 2 years with presenting symptoms of persistently high fever, inflammatory eye symptoms, and fatigue. The patient was diagnosed initially with Giant Cell Arteritis and treated with pulse therapy with methylprednisolone, followed by maintenance doses. The peripheral blood showed persistent megaloblastic anaemia, moderate thrombocytopenia, and neutropenia. All autoantibodies' titers came negative and persistently very high CRP (C-reactive protein) and ERS (erythrocyte sedimentation rate) was noted. Later, on the course of the disease the patient, despite the maintaining dose of steroids, had recurrent fever, arthralgia, palpable purpura and lately, shortness of breath, dry cough, and polyposis of colon.

The peripheral blood and bone marrow aspiration raised high suspicion for myelodysplastic syndrome and UBA1 gene mutations was ordered.

Findings: A hemizygous pathogenic variant in UBA1, c.121A>G (p.Met41Val) gene was detected and a diagnosis of VEXAS Syndrome was concluded. For the time being we are considering the therapeutic strategy regarding myelodysplastic syndrome

Conclusions: We must take in consideration VEXAS Syndrome every time we face symptoms of autoinflammatory disease refractory to conventional treatment, man over 45 years old, macrocytic anaemia, and thrombocytopenia.

Keywords: *autoinflammatory, VEXAS syndrome, myelodysplastic*

[Abstract:0793]

WOLF IN THE MARROW SPINAL APLASIA DURING LUPUS

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Hematological abnormalities of lupus are common; they affect all lineages; bone marrow aplasia is rare and exceptionally.

B.A aged 22, followed for cutaneous lupus for 4 years, under plaquenil. Hospitalized for treatment of long-term fever evolving in a context of deterioration in general condition. On clinical examination, the patient presented: an altered general condition, febrile at 40°C, hemodynamically stable, butterfly-wing malar erythema, oral and nasal ulceration, superficial lymphadenopathy. We did not find any obvious infectious focus. Biological exploration has objectified. Leukopenia: 1200 - neutropenia: 300 - Hb: 12.2 Thrombocytopenia: 79,000 a-Bone marrow: bone marrow aplasia, CRP at 5 and negative procalcitonin, cytolysis syndrome, elevated LDH, negative viral serology (HBV, HCV, CMV) and renal function with urinary sediment without abnormalities. Immunological assessment was positive: Anti DNA strongly positive: 800, profound hypo complementemia. SAPL search came back negative.

ECG: Regular sinus rhythm at 90b/min, no conduction or repolarization disturbances, Heart echo: Correct kinetics, minimal MI, moderately dilated LA, non-dilated LV, non-dilated right chambers, PAH unlikely.

All the clinical, biological and immunological data made it possible to identify a severe haematological flare-up of his lupus, i.e. SLEDAI score of 15. Emergency treatment with a corticosteroid bolus was initiated with a double antibiotic: Augmentin 3g/24h-Ciprolan800mg/h with good clinicobiological evolution (apyrexia-improvement of general condition-normalization of biological parameters: GB: 3400-PLQ: 204000).

Hematological damage in systemic lupus erythematosus is mainly manifested by the presence of peripheral cytopenia, but central damage which can be misleading is described.

Keywords: *put, make, wait*

[Abstract:0848]

LAMOTRIGINE-ASSOCIATED TOXIC EPIDERMAL NECROLYSIS: A CASE REPORT

Muzeyyen Yilmazoglu[1], Erdem Yalcinkaya[2], Umut Sabri Kasapoglu[2], Huseyin Arikan[2], Sait Karakurt[2]

[1] Department of Internal Medicine, Marmara University School of Medicine, Istanbul, Turkey

[2] Department of Pulmonary and Critical Care Medicine, Marmara University School of Medicine, Istanbul, Turkey

This case report discusses a rare dermatological complication, toxic epidermal necrolysis, emerging after initiating Lamotrigine treatment in a 31-year-old male with major depression. It emphasizes the importance of a multidisciplinary approach in diagnosing and managing TEN, with high mortality potential. Stevens-Johnson Syndrome, a severe hypersensitivity reaction causing vesiculobullous lesions, is classified as SJS when affecting less than 10% of the body's epidermal surface and as toxic epidermal necrolysis when exceeding 30%. While antiepileptic drugs like Carbamazepine and Phenobarbital are known triggers for SJS, reports associating Lamotrigine with SJS are infrequent. The patient was initiated Lamotrigine, leading to eruptions on lower extremities within 7-10 days. Initially diagnosed with Stevens-Johnson syndrome, the patient received methylprednisolone, but

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unresponsive lesions prompted admission to the intensive care unit for toxic epidermal necrolysis management. Intensive care measures, including hydration, electrolyte replacement, enteral nutrition, IVIG treatment, and Etanercept administration, were implemented. Collaboration among dermatology, ophthalmology, infectious diseases, and psychiatry contributed to successful treatment. Meticulous monitoring, focusing on skin care, eye health, and infection control, underscored the potential severe dermatological side effects of anticonvulsant medications during major depression treatment, necessitating vigilance for mucosal side effects and prompt intervention. After approximately 20 days in the ICU, the patient transitioned to dermatology service. Discharge planning commenced after approximately 15 days of follow-up, with significant progress in re-epithelialization. In conclusion, this case highlights the effective management of rare dermatological complications like TEN through a multidisciplinary approach, positively influencing clinical outcomes. It emphasizes the imperative need for awareness regarding dermatological side effects of anticonvulsant medications.

Keywords: *Stevens-Johnson syndrome, toxic epidermal necrolysis, lamotrigine, depression*

Figure 1. *Body Involvement.*

Figure 2. *Intensive Care Admission.*
Erythematous, targetoid, annular, or purpuric macules, Flaccid bullae, Large painful erosions.

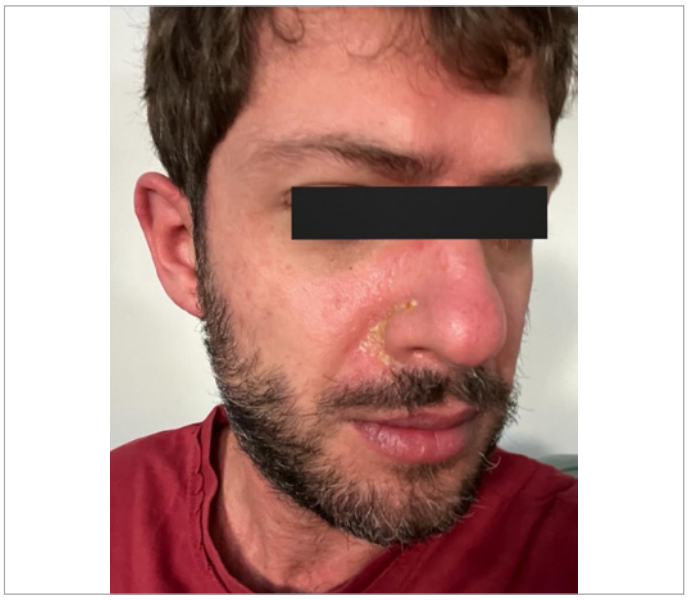

Figure 3. *Intensive Care Discharge.*

[Abstract:0870]

MUCOPOLYSACCHARIDOSIS TYPE IV: A CASE REPORT OF MORQUIO SYNDROME

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[1] Department of Internal Medicine, Marmara University School of Medicine, Istanbul, Turkey

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Mucopolysaccharidosis type IVA (MPS IVA), or Morquio syndrome, is an autosomal recessive lysosomal disorder resulting

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from a deficiency of the GALNS enzyme, causing the accumulation of glycosaminoglycans in bones and cartilage. Our 19-year-old Type4A MPS patient, previously evaluated for obstructive sleep apnoea syndrome (OSAS), presented with severe respiratory distress. Despite non-invasive mechanical ventilation for up to 20 hours daily, persistent hypercarbia and acidosis led to considerations of elective tracheostomy. This was complicated by atlantoaxial joint laxity, posing a risk of quadriplegia. Elosulfase alfa, administered weekly, had limited impact on airway obstruction. Imaging revealed intricate airway abnormalities, with the upper and lower airways showing narrowing and tortuosity due to GAG deposition and structural anomalies. The "sniffing position" was employed to alleviate airway obstruction. A 14-day multidisciplinary approach, involving paediatricians, pulmonologists, cardiologists, and anesthesiologists, addressed the patient's decreased physical activity, irregular nutrition, and weight gain. Despite the patient's limited lung capacity, physical therapy, appropriate exercise, and antibiotic treatment were implemented. The NIMV support, initially provided for 20 hours, was successfully reduced to 5 hours, resulting in symptom resolution and discharge. The patient's echocardiogram indicated mild cardiac insufficiencies, emphasizing the systemic impact of Morquio A syndrome. Respiratory impairment is a significant contributor to morbidity and mortality in Morquio A syndrome. While non-invasive ventilator support can manage sleep-disordered breathing, tracheostomy may be considered in severe cases. The heterogeneous and progressive nature of Morquio A syndrome necessitates a multidisciplinary approach for effective management.

Keywords: *mucopolysaccharidosis type IVA, Morquio syndrome type A, OSAS, NIMV, tracheostomy*

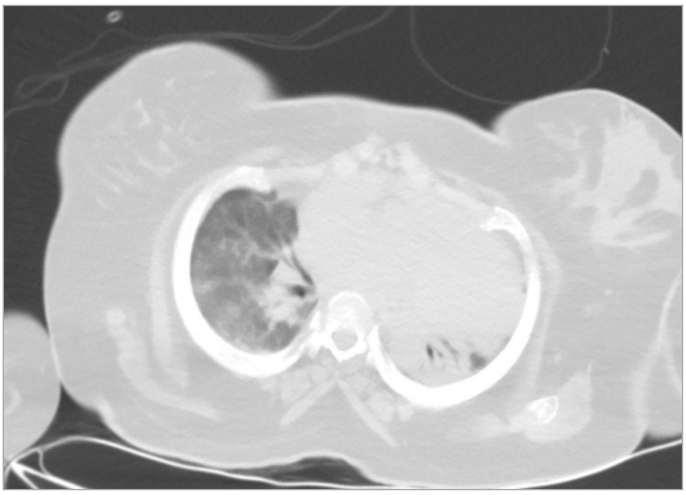

Figure 1. *Intensive Care Admission CT.*

Figure 2. *Intensive Care Discharge.*
The patient who was discharged without the need for tracheostomy

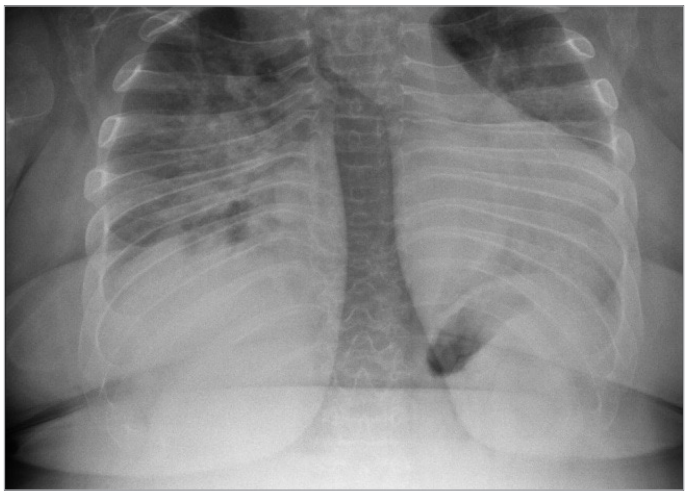

Figure 3. *Intensive Care Discharge Chest X-Ray.*

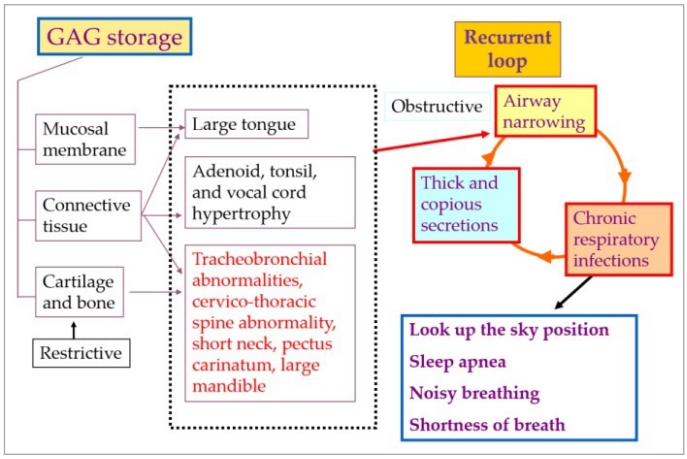

Figure 4. *Pathophysiology of airway compromise in MPS IVA patients.*

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[Abstract:0898]

FROM LUNG TO ORBITS: PERIVASCULAR EPITHELIOID CELL NEOPLASM (PECOMA)

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Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates

Introduction: Perivascular epithelioid cell tumour, also known as PEComa, is a group of rare mesenchymal tumours that are characterized by the presence of cells around blood vessels in a variety of organs.

Case Presentation: A 43-year-old female with a history of Tuberous Sclerosis Complex (TSC) presented with a one-month history of left eye protrusion, accompanied by pain, blurry vision, left-sided headache, and periorbital swelling. She also reported a painful large mass on her upper back. Imaging revealed a solid, infiltrative lesion in the left orbital area displacing the optic globe and a 12.2 cm dumbbell-shaped chest mass with metastatic bone disease. Biopsy confirmed malignant pulmonary PEComa with strong immunohistochemical markers. The multidisciplinary team deemed the orbital mass surgically unresectable, with limited responsiveness to available systemic therapies, and recommended referral to a specialized PEComa centre. Palliative radiotherapy to the orbit was suggested to alleviate discomfort, though the impact on tumour shrinkage remains uncertain.

Discussion: PEComas are associated with genetic changes linked to Tuberous Sclerosis Complex (TSC). These tumours typically express melanocytic markers like HMB-45 and/or Melan-A, as well as smooth muscle markers like actin and/or desmin. Diagnosing PEComas lacks a gold standard imaging study, but they often appear as low-density, hypointense on CT, hypointense on T1-weighted MRI, and hyperintense on T2-weighted MRI. Surgical excision is the primary treatment, although guidelines are lacking due to the rarity of cases. Emerging research explores hormonal and targeted therapies, particularly mTOR inhibitors, for aggressive metastatic PEComas

Keywords: *PECOMA, perivascular epithelioid cell neoplasm, orbit pecoma, lung pecoma, cancer*

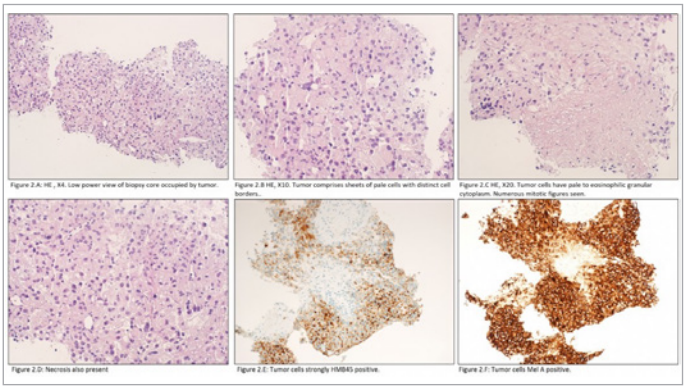

Figure 1. *Histopathology findings of PECOMA.*

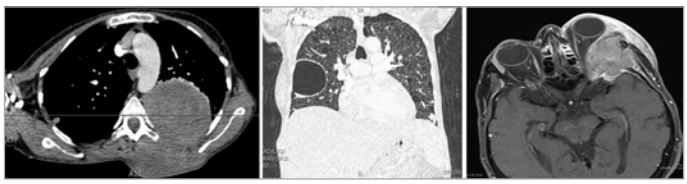

Figure 2. *Radiological images of PECOMA.*

[Abstract:0935]

PREGNANCY IN GAUCHER DISEASE: NEW SUCCESS OF IMIGLUCERASE

Nabila Slimani, Imene Bradaia, Chahra Kamar, Aicha Saidj, Ouassila Hocine, Nadjib Abdelghafour, Mouad Boucherit, Djenette Hakem, Samia Zekri, Amar Tebaibia

Internal Medicine Department, El Biar University Hospital, Algiers, Algeria

Introduction: Gaucher disease (GD) is a rare genetic disorder, it is a lysosomal storage disorder resulting from a deficiency of the enzyme glucocerebrosidase. The association with pregnancy exposes the worsening of the disease and complications of pregnancy and puerperium. We report a case of pregnancy in a woman of 29 years, suffering from GD type 1 successfully treated with Imiglucerase.

Observation: MS was a 29 years-old, who was first diagnosed with GD type 1 at the age of 17 years, stabilized under enzyme replacement therapy (ERT), primigravida. In the absence of adverse effects, we maintained ERT with 30 U/kg per 2 weeks. At the 20th week of gestation, she reported dyspnoea without bone pain or hepatosplenomegaly. She had an oligohydramnios associated with fluctuating thrombocytopenia, normocytic normochromic anaemia at 9.8 g/dl of haemoglobin. No side effects following the use of Imiglucerase have been reported. The course of the pregnancy was marked by the occurrence of a preterm premature rupture of membranes, which justified delivery at 32 weeks. She had a healthy male infant weighing 2030 g. She presented no postnatal complications with a good progress after a 6-month follow-up.

Conclusions: Increasing hypermetabolism in GD during pregnancy is associated with the risk of increased disease activity. The particularity of this observation is the effectiveness of ERT during pregnancy, with limited the risk of delivery haemorrhage in our patient. A large number of publications report that ERT appears to be safe both for the mother and the foetus.

Keywords: *Gaucher disease, pregnancy, imiglucerase*

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[Abstract:0970]

ACUTE PORPHYRIA: BETWEEN ERRANT DIAGNOSIS AND UNUSUAL ASSOCIATED METABOLIC DISORDERS; CASE REPORT

Besma Kletin[1], *Nabila Slimani*[1], *Nadjib Abdelghafour*[1], *Amine Diah*[1], *Meriem Lebdjiri*[1], *Amel Mammeri*[1], *Ammar Tebaibia*[1], *Abdelaziz Tarzali*[2], *Gilles Pantex*[3], *Francois Cornu*[3]

[1] Department of internal medicine, Elbiar University Hospital, Algiers, Algeria

[2] Tarsali Medical Medical Analysis Laboratory, Algiers, Algeria

[3] L.Gouya biology pole, Louis Mourier University hospital, Paris, France

Acute intermittent porphyria AIP is a rare inherited metabolic disorder. It presents with acute episodes of neurovisceral symptoms which are non-specific, therefore diagnosis is frequently missed or delayed. AIP is rarely associated with dyslipidaemia, and is exceptionally accompanied by copper disorders, or non-iatrogenic hepatic iron overload. We report one case.

A 20-year-old female was referred to us for a recurrent attacks of abdominal pain and vomiting which has been evolving for four months, associated with electrolyte disorders, for which etiological assessment came back negative, and were eventually linked to a psychiatric origin, and put on antidepressants.

On clinical examination, in-addition to the symptoms described above, we noted tachycardia, high blood-pressure, accompanied by resting tremor of the right upper limb.

Laboratory tests revealed moderate liver cytolysis, hyponatremia, acute renal failure, hypercholesterolemia, slightly low ceruloplasmin 1.6 µmol/l, and high urinary copper levels. Urinary porphobilinogen and ADA levels came back very high (180.8/ 83.5 µmol/l), faecal coproporphyrin was normal.

Hepatic-MRI identified slight hepatic iron overload. Cerebral-MRI showed discrete T2-hyposignal of the red nuclei and substantia nigra (Wilson's disease).

The diagnosis of AIP associated with hepatic iron overload, copper overload, and dyslipidaemia was made.

She was put on dextrose solutions, opioids antalgics, zinc supplement, and low-cholesterol diet. Haemin was unavailable. Symptoms have resolved within a week. Three months later, she had another attack due to exposure to a solvent eventually resolved under treatment.

AIT is rare, misdiagnosed disease. Its association with copper and iron overload outside of heminic-treatment is exceptional; coincidence or cause-and-effect relationship? This remains to be elucidated.

Keywords: *acute intermittent porphyria, misdiagnosed, copper disorders, non-heminic related hepatic iron overload, dyslipidaemia*

[Abstract:0996]

CLINICAL AND COURSE CHARACTERISTICS OF ADULT RHEUMATOID PURPURA: STUDY OF A TUNISIAN POPULATION

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Introduction: Rheumatoid purpura (RP) is a systemic immune vasculitis affecting small vessels. The aim of our study is to identify the different organ affected, as well as the treatment and course of adult RP.

Methods: A single-centre retrospective descriptive study over a period of 8 years. Including patients with RP based on clinical and biopsy findings and the EULAR/PRINTO/HSP PRES 2008 classification.

Results: Thirty patients were included, sex ratio M/F 0.87, with a mean age of 45.6 years. Skin involvement: Petechial purpura in 28 cases, associated with necrosis in 5 cases and ecchymosis in 3. Skin biopsy revealed leukocytoclastic vasculitis in 26 cases and fibrinoid necrosis in 11. DFI revealed IgA deposits in 25 cases, C3 deposits in 16. Digestive involvement in 20 patients. Bleeding occurred in 50% of cases and an occlusion in 15%. Joint involvement in 17 patients, arthralgia in 10, arthritis in 5. Kidney damage in 11 patients, with proteinuria ranging from 0.82 g/24h to 2.6 g/24h. Haematuria in 23% of cases. Neurological involvement in 4 patients (peripheral neuropathy in 3 patients and a seizure in one patient).One patient had a pericarditis and another had orchiepididymitis. Bed rest was indicated for all patients. Corticosteroids were prescribed to 20 patients, Colchicine for 9 patients. The immunosuppressive treatments prescribed were azathioprine in 2 patients and cyclophosphamide in 2 patients. Disease remission was observed in 23 patients, recurrence in 7.

Conclusions: Adult rheumatoid purpura or IgA vasculitis is a truly systemic disease, affecting several organs, potentially life threatening, leaving sequelae with a significant potential for relapse.

Keywords: *rheumatoid purpura, kidney, skin*

[Abstract:1011]

THROMBOTIC MICROANGIOPATHY ASSOCIATED TO NEWLY DIAGNOSED SJOGREN'S SYNDROME: CASE REPORT

Sameh Sayhi[1], *Arij Ezzouhour Yahyaoui*[1], *Nour Elhouda Guediche*[1], *Bilel Arfaoui*[1], *Faida Ajili*[2], *Najeh Boussetta*[1], *Nadia Ben Abdelhafidh*[1]

[1] Military Hospital of Tunis, Tunisia

[2] ⚠ The author did not provide affiliation upon requests from the event organizer

Introduction: Sjogren's syndrome (SS) is an autoimmune disease characterized by ocular and oral dryness and a variety of other

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systemic manifestations. Thrombotic microangiopathy (TMA) is rarely associated with SS. We report a case that illustrates this association in a female patient, who also presents autoimmune hypophysitis.

Observation: A 65-year-old patient was referred for investigation of an axonal sensorimotor neuropathy that has been evolving for 5 months. Possible infectious and neoplastic causes were ruled out by examination, laboratory tests and imaging. The patient reported ocular and oral dryness. Minor salivary gland biopsy highlighted the presence of focal lymphocytic sialadenitis with a focus score of 1 foci/ 4 mm^2. Schirmer's test was inferior to 5 mm/5 min in both eyes. Laboratory investigations revealed anterior pituitary failure including secondary adrenal insufficiency, central hypothyroidism and hypogonadotropic hypogonadism. Magnetic resonance imaging of the hypothalamo–pituitary region demonstrated signs of autoimmune hypophysitis. During hospitalization, the patient developed anaemia and thrombocytopenia with schizocytes count at 4%. The diagnosis of TMA associated to SS, without renal failure was made. The patient was commenced on intravenous immunoglobulin, corticosteroids, azathioprine and pregabalin. An improvement was noticed in her neuropathic pain, anaemia and thrombocytopenia, schizocytes count was reduced progressively.

Conclusions: Previous systematic reviews highlighted the rarity of SS associated with TMA. Our case also illustrates two manifestations of SS: axonal neuropathy and autoimmune hypophysitis.

Keywords: *Sjogren's syndrome, autoimmune disease, thrombotic microangiopathy*

[Abstract:1031]

NAVIGATING THE CHALLENGES OF GLYCOGEN STORAGE DISEASE TYPE IB: DIETARY MANAGEMENT, NEUTROPENIA, AND THE ROLE OF LIVER TRANSPLANTATION

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Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates

Glycogen Storage Disease Type Ib (GSD-Ib) is a rare and complex metabolic disorder characterized by impaired glycogen metabolism due to a deficiency in glucose-6-phosphatase enzyme, leading to a wide range of clinical challenges and complications. This genetic condition poses significant management hurdles, often requiring a multidisciplinary approach for effective care.

We present a 22-year-old patient with longstanding GSD-Ib who meticulously adhered to a modified diet, excluding complex carbs, sugars, and lactose. Previous liver biopsies in 2001 and 2002 confirmed GSD-Ib with glucose-6-phosphatase deficiency (von Gierke disease). Despite strict dietary compliance, the patient experienced recurrent and severe lactic acidosis and hypoglycaemia, resulting in multiple hospital admissions. Imaging revealed significant hepatomegaly, leading to discussions about the potential need for liver transplantation to manage these persistent metabolic issues. Additionally, during a recent hospitalization, the patient developed neutropenia, with a granulocyte count as low as 250. Although GSD-Ib itself can contribute to neutropenia, an extensive investigation, including a bone marrow aspirate and biopsy, was initiated to rule out other causes. To address neutropenia and anaemia, the patient received G-CSF and erythropoietin therapy, which improved haemoglobin levels. However, severe neutropenia persisted, necessitating continuous G-CSF treatment as part of the preparation for liver transplantation.

This case sheds light on the intricate clinical trajectory of GSD-Ib, emphasizing its potential haematological complications. It underscores the necessity of a multidisciplinary approach to manage this challenging disorder effectively. Timely consideration of liver transplantation becomes crucial in cases involving unresponsive metabolic derangements, such as recurrent lactic acidosis despite strict dietary interventions.

Keywords: *inborn errors of metabolism, glycogen storage disease type Ib, glucose-6-phosphatase deficiency, von Gierke disease*

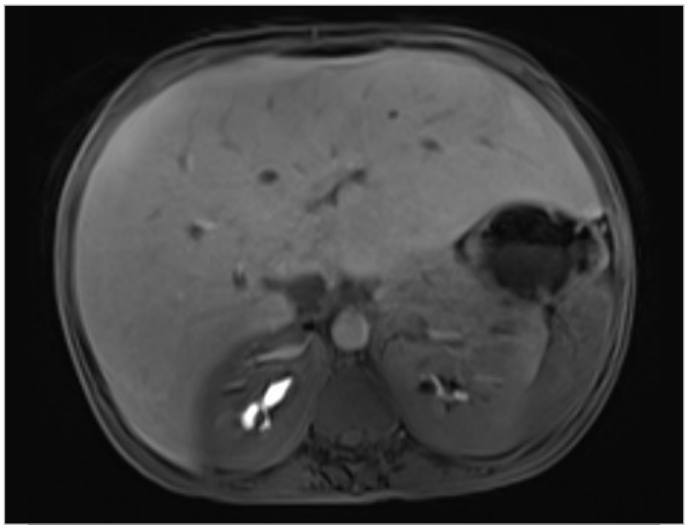

Figure 1. *MRI of liver: evidence of hepatomegaly with steatosis. No discrete hepatic lesions.*

[Abstract:1060]

A CRUISE THROUGH MOYAMOYA: A CASE STUDY

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Moyamoya is a rare progressive cerebrovascular condition defined as stenosis of the large intracranial arteries - internal carotid arteries and its proximal branches – and, hence the compensatory mechanisms of reduced blood flow to the brain, a development of the small collateral vessels. The pathognomonic feature of this

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condition is a hazy or smoky image on a brain angiogram, which as first described by the Japanese neurosurgeons as "moyamoya". A disease surges when there are no associated conditions versus a syndrome when these alternative diseases are present. Although ischemic symptoms are the most prevalent at presentation, in adults the rate of hemorrhage stroke increases significantly. In this case study we discuss a 36-years old man that presented with an intense pulsatile headache limited to the occipital region with irradiation to the supraorbital area, treated with analgesics. Associated symptoms such as nausea, vomiting, asthenia, and fever were denied. Three days later, the headache reoccurred with the same intensity, characteristics, nausea, and no other symptoms. Admission brain magnetic resonance (MR) revealed a subacute thalamus hematoma, and the MR angiographic (MRA) exposed a bilateral stenosis of the internal carotid arteries, low signal from the bilateral middle and anterior cerebral arteries, and multiple collateral small vessels. These findings support the diagnosis of Moyamoya disease/syndrome. With this work we aspire to empathize the importance of quality clinical history taking in the process of prompt diagnosis and treatment, while also doing a literature review of this condition.

Keywords: *moyamoya, moyamoya disease, moyamoya syndrome*

[Abstract:1118]

NON-HAEMATOLOGICAL CLINICAL MANIFESTATIONS IN TTP

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Introduction: TTP is a rare disease. The diagnosis is confirmed by collapsed ADAMS-13 activity (<10% of normal) responsible for a clinical picture of MAT combining haematological manifestations such as thrombocytopenia and mechanical haemolytic anaemia, with extra-haematological manifestations secondary to ischaemia in the organs affected.

Methods: A Retrospective descriptive study including patients with TTP hospitalised in our university hospital over an 18-year period.

Results: Sixteen patients were included, sex ration=1. The mean age at diagnosis was 46. The clinical presentation: fever in 2 patients, Neurological symptoms included headache in 5 patients, confusion in 4 patients, motor deficit in 4 patients, seizures in 3 patients, aphasia in 3 patients, coma in 3 patients and dizziness in 2 patients. Cerebral CT were performed in 4 patients, revealing ischaemic stroke in three. Digestive complaints in 6 cases, abdominal pain (n=6), nausea and vomiting (n=3). An abdominal CT was performed in these patients: normal. Cardiovascular manifestations included chest pain in 4 patients, rhythm and conduction disorders, coronary insufficiency and superficial femoral DVT in one patient each. Urine dipstick tests were performed in 5 patients, showing haematuria and single-cross proteinuria in 2 cases in which renal function was not impaired. Renal failure was observed in 2 patients with creatinine clearance of 53 ml/min/1.73m^2 in one case and 22 ml/min/1.73m^2 in the other.

Conclusions: The aetiologies in our study were: idiopathic TTP in 12 patients. PTT associated with breast cancer in two patients, one of whom was a known tumour carrier. Post-vaccination TTP in 2 patients.

Keywords: *TTP, haematology, thrombosis,*

[Abstract:1134]

A RARE CASE REPORT OF HUS ASSOCIATED WITH NON-BLOODY DIARRHOEA IN ADULTS

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A 51-year-old female patient presented to the emergency department with back pain and non-bloody mucoid diarrhoea. These symptoms had started 2 days before. There was no significant medical history, no history of drug use and contaminated raw food or water. Physical examination and vital signs were normal. Pathological laboratory results were urea: 122 mg/dl, creatinine: 3.01 mg/dl, GFR: 17 ml/dk/1.73m^2, LDH: 1695 u/l, total/indirect bilirubin: 3.1/2.5 mg/dl, hb: 12.1 g/dl, plt: 85x10^9/l. Stool cultures were negative that no erythrocytes, only 4-5 leukocytes. Blood samples showed schistocytes. Laboratory findings were remarkable for thrombotic thrombocytopenic purpura (TTP)/ HUS called trombotic microangiopathy(TMA). Plasmapheresis and haemodiafiltration were performed daily. On the second day, the ADAMTS-13 activity result was 87%, TTP was excluded. On the fourth day, she had hypertension, anuria and the highest urea (201 mg/dl), creatinine (9.98 mg/dl), LDH (2085 u/l), the lowest haemoglobin (6.2 g/dl) and platelets (37 x10^9/l) values despite dialysis and plasmapheresis. She developed seizures, mental fog and required intubation. Diffusion MR showed vasogenic oedema and hyperintense areas in the parietooccipital cortical region were observed in the Flair sequence. The preliminary diagnosis was posterior reversible encephalopathy syndrome (PRES) secondary to HUS. The first dose of eculizumab was administered with a presumptive diagnosis of atypical HUS. On day 15, in *E. coli* 0157:H7 culture results were positive for Verotoxigenic and Shiga-like-toxin-producing *E. coli*. The diagnosis of typical HUS was confirmed. Eculizumab was discontinued. Haemodialysis was continued throughout the day. The patient was extubated on day 21 and discharged on day 33 with improved values and clinical status. The presence of non-bloody diarrhoea does not exclude the HUS. In TMA, treatment should be initiated without waiting for subtype differentiation.

Keywords: *haemolytic uremic syndrome, non-bloody diarrhoea, posterior reversible encephalopathy syndrome (PRES)*

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[Abstract:1183]

PSEUDOXANTOMA ELASTICUM-LIKE IN A PATIENT WITH HEMOLYTIC ANAEMIA

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A 47-year-old woman with a diagnosis of haemolytic anaemia caused by a congenital pyruvate kinase deficiency. She was on chelation therapy to control iron overload due to repeated transfusions.

A routine ophthalmic exam revealed a chronic exudate in the inferior temporal arcade of the right eye, far from the macular area. One month later, peripapillary striated images suggestive of angioid streaks were observed, with exudate in the upper arcade of the left eye.

During physical examination, the skin on the neck and the axillae was rough and lax, with small yellowish papules in a reticular pattern. Its histological examination was compatible with pseudoxanthoma elasticum. An echocardiogram and the ischemia tests excluded cardiac abnormalities.

Pseudoxanthoma elasticum (PXE) or Groenblad-Strandberg syndrome (OMIM: 177850 264800) is a rare congenital dysplastic disorder of the connective tissue, characterized by an abnormal mineralization of elastic tissues and caused by mutations in the ABCC6 gene. It predominantly affects tissues rich in elastic fibers. The main clinical manifestations include cutaneous (pseudoxanthoma elasticum), ocular (angioid streaks), vascular and gastrointestinal. This prompted the sequence analysis, but it did not reveal ABCC6 mutations.

Therefore, although the patient had ocular and cutaneous manifestations of PXE, the absence of mutations in ABCC6 suggested an alternative diagnosis of pseudoxanthoma elasticum-like disorder. This is an acquired disorder, with clinical and histological manifestations similar to PXE. However, as seen in this patient, it is associated with hemoglobinopathies and other chronic hemolytic anaemias. The pathogenesis remains unclear: it may involve an erythropoietin-related increase in FGF23.

Keywords: *pseudoxanthoma elasticum, haemolytic anaemia, pseudoxanthoma elasticum-like*

Figure 1. *Right axilla.*
Lax skin, with small yellowish papules in a reticular pattern.

[Abstract:1188]

ATYPICAL COGAN SYNDROME

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Introduction: Cogan syndrome is a systemic inflammatory disease affecting mainly the eye and the auditory-vestibular system, and is associated with systemic vasculitis. Two typical and atypical clinical forms have been described for this rare syndrome, the aetiology of which remains unknown. We report a case of Cogan syndrome atypical for its ocular involvement of episcleritis and anterior uveitis.

Case Presentation: Mrs B.N, aged 26, with no previous pathological history, initially consulted an otorhinolaryngologist (ENT) for sudden deafness of the right ear, with tinnitus and vertigo. ENT examination revealed a vestibular syndrome. Audiometry revealed a sensorineural hearing loss of 80 dB in the right ear.

The aetiological investigation was negative. Syphilis, cytomegalovirus and herpes simplex virus serologies were negative. Cerebral MRI to look for a lesion in the inner ear or in the course of the VIII nerve showed no abnormalities. The patient also had bilateral ocular redness. Ophthalmological examination revealed episcleritis and bilateral anterior uveitis.

Given the association of the atypical inflammatory ocular picture with rapidly progressive deafness spaced a few weeks apart in a young patient, atypical Cogan syndrome was retained.

In view of the severe hearing impairment, treatment with high dose of corticosteroids was indicated. Clinical outcome was favourable.

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Conclusions: Cogan syndrome is a rare disease that should be considered in the presence of a recurrent audiovestibular picture associated with inflammatory ocular involvement. Diagnosis, which remains clinical, is difficult, especially in the atypical form. Early treatment is essential, given the risk of permanent deafness.

Keywords: *Cogan syndrome, episcleritis, deafness*

[Abstract:1343]

SNEDDON'S SYNDROME WITHOUT ANTIPHOSPHOLIPID ANTIBODIES: A NEW ENTITY

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Introduction: Sneddon's syndrome is a rare entity, characterized by generalized livedo racemosa and recurrent cerebrovascular events. Its singular revelation with negative antiphospholipid antibodies (aPL) indicate that this syndrome may be a distinct entity or perhaps a group of different disorders.

Findings: N,65 years- old, G1P1A0, with no cardiovascular risk factors. Clinical history began 3 years ago with hemiparesis, migrainous headache. these symptoms, initially linked to cerebral vasculitis, justified a corticosteroid and antiplatelet therapy.

On clinical examination, an enlarged livedo racemosa, non-infiltrated, generalized over the entire body. Raynaud's phenomenon on the hands, with capillary dystrophy on nailfold capillaroscopy. Neurological examination show a pyramidal syndrome and psychiatric disturbances including depression with no extra-neurological symptoms. Cerebral MRI shows multiple micro ischemic lacunes, cardiovascular investigations show no abnormalities, Autoimmune assessment (anti- nuclear antibodies, aPL), ANCA search, and cryoglobulinemia are negative. Skin biopsy of the livedo mesh patterns came back inconclusive.

After well-managed follow-up with antiplatelet therapy and hydroxychloroquine, the patient has not presented recurrent ischemic manifestations.

Conclusions: The presence of cutaneous signs such as (livedo racemosa) coupled with ischemic stroke featuring lacunar lesions, and especially considering the absence of major cardiovascular risk factors or a history of placental vascular pathology. After thorough investigation, the ischemic stroke is attributed to Sneddon syndrome due to the contextual presence of livedo.

However, it is noteworthy that the revelation of Sneddon syndrome at a late age without aPL is not trivial and is often indicative of the potential onset of vascular dementia.

Keywords: *Sneddo's syndrome, antiphospholipid antibodies, late age*

[Abstract:1362]

DIAGNOSIS AT FIRST SIGHT: MELKERSSON-ROSENTHAL SYNDROME

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A 42-year-old woman with episodes of recurrent peripheral facial paralysis with no other personal history of interest. First episode on the left side at age 7 with subsequent ipsilateral episodes at ages 14 and 37, with last episode at age 41 on the right side with mild residual eyelid ptosis.

She attended the Internal Medicine consultation due to facial angioedema without other associated symptoms that had improved with a single dose of prednisone 60 mg. On physical examination, a fissured tongue was observed, with the rest of the examination normal. A complete analytical study was carried out in which she did not present any alterations of interest. Functional inhibitor C1, angiotensin converting enzyme, IgE and tryptase were normal. Serology ruled out acute infection by *(Coxiella burnetti, Borrelia burgdorferi)* and herpes simplex virus type 1 and 2. Given the characteristic clinical trial, once other causes being ruled out, she was diagnosed with Melkersson-Rosenthal syndrome. High-dose prednisone treatment was initiated with tapering afterwards up to a low maintenance dose with good clinical response and no new episodes during follow-up.

Melkersson-Rosenthal syndrome is a rare of unknown aetiology characterized by the triad of oro-facial oedema, facial nerve palsy and fissured tongue. The onset of symptoms is most commonly between 25 and 40 years with a female preponderance and it occurs more often in its incomplete form with only two of the three mentioned features. Differential diagnosis should include allergy, hereditary angioedema, acute infections, sarcoidosis and inflammatory bowel disease among others.

Keywords: *facial oedema, facial palsy, fissured tongue*

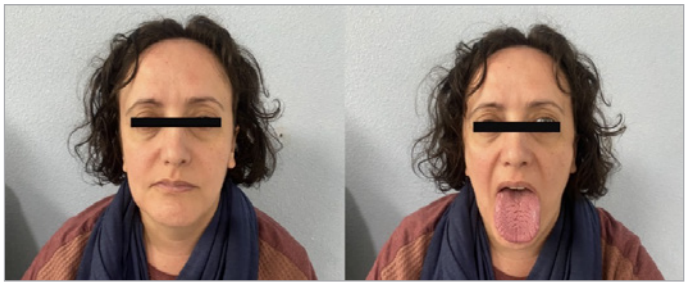

Figure 1. *Complete triad of Melkersson-Rosenthal syndrome. The patient authorizes the publication of these images.*

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[Abstract:1364]

EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

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Eosinophilic Granulomatosis with polyangiitis (EGPA) also known as Churg-Strauss Syndrome (CSS) is an extremely rare autoimmune condition belonging to ANCA (Anti-neutrophil cytoplasmic antibody) – associated systemic small vessel vasculitis. Which is primarily characterized by hypereosinophilia, history of asthma and necrotizing granulomas.55-year-old Caucasian female was referred for evaluation for Asthma, dyspnoea and chronic cough. Patient has been intermittent without consistent pattern for these problem for the past few years. Patient's previous labs did show persistent eosinophilia. Patient had been previously prescribed bronchodilators MDI which usually gets temporary response without complete improvement. On examination patient appeared dyspnoeic and had a low-grade fever, lab work was found to have an eosinophil count of 81% in total leucocyte count and positive for rheumatoid factor. Chest radiograph showed diffuse irregular opacities throughout both lungs, computed tomography (CT) of chest showed multifocal ill-defined infiltrates in both lungs with multiple perivascular lymphadenopathies. The patient was then subjected to endobronchial ultrasound bronchoscopy (EBUS) biopsy of mediastinal lymphadenopathy which on histopathologic examination revealed eosinophilic infiltration. With a high diagnostic suspicion of EGPA, we ordered ANCA tests which came back positive for P-ANCA (anti-myeloperoxidase) confirming Eosinophilic granulomatosis with polyangiitis involving multiple lobes of both the lungs. Patient was started on anti-interleukin-5 monoclonal antibody mepolizumab 750 MG IV once monthly. Although it is a very rare condition, it must remain in the differential due its slowly progressive nature that can transition into a highly destructive disease without proper surveillance and treatment.

Keywords: *Churg Strauss syndrome, ANCA, vasculitis, granuloma, eosinophilia, asthma*

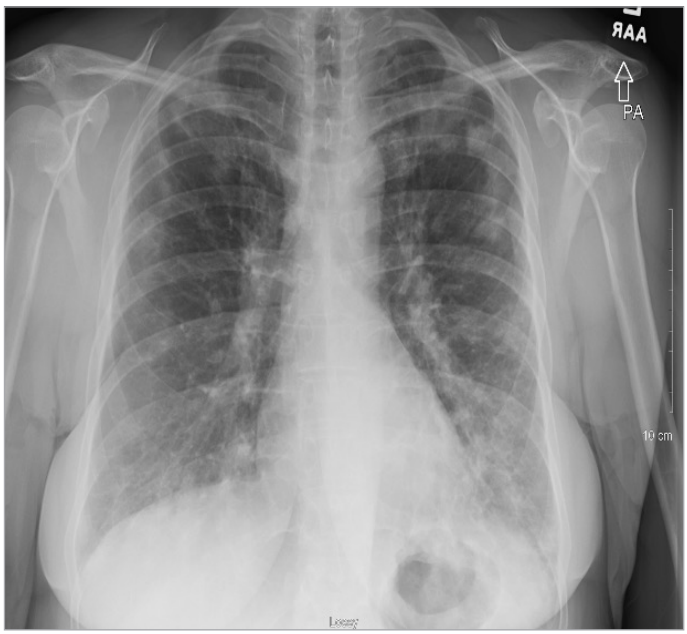

Figure 1. *Chest Radiograph showing diffuse irregular opacities throughout both lungs.*

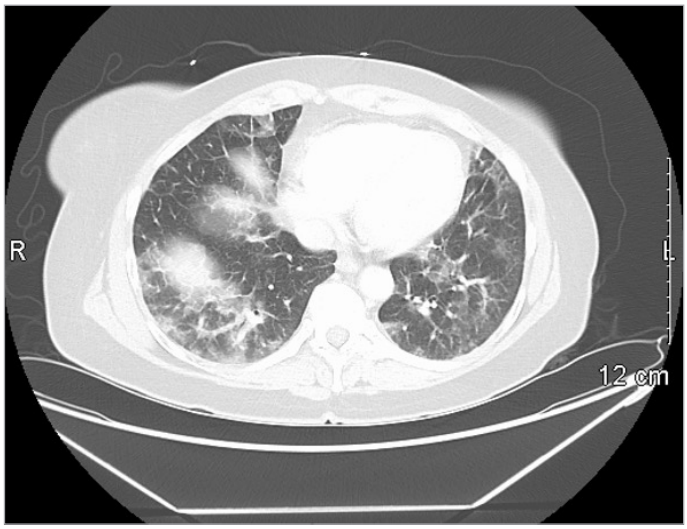

Figure 2. *Computed Tomography Of Chest showing ground glass opacities with multifocal ill-defined infiltrates in both lungs.*

[Abstract:1374]

ERDHEIM-CHESTER DISEASE: A DIAGNOSTIC CHALLENGE

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Erdheim-Chester disease is a rare entity that consists of non-Langerhans cell histiocytosis with multisystem involvement that frequently includes bone, heart, lungs, retroperitoneum and central nervous system, among others.

We present the case of a 56-year-old man who consulted for decreased libido, impotence, polyuria, polydipsia and intense nocturia. With pituitary MRI without alterations, negative

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antipituitary antibodies and compatible hormonal study, he was diagnosed with primary hypergonadotropic hypogonadism and diabetes insipidus. The treatment with intramuscular testosterone and nasal desmopressin had a good clinical and analytical response. Furthermore, he reported frequent pain in the jaws, knees and hips with non-specific MRI study. Next, he went to the Emergency Department due to acute abdomen, visualizing mesenteric panniculitis and signs of intestinal ischemia on abdominal-pelvic CT. An urgent laparotomy was performed that revealed peritoneal implants and polyadenopathy that were biopsied with a histological study without signs of malignancy or other alterations of interest. Therefore, a PET-CT was performed with suspicion of peritoneal carcinomatosis without evidence of a primary lesion, as well as probable diffuse spinal infiltration (scapular and pelvic girdles, both rib cages, humeral and femoral shafts) with bone metastasis in the left maxilla, spine (D12, L2) and pelvis. A biopsy of the left iliac blade was performed with an immunophenotype study compatible with infiltration due to histiocytosis (CD1a), allowing the final diagnosis of Erdheim-Chester disease to be made. Initially it was treated with IFN and, after confirming the BRAF V600E mutation, it was modified to vemurafenib with good response and evolution to date.

Keywords: *Erdheim-Chester disease, non-Langerhans cell histiocytosis, immunohistochemistry*

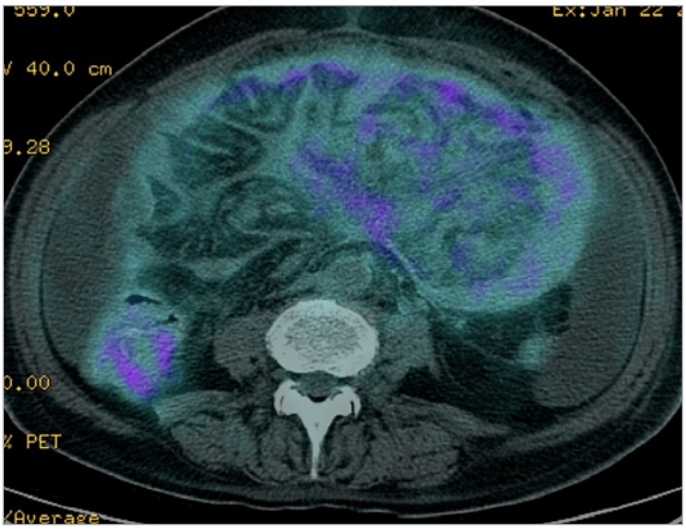

Figure 1. *Abdominal involvement by PET-CT in Erdheim-Chester disease.*
Histiocytic infiltration at the mesenteric and peritoneal level.

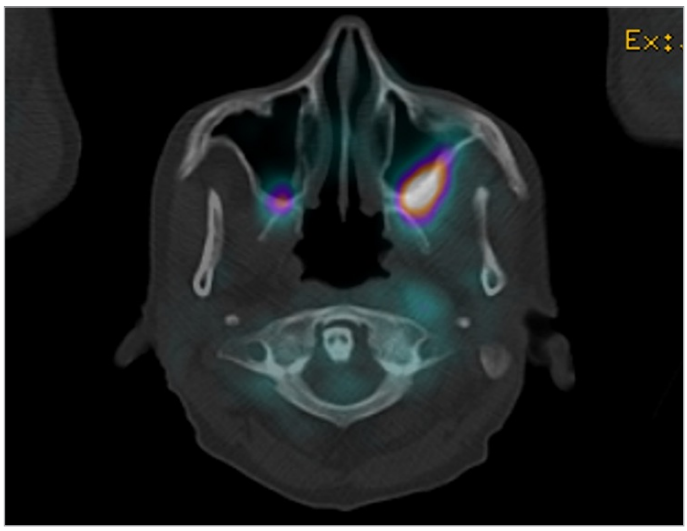

Figure 2. *Bone involvement by PET-CT in Erdheim-Chester disease. Histiocytic infiltration of the left maxilla; it was the affected area with the highest radiotracer uptake in PET-CT (SUVmax 9.8).*

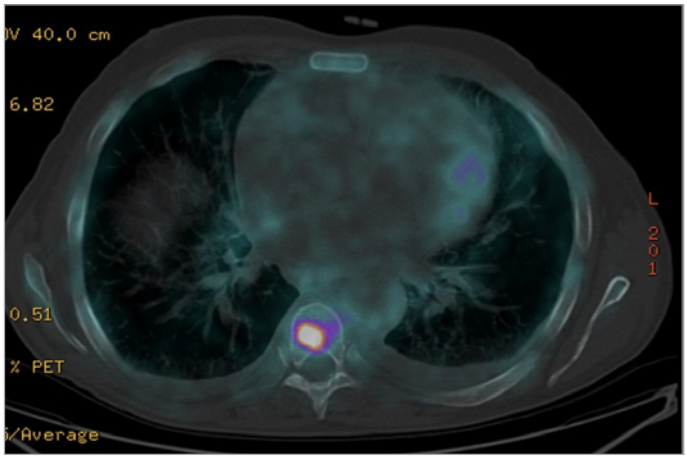

Figure 3. *Bone involvement by PET-CT in Erdheim-Chester disease (II). Histiocytic infiltration of the 12th dorsal vertebral body.*

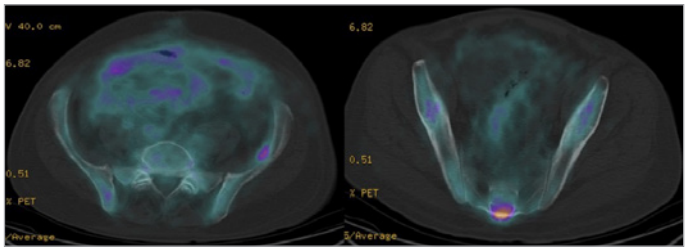

Figure 4. *Bone involvement by PET-CT in Erdheim-Chester disease (III). Spinal infiltration at pelvic girdle with bone metastasis in sacrum.*

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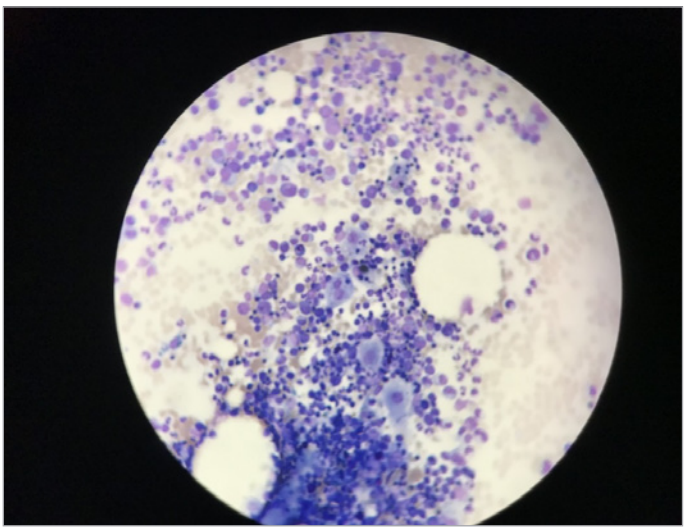

Figure 5. Microscopic findings in Erdheim-Chester disease. Infiltration is observed by large cells with the appearance of foamy histiocytes, sometimes spindle-shaped, and also macrophages with a reactive appearance. All morphological varieties have great phagocytic capacity; findings compatible with infiltration due to histiocytosis.

[Abstract:1389]

DESCRIPTION OF THE CLINICAL-EPIDEMIOLOGICAL CHARACTERISTICS OF PATIENTS DIAGNOSED WITH STILL'S DISEASE IN A THIRD LEVEL HOSPITAL

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Purpose: To describe the clinical-epidemiological characteristics of patients under follow-up for Still's disease in a tertiary hospital until 2023.

Methods: It is a retrospective descriptive case series that includes patients under follow-up in the Internal Medicine outpatient clinics of our centre between 1997 and May 2023 with a diagnosis of Still's disease. The data was obtained from the Clinical Documentation records, and from the digital history of the Andalusian Public Health System. The analysis was performed with IBM-SPSS®.

Findings: 14 patients were identified, of which 12 were women (85.7%). Their mean age was 43.57 years (range 14-74). 92.9% presented fever, the rest of the symptoms appear in Figure 1. 100% of the patients presented negative Rheumatoid Factor and Antinuclear Antibodies, as well as C3 and C4 complement proteins within normal limits, the rest of the values are shown in Figure 2. The complementary tests performed appear in Figure 3. 28.57% of the patients did not meet diagnostic criteria (Figure 4).

Conclusions: Adult Still's disease is an inflammatory disease of unknown aetiology, whose prevalence is estimated at 0.16-1 case per 100,000 adults. It is an underdiagnosed entity. Compared to the reviewed literature, the age of presentation is similar, with a slight predominance in women in our review. Fever, arthralgia, arthritis and rash are the most common symptoms. The diagnosis was established based on the doctor's criteria.

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Keywords: *Still's disease, fever, arthralgia, rash*

Symptoms	Percentage of patients who have presented the symptom			
Fever	92,9%			
Arthralgia	87,7%			
Arhritis	Monoarthritis	Oligoarthritis	Polyarthritis	Total
	7,1%	14,3%	28,6%	50%
Exanthema	Evanescent	Hives	Total	
	28,6%	57,1%	85,7%	
Lymphadenopathy	28,8%			
Hepatomegaly	21,4%			
Splenomegaly	21,4%			
Odynophagia	42,9%			
Abdominal pain	14,3%			
Pleutiris	14,3%			

Figure 1.

Analytical Parameter	Average	Range
Hemoglobin (g/dl)	12,21	6,4-14,5
Leukocytes (/l)	13.180	4500-30600
Neutrophils (/l)	11.700	4230-29000
Ferritin (ng/ml)	7.508,15	94-40.000
C Reactive Protein (mg/l)	134,78	14-373
Erythrocyte Sedimentation Rate (mm/h)	44,18	3-123

Figure 2.

Complementary Tests	Number of patients in whom it has been performed	Percentage
Chest x-ray	14	100%
Joint x-ray	3	21,4%
Erosion x-ray	2	14,3%
Transthoracic echocardiography	4	28,6%
Abdominal ultrasound	7	50%
TAC	12	88,4%
PET-TC	4	28,6%

Figure 3.

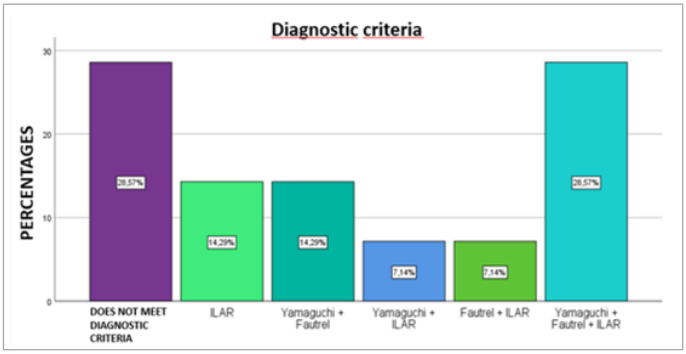

Figure 4.

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[Abstract:1391]

SLEROSING/INFLAMATORY DISEASE. RELATED WITH IGG4?

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The case involves a 56-year-old male, from Morocco, presenting odynophagia, bilateral submandibular lumps and a loss of 1.5 kg in the last month. Evaluation revealed hard, painful submandibular masses. Blood tests showed acute phase reactant elevation. Further investigation indicated suspected Mikulicz syndrome, with neck ultrasound and thoraco-abdominal CT showing inflammatory involvement of submandibular glands, ascending aorta and pericardial thickening, and doubtful alteration of pancreatic tail enhancement that could indicate a systemic inflammatory process. An immunoglobulin study, including IgG4, was in normal range except for an elevation of IgE. The autoimmunity profile was negative as well as the microbiological study. Due to suspicion of IgG4 disease, treatment was started with corticosteroids with clear improvement in symptoms.

While the study was being carried on, the patient returned twice with chest pain, syncope, and pericardial effusion. Pericardiocentesis and pericardiectomy were performed. Recurrences led to rituximab and mycophenolate combination therapy. Pericardial and submaxilar biopsies results showed non-IgG4-related inflammation.

After two months of treatment, the patient maintains low doses of corticosteroids, mycophenolate at a dose of 2 g daily and remains asymptomatic

Despite not meeting the ACR/EULAR 2019 classifying criteria for IgG4 disease, this pathology is very heterogeneous and these criteria are not intended for diagnosis in clinical practice. Therefore, when there is a clinical diagnosis, the fact of not meeting them should not prevent starting the most appropriate treatment as was done in this case, in order to avoid progression and evolution to fibrosis and its associated comorbidity.

Keywords: *IgG4, Pericarditis, sialoadenitis*

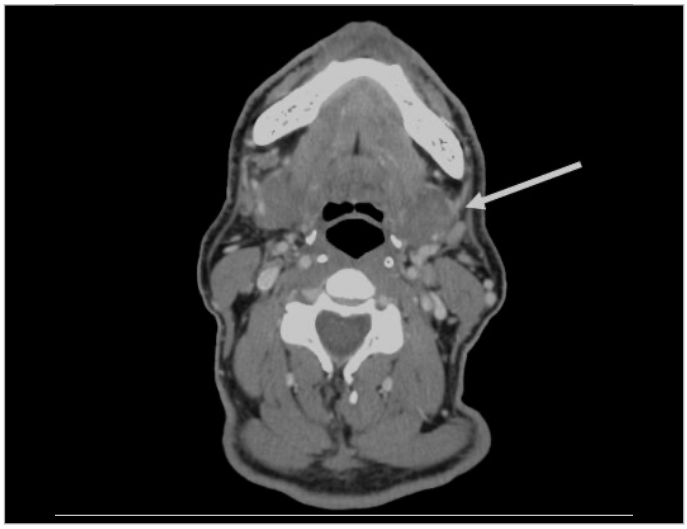

Figure 1. *Contrast-enhanced CT scan of the neck showing moderate diffuse enlargement of both submandibular glands without evidence of collections.*

[Abstract:1392]

RARE OR NOT RARE: THE NEED FOR A HOLISTIC APPROACH

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We present the case of a 72-year-old male, with a two year history of obstructive jaundice caused by increased common bile duct's wall thickness, requiring the placement of a metallic prosthesis. Multiple biopsies were negative for malignancies. A follow-up CT scan showed diffuse lymphadenopathies, and kidneys' hypertrophy with a poor cortico-medullary differentiation, both confirmed at PET. An axillary lymph node biopsy was then performed, showing a reactive lymphadenitis with plasmacytosis. Several diagnostic tests were performed to evaluate possible lymphoproliferative disease versus Castleman disease; noteworthy, we found complement consumption, elevated serum IgG and IgG4 and persistent altered liver function.

First, we performed a kidney biopsy whose result was not diriment. Considering the altered liver function, we then performed a liver biopsy showing destructive lesions of the biliary tract and focal periductal fibrosis with an inflammatory and plasmacellular IgG4 component markedly above the norm, creating a picture highly compatible with a secondary sclerosing cholangitis (SSC) IgG4-related. A cholangio-MRI was repeated, showing a dilation of the intrahepatic bile ducts and the common bile duct,

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shranking abruptly at the papilla needing endoscopic ballooning. Furthermore, a salivary gland ultrasound showed involvement of the glands.
Considering the typical organ involvement despite a non-definitive histopathology we supposed a diagnosis of IgG4 related disease with SSC and started steroid therapy first, followed by rituximab, with regression of symptoms, normalization of liver and kidney function.
IgG4-RD is a complex condition, with intrinsically deceptive nature, whose picture can be clearly interpreted only by looking at it in a holistically way.

Keywords: *IgG4 Related disease, secondary clerosing cholangitis, Castleman disease*

[Abstract:1394]

IGG4-RELATED INFLAMMATORY PSEUDOTUMOR OF LIVER: THE IMPORTANCE OF DIFFERENTIATING FROM MALIGNANT HEPATIC TUMORS

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Purpose: Inflammatory Pseudotumor (IPT) of the liver is a rare and benign lesion often misdiagnosed as a malignancy such as hepatocellular carcinoma; thus, it can be considered as a diagnosis when IgG4 is positive.
Case Description: A 43-year-old woman presented with progressive right upper quadrant pain with elevated CRP, negative procalcitonin and high sedimentation rate. Liver function tests were within normal ranges except low albumin. Ultrasound imaging mimicked malignant lesion of the liver; yet tumour markers were negative. Advanced imaging reported probable indication as a liver abscess. Percutaneous drainage catheter collected purulent aspirate that microbiology culture resulted in no growth and microorganism antibody assays were negative. Metronidazole was administered and CRP levels dropped. Pathology of liver biopsy reported dense inflammatory reaction with fibrosis and focal IgG4(+) plasma cells and a pathologic diagnosis as IPT.
Discussion: Inflammatory pseudotumors have favourable prognosis with spontaneous regression, remission with antibiotics, or recovery after complete resection. Some IPTs were associated with IgG4-related sclerosing disease, while others were reported to have microorganisms as the cause. Combination of accurate radiologic assessment and histological pathology showing fibrosis, foamy histiocytes, and plasma cells can effectively lead to correct diagnosis and proper treatment of IPT.

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Keywords: *inflammatory pseudotumor, liver abscess, IgG4*

[Abstract:1411]

A RARE CAUSE OF LUNG PSEUDOTUMOR

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We report the case of a 50-years old woman admitted to our ward for septic shock. She had a history of neonatal cognitive impairment, treated breast infiltrating ductal carcinoma, with negative follow-up and a recently diagnosed diffuse mass at the left lung with infiltration of the mediastinum, homolateral paravertebral muscles, vertebrae and ribs. She had undergone several biopsies that showed an inflammatory infiltrate with no sign of malignancies. All infective and autoimmunity screening tests resulted negative.
At admission she was treated with crystalloids, amines, and broad-spectrum antibiotic therapy (piperacillin/tazobactam plus vancomycin) with no sign of clinical improvement. Blood and urine cultures were negative. A chest CT scan showed a superinfection of the lung mass with multiple abscesses. Urgent thoracoscopy with abscesses drainage and pleural surgical toileting was performed with significant clinical improvement in the next days.
Pleural fluid culture resulted positive for penicillin susceptible Actinomyces spp and *Streptomyces griseus*. Antiobiotic therapy was de-escalated to iv ampicillin and then to oral amoxicillin after clinical improvement.
The patient was discharged with indication to long course antibiotic treatment (12-16 months) and ambulatory follow up. After 4 months she was in good clinical conditions and the CT scan showed a significant reduction of the lung mass at all sites of infiltration.
Invasive actinomycosis is a rare subacute to chronic infection that can simulate a tumour, usually involving the oral cavity, the gastrointestinal or genitourinary tract, rarely the lungs. It is crucial to diagnose it early because the prognosis correlates with the timeliness of treatment.

Keywords: *lung pseudotumor, invasive actinomycosis, lung abscesses*

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[Abstract:1470]

BRANCHIO-OTO-RENAL SYNDROME: A CASE REPORT

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Branchio-oto-renal syndrome (BORS) is a rare autosomal dominant disorder which includes ear malformations accompanied by hearing loss, branchial fistula and cysts in the neck and renal malformations. A 21-year-old female patient with right renal agenesis with a baseline creatinine level of 1.0 mg/dL was hospitalized with acute kidney injury (AKI). Her blood pressure was 140/90 mmHg, and no pathological finding was found except bilateral pretibial edema and high blood pressure. In her biochemistry, serum creatinine level was 1.6 mg/dL (reference: 0.5-1.1 mg/dL), albumin was 3.1 g/dL (reference: 3.2-4.8 g/dL), 4+ protein was observed in the urinalysis, and UP/CR was found 3000 mg/g (reference:<200 mg/g). Renal Ultrasound (USG) demonstrated her right kidney was congenitally agenetic and the left kidney dimensions were increased compensatorily (145x80x40 mm). When her anamnesis was detailed, it was learned that she had a branchial fistula operation in her childhood, detailed physical examination revealed an operation scar in the left cervical region (Figure 1A) and a fistula in the left preauricular region (Figure 1B). Temporal bone CT (Computed Tomography) scan revealed dysplasia in bilateral middle ear ossicles and hypoplasia in bilateral semicircular canals. It was learned that her father, uncle and aunts also had hearing loss and branchial cysts. There is also mixed type hearing loss detected in the patient's hearing test. Renal biopsy result was compatible with tubulointerstitial nephritis and focal segmental glomerulosclerosis. We aimed to show the importance of screening family members and to emphasize in which cases BORS should be considered.

Keywords: *branchio-oto-renal syndrome, BORS, acute kidney injury, AKI*

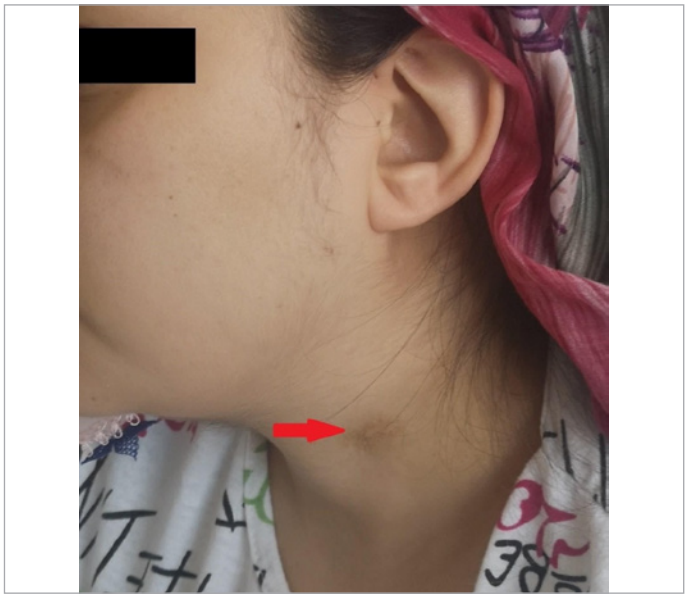

Figure 1A. *Operation scar in the left cervical region(arrow).*

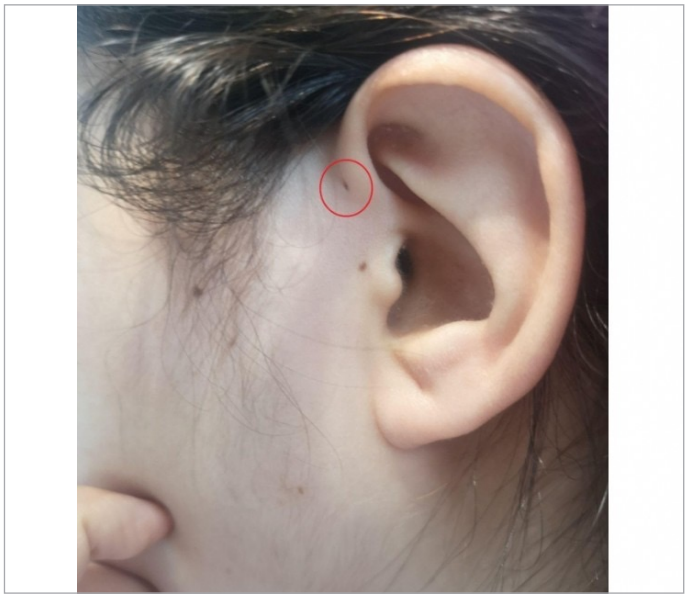

Figure 1B. *Fistula in the left preauricular region(circle).*

[Abstract:1484]

HYPERCALCEMIA AS A PRESENTATION OF DISSEMINATED BCG INFECTION

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An 80-year-old man was admitted to Internal Medicine unit because of abdominal pain, vomiting and exertional dyspnoea. He reported involuntary weight loss and asthenia in the last six months. His past medical history included multiple relapses of low-grade non-invasive bladder urothelial carcinoma treated with transurethral resection and Bacillus Calmette-Guerin (BCG)

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instillations. At admission, blood tests showed hypercalcaemia with low PTH and a slight increase of cholestatic markers.
He did not take any medication known to cause hypercalcaemia and paraneoplastic hypercalcaemia was ruled out after extensive tests. A possible granulomatous disease was then considered. For persistence of increased cholestasis indices and evidence of hepatomegaly we performed a liver biopsy which showed granulomatous hepatitis.
Considering the history of intravesical instillation of BCG, disseminated BCG infection vs. idiopathic systemic granulomatous reaction was suspected. QuantiFERON tuberculosis, DNA and microscopic analysis for M. tuberculosis and nontuberculous mycobacteria on liver sample resulted negative while mycobacterial tests (microscopic and polymerase chain reaction, PCR) on urine resulted positive. Steroid therapy was started, and the patient was discharged with close follow-up.
Two months later the patient developed fever and increased inflammatory indices. A CT scan showed new onset ground-glass lung infiltrates. BCG detection and PCR on sputum gave positive results. Thus, specific therapy with isoniazid, rifampicin and ethambutol was started.
Although BCG instillation is generally safe, disseminated *M. bovis* disease is a rare and serious adverse reaction that can occur following intravesical BCG therapy so that a high index of suspicion is required.

Keywords: *hypercalcemia, Bacillus Calmette-Guerin, disseminated M. bovis disease, granulomatous hepatitis*

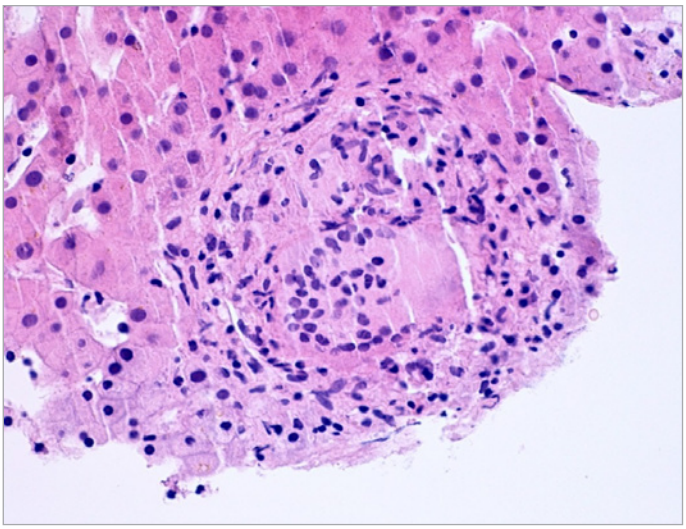

Figure 1. *Granulomatous hepatitis with noncaseating granuloma.*

[Abstract:1487]

SUDOSCAN AS A PREDICTOR TOOL OF DISAUTONOMY IN ATTRV

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Patients with hereditary transthyretin amyloidosis (ATTRv), especially Val50Met mutation, have small fibre dysfunction with disautonomy. Sudoscan is a non-invasive test measuring the sudomotor function in palms/plants, providing electrochemical skin conductance (ESC). It's used in many diseases with disautonomy. Analyse Sudoscan for the diagnosis of disautonomy in patients with ATTRv, and correlation with Compass-31 and Norfolk questionnaires.
A retrospective study with patients ATTRv (Val50Met) and asymptomatic carriers. Autonomic dysfunction described as: postural hypotension, nausea/vomiting, diarrhoea, sphincter abnormalities, sexual dysfunction. The last Sudoscan measure (palms/plants) and Compass-31 questionnaire were collected. Validity of Sudoscan measured with ROC curve. Optimal cut-off point measured by Youden Index. Simple correlation model between results from Sudoscan and Compass-31/Norfolk questionnaires.
Total 164 individuals; 107 asymptomatic carriers. 85 women. Mean age of 52. 49 disautonomy. 8 patients with disautonomy were carriers of Val50Met mutation without ATTRv. 12 were diabetic; 6 of them were Val50Met carriers and none of which had disautonomy. The other 6 had ATTRv and 5 with disautonomy. The results of Sudoscan show in disautonomy lower results ($p>0.05$). The area under the curve (AUC) was of 0.85 (IC 0.78-0.92) in plants and AUC of 0.73 (IC 0.63-0.82) in palms. The optimal cut-off point was 71 plants / 69 palms, similar to the literature. Correlation between Compass-31 and Sudoscan was weak, (R-squared 0.17 plants / 0.20 palms). Higer between Norfolk and Sudoscan (0.42 plants / 0.71 palms).
Sudoscan is a useful tool for the diagnosis of disautonomy in ATTRv Val50Met. The correlation with Compass-31 and Norfolk was weak.

Keywords: *ATTRV, Val50Met, disautonomy, sudoscan, small fibre dysfunction*

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[Abstract:1489]

ASSOCIATION OF DIABETIC KETOACIDOSIS, PERIORBITAL CELLULITIS AND CEREBROVASCULAR EVENT IN A LIVER TRANSPLANT PATIENT

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A case of a fifty-two-year-old liver-transplanted male patient presenting with diabetic ketoacidosis and periorbital cellulitis in the left eye is reported. Acute diffusion restriction was observed in the imaging performed in the case with neurological changes. Anticoagulant treatment was started. Multiple antibiotics and antifungal treatments were started in the early period. Because diabetic ketoacidosis had an acute onset, and the patient was receiving immunosuppressant treatment. The blood glucose of the patient was regulated by insulin therapy. Since fungal infections are considered in the differential diagnosis in immunosuppressed patients, the added amphotericin b is thought to have a major contribution to reducing mortality. In addition, the patients taking the calcineurin inhibitors should be aware of the possibility of a hyperglycaemic crisis, which occurs as a sudden onset of diabetic ketoacidosis. In our case, we want to question the use of drugs in the diabetic ketoacidosis clinic and show the contribution of supporting periorbital cellulitis with systemic antibiotherapy and antifungal therapy to the progression in immunosuppressed patients.

Keywords: *diabetic ketoacidosis, periorbital cellulitis, liver transplant, tacrolimus*

Figure 1. *Before therapy.*

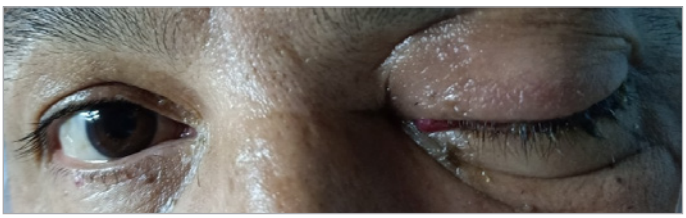

Figure 2. *After therapy.*

[Abstract:1497]

A SINGULAR FORM OF SYSTEMIC SARCOIDOSIS: A CASE REPORT

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Involvement of the central nervous system during the course of sarcoidosis is rare. Medullary neurosarcoidosis (MNS) is considered rare, and it's exceptional for it to be inaugural, or for it to occur in isolation without associated cerebral involvement. We report one case.

A 65years-old female was admitted to our clinic on suspicion of systemic granulomatosis, following the onset of neurological disorder consisting of paresis and paresthesia of all limbs, progressing gradually over the past year, associated with bilateral mediastinal lymph-nodes.

On clinical examination, she presented with posterior cord syndrome, pyramidal syndrome predominantly in the right hemicorpus, superficial sensitivity disorders, and anal-urinary sphincter disorders.

Biological tests revealed hypercalciuria (613 mg/l), hyperphosphatiuria (1444.5 mg/24h) and normal calcaemia. Serum lysozyme was elevated (11.7 mg/l). Onco-neuronal tests, autoimmunity tests (FAN, ANCA, anti-NMO, anti-MOG). The alveolobronchial fluid showed non-specific inflammatory fluid. Cerebral-medullary MRI revealed medullary hypersignal with the appearance of large medulla and the presence of a nodular lesion opposite C5-C6. Thoracoabdomino-pelvic CT revealed bilateral non-compressive mediastinal adenomegalic, lung parenchymal nodules.

In accordance with the 2018 consensus diagnostic criteria for neurosarcoidosis, the diagnosis of MNS associated with systemic involvement were made. She was started on corticosteroids bolus and cyclophosphamide. After 3 months of treatment, we noted an improvement in the neurological deficit and bladder sphincter disorders.

NSM is rare, even exceptional if it's not accompanied by cerebral involvement. It's difficult to diagnose, especially when it first appears clinically. It's an inflammatory myelopathy that can be potentially disabling, but which may be reversible if diagnosed and treated in time.

Keywords: *medullary neurosarcoidosis, inaugural manifestation, without cerebral involvement, difficult to diagnose, disabling myopathy*

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[Abstract:1498]

TRANSPLANTATION IN HYPER-IGM SYNDROME IN ADULT PATIENTS, OUR EXPERIENCE

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Introduction: Hyper IgM syndromes present with normal or elevated levels of IgM and low levels or absence of IgG, IgA and IgE.

Case 1: Male, 22 years old. History of multiple infections at different levels and some with need of intensive care. It was decided to be included in the list of liver transplants in 2019. haematology was consulted on the possibility of performing HCT but it was ruled out due to severe liver involvement. Liver graft is performed in January 2020. In May 2020, the patient was admitted for CMV infection with gastrointestinal and hepatic involvement. Also found infection by Entamoeba. The HCT is again valued but the patient progressively deteriorates and finally dies at the age of 25.

Case 2: Male, 18 years old. History of multiple infections at different levels, is carrier of CMV and HBV and has developed sclerosing cholangitis. In conjunction with Infectious diseases and haematology we decided to add nitazoxamide prophylaxis until the HCT. There was a reactivation of Cryptosporidium despite prophylaxis which was successfully treated by doubling doses of nitazoxamide. After a month of hospitalization, the patient was discharged, during the following months the liver function was normalized and treatment was progressively reduced until he left follow-up a year later.

Conclusions: HCT in the early years of life is curative. Once the patient reaches advanced hepatopathy, transplant options are complicated. The best results are achieved by performing HCT at the same time as the liver transplant or with little delay of the latter.

Keywords: hyper IgM syndrome, nitazoxamide, cryptosporidium

[Abstract:1507]

DYSAUTONOMIA IN EHLERS-DANLOS: INQUIRING DYSFUNCTION AND ITS IMPACT ON QUALITY OF LIFE AMONG DIFFERENT FORMS OF DISEASE

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Summary: Ehlers-Danlos syndrome (EDS) is a group of heritable connective tissue disorders resulting from impaired collagen formation. Besides joint hypermobility and tissue fragility, chronic pain and multisystemic autonomic dysfunction are major symptoms in EDS; furthermore, patients experience higher rates of depressive symptoms, anxiety, and sleep disturbances compared to healthy controls. Variability in clinical features permits distinguishing 13 different forms of EDS; however, autonomic profile characterization of specific disease subsets is still lacking.

Purpose: To compare dysautonomic alterations among different EDS subtypes and to investigate their impact on anxiety and sleep quality.

Methods: 17 patients with hypermobile EDS, classical form, or hypermobility spectrum disorder (HSD) were consequently enrolled in our EDS clinic (Policlinico Hospital, Milan) in a cross-sectional analysis (Table 1). They completed surveys about dysautonomia, sleep quality, and anxiety. We performed one-way ANOVA to compare scores from EDS subtypes, and Spearman correlation to investigate relationships between dysautonomia, sleep quality, and anxiety.

Findings: Between HSD and hypermobile EDS, overall dysautonomia scores were significantly different ($p<0.05$) along with gastrointestinal and bladder dysfunction sub-scores (both $p<0.05$). A positive significant correlation was found between dysautonomia and sleep disturbances scores ($\rho=0.652$, $p=0.005$) and between dysautonomia and anxiety ($\rho=0.629$, $p=0.0193$). No other significant difference or correlation was observed.

Conclusions: Hypermobile EDS patients present higher grades of dysautonomia compared to HSD forms; moreover, dysautonomia correlates to worse sleep and greater anxiety symptoms. Further research is required to deeply assess differences in autonomic profiles of different EDS subtypes, possibly contributing to better disease management.

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Keywords: *Ehlers-Danlos, dysautonomia, quality-of-life*

	Number of patients	Age – yo (median; RIQ)	Female (number; %)
Hypermobile EDS	7	34; 28-45	7; 100%
Classical EDS	5	33; 26-51	4; 80%
HSD	5	38; 28-39	3; 60%

Table 1. *Characteristics of the patients [yo = years old; RIQ = range interquartile].*

[Abstract:1557]

FAHR'S DISEASE: A CASE REPORT

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Case Presentation: A 56-year-old man with a history of type 1 diabetes mellitus arrived to the emergency department with a chief complaint of dizziness for the previous months, which had progressively worsened. The patient reported inability to walk.

Neurological examination revealed an ataxic gait, being otherwise unremarkable. A cranial computerized tomography (CT) scan showed bilateral and symmetrical calcifications in both dentate nuclei of the cerebellum, millimetric foci of calcification in both globus pallidus and lacunar infarcts (figure 1).

A complete blood test showed calcium 9.3 mg/dL, free calcium 0.94 mmol/L, 24-hour urine calcium 161 mg/24 h, parathormone 57 ng/L and phosphate 3.1 mg/dL. A complete autoimmunity panel, tumour markers, proteinogram and peripheral blood smear were also normal. The diagnosis of Fahr's disease was thus reached. A genetic test was ordered and showed no alterations.

Treatment with levodopa and carbidopa was started, showing clinical improvement.

Discussion: Fahr's disease is a rare disease with a prevalence of 1 case per 100,000 population1. It follows an autosomal dominant pattern of inheritance with incomplete penetrance. Clinical manifestations begin between fifth and sixth decade, including gait disturbances, dystonia, asthenia, dizziness, neuropsychiatric disturbances, tetany and epileptic seizures1.

On cranial CT, calcifications of the basal ganglia are seen. Endocrinopathies, mitochondrial diseases, autoimmune diseases, infections, toxins or trauma must be excluded1. There is no curative treatment.

References:

1. Saleem S, Aslam HM, Anwar M, Anwar S, Saleem M, Saleem A, et al. Fahr's syndrome: literature review of current evidence. Orphanet J Rare Dis. 2013;8(1):1-9.

Keywords: *Fahr disease, calcification, rare diseases*

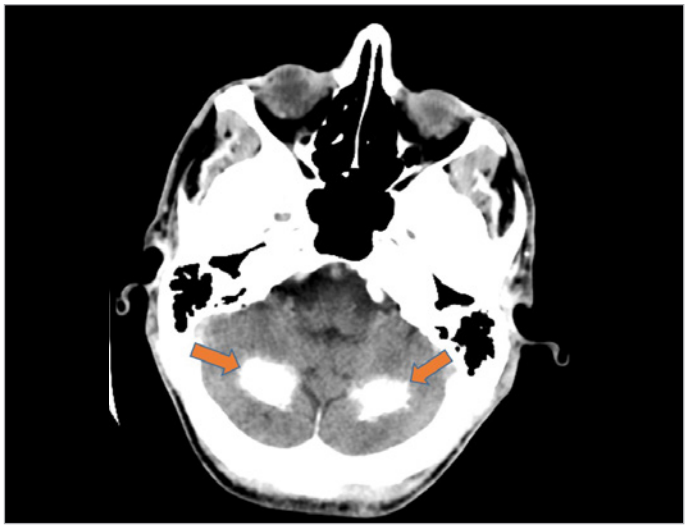

Figure 1. *Bilateral and symmetrical calcifications in the dentate nuclei of the cerebellum (arrows).*

[Abstract:1561]

A RHABDOMYOLYSIS WITH A SURPRISE

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We present the case of a 35-year-old male from China who has been living in Spain for 17 years. Personal history of tuberculous pleuritis and episodes of intense myalgias since childhood related to prolonged fasting and physical exercise that were self-limited by resting. Also, episode of rhabdomyolysis during admission for tuberculous pleuritis at 26 years of age and new episode at 29 years of age after intense exercise.

He was admitted to Internal Medicine for severe acute renal failure secondary to rhabdomyolysis in the context of asymptomatic SARS-CoV-2 infection. During admission, he presented an episode of dyspnoea associated with oligoanuria. A chest X-ray was requested, showing a predominantly central alveolar infiltrate compatible with acute pulmonary oedema. For this reason transthoracic echocardiography was requested, showing severely depressed systolic dysfunction probably secondary to myocarditis. Otherwise, blood test showed an elevation of creatinine levels (9.18 mg/dL) and creatine kinase (110054 U/L).

He was admitted to intensive care and treatment was started with steroids and hemodialysis/ultrafiltration sessions due to persistent oligoanuria. The clinical and analytical evolution was favourable with recovery of the ejection fraction and renal

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function. A metabolic myopathy was suspected so a complete autoimmune study was requested, which was negative. In addition, a muscle biopsy and a genetic study were requested, which confirmed the diagnosis by identifying a pathogenic variant in the CPT2:c.1148T>A;p.(Phe383Tyr) gene, and the patient was discharged with the diagnosis of carnitine palmitoyltransferase II deficiency expressed in its myopathic form and myocarditis secondary to SARS-CoV-2 viral infection.

Keywords: *myopathy, rhabdomyolysis, myocarditis*

[Abstract:1574]

STUDY OF NEW PROGNOSTIC PARAMETERS IN PULMONARY HYPERTENSION (I): RELATIONSHIP BETWEEN SST2 AND CA-125 WITH RESPECT TO NT-PROBNP, FUNCTIONAL CLASS (NYHA) AND DISTANCE TRAVELLED IN THE TM6M

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Objectives: To investigate the relationship between sST2 and CA-125 and the values of NT-proBNP, functional class (NYHA) and distance travelled in the TM6M.

Materials and Methods: Prospective cohort study approved by the research ethics committee. Group of patients with PH (n=48), clinically stable at baseline assessment versus a control group composed of patients with cardiac and pulmonary disease without PH (n=23). At baseline, clinical assessment, echocardiography and serum NT-ProBNP, sST2 and CA-125 were performed. Correlations were performed using Spearman correlations.

Results: When evaluating the totality of individuals studied, a statistically significant correlation was detected between the serum concentration of the three biomarkers with respect to functional class (NYHA) (table 1). There was a statistically and inversely significant correlation between serum NT-proBNP, sST2 and CA-125 concentration and distance travelled in metres in the TM6M (NT-proBNP, r=-0.440, p=0.002; sST2, r=-0.460, p=0.001; CA-125, r=-0.394, p=0.006).

Discussion: Our study analysed the relationships between the concentrations of the three biomarkers and classical prognostic risk parameters in patients with pulmonary hypertension (PH) such as NYHA dyspnoea and exercise breathing capacity using the 6-minute walk test. Both biomarkers correlated with the classical parameters in a statistically significant manner.

Conclusions: In summary, we can consider that, in addition to the classic parameters such as NT-proBNP or TM6M, new serum biomarkers such as sST2 and CA-125 could be useful tools in the follow-up and prognostic estimation of patients with PH, complementary to the other studies recommended by clinical practice guidelines.

Keywords: *pulmonary, hypertension, biomarkers, prognosis*

-	NT pro BNP	p	sSt2 (ng/ml)	p	CA-125 (U/ml)	p
NYHA	-	-	-	-	-	-
I o II (n=27)	282 (91-492)	0.001	24 (19-40)	< 0.001	12 (9-19)	0.002
III o IV (n=21)	1746 (732-5968)	0.001	50 (36-89)	< 0.001	24 (15-76)	0.002

Table 1.

[Abstract:1578]

STUDY OF NEW PROGNOSTIC PARAMETERS IN PULMONARY HYPERTENSION (II): TO EVALUATE THE CORRELATION BETWEEN SERUM LEVELS OF TSS2 AND CA-125 AND ECHOCARDIOGRAPHIC PARAMETERS OF RIGHT VENTRICULAR FUNCTION

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Internal Medicine, Hospital Universitario de Jerez, Servicio Andaluz de Salud, Jerez de la Frontera, Spain

Objectives: To assess the correlation between serum sST2 and CA-125 levels and echocardiographic parameters of right ventricular function in the field of pulmonary hypertension.

Materials and Methods: Prospective cohort study approved by the research ethics committee. A group of patients with PH (n=48), clinically stable at baseline assessment versus a control group consisting of patients with cardiac and pulmonary disease without PH (n=23). At baseline, clinical evaluation, echocardiography and determination of serum NT-ProBNP, sST2 and CA-125 levels were performed. Correlations were performed by Spearman correlations.

Results: In table 1.

Discussion: Our study analysed the relationships between the concentrations of the three biomarkers and the echocardiographic parameters of the total sample. NT-proBNP, a classic marker in the clinical follow-up of HF and PH, showed statistically significant correlations with all parameters measured by echocardiography, both those estimating pulmonary pressures (PAPS, PAPm, TRPV) and those reflecting RV function (TAPSE, DTI, DTDVD, PAAT, VAC); correlations that were overwhelmingly also observed with serum concentrations of both sST2 and CA-125, supporting the value of these two biomarkers.

Conclusions: In summary, we can consider that, in addition to the classic values of PAPS, TRPV or NT-proBNP, new echocardiographic parameters such as PAAT, TAPSE or VAC and serum biomarkers such as sST2 and CA-125 are useful tools in the prognosis of PH, complementary to the other studies recommended by clinical practice guidelines.

Keywords: *hypertension, pulmonary, prognosis, echocardiography, ventricle*

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Ecographic variables	NT-proBNP (pg/ml)	NT-proBNP (pg/ml)	sSt2 (ng/ml)	sSt2 (ng/ml)	CA-125 (U/ml)	CA-125 (U/ml)
-	r	P	r	P	r	P
systolic pulmonary artery pressure (PAPS) (mmHg)	0.712	<0.001	0.241	0.047	0.446	<0.001
mean pulmonary arterial pressure. (PAPm)	0.643	<0.001	0.394	0.017	0.330	0.049
tricuspid regurgitation velocity (VRT) (m/seg)	0.635	<0.001	0.186	0.120	0.324	0.006
right atrium area (cm2)	0.645	<0.001	0.326	0.007	0.443	<0.001
displacement systolic displacement of the tricuspid annulus plane (TAPSE) (mm)	-0.608	<0.001	-0.330	0.006	-0.424	<0.001
TDI-S: tricuspid systolic wave by tissue Doppler. (cm/seg)	-0.433	<0.001	-0.009	0.947	-0.388	0.002
right ventricular end-diastolic diameter. DTDVD (mm)	0.562	<0.001	0.296	0.016	0.363	0.003
PAAT: pulmonary artery acceleration time. (milliseconds.)	-0.754	<0.001	-0.339	0.021	-0.440	0.002
VAC: ventricle-arterial coupling. (mm/mmHg)	-0.794	<0.001	-0.329	0.007	-0.516	<0.001

Table 1.

[Abstract:1580]

NEW PROGNOSTIC PARAMETERS IN PULMONARY HYPERTENSION III. RISK OF HOSPITALISATION AND/OR DEATH AT 12 MONTHS

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Objectives: To analyse the prognostic value of echocardiographic parameters, sST2 and CA-125 in patients with pulmonary hypertension, considering as end-point the combined variable of admission for heart failure and/or death.

Materials and Methods: Prospective cohort study of patients with PH (n=48), stable at baseline assessment. At baseline clinical and echocardiographic assessment and serum NT-ProBNP, sST2 and CA-125 determination were performed. They were followed for 12 months, recording the number of admissions and/or death as a consequence of PH, performing a bivariate analysis of the parameters associated with them. Variables significantly associated with admission/death were entered into a multivariate analysis using Cox logistic regression, where time was considered as the period from inclusion to first hospital admission, exitus or end of follow-up. Variables associated with hospital admission or survival were categorised according to the values recommended by the European Society of Cardiology and European Respiratory Society Guidelines or the median in the case series. Survival curves were determined using the Kaplan-Meier method.

Results: (Table 1).

Discussion: In the bivariate analysis the variables associated with hospitalisation and/or death were NYHA, TM6M, PAPS, RAA, TAPSE, DTDVD, VAC and levels of NT-proBNP, sST2 and CA-125. Finally, the most convincing model was the one including NT-proBNP, TM6M, sST2 and TAPSE (Figure 1).

Conclusions: Both clinical (TM6M) and functional echocardiographic (TAPSE) and biochemical (NT-proBNP and sST2) parameters independently predict the evolution of patients with pulmonary hypertension, understood as a higher incidence of hospitalisations due to decompensation of heart failure or death.

Keywords: *hypertension, pulmonary, hospitalisation, parameters, prognosis*

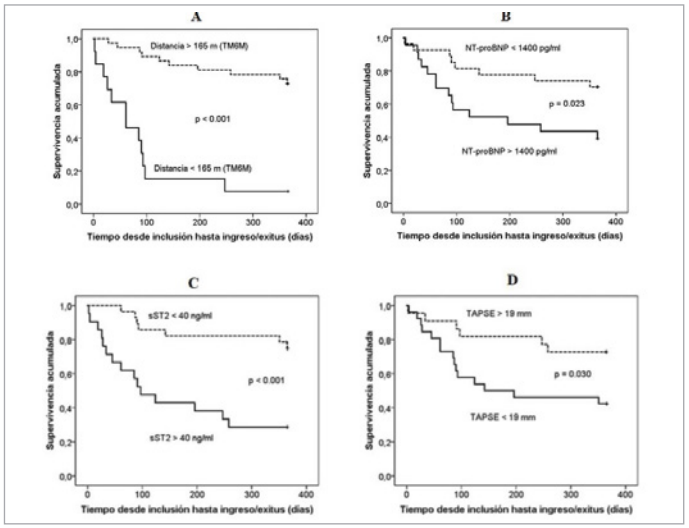

Figure 1. Survival curves.

CLINICAL FEATURES	No admission or death (n=26)	≥ 1 admission and/or death (n=22)	p
age (years)	68 (60-74)	72 (62-78)	0.379
Sex, male (n, %)	10 (39)	6 (27)	0.542
NYHA > 3 (n, %)	3 (12)	18 (82)	<0.001
TM6M (metres)	490 (350-550)	125 (50-325)	<0.001
ECOGRAPHIC VARIABLES	-	-	-
left ventricular ejection fraction (%) FEVI	63 (58-66)	65 (62-69)	0.159
PAPS (mmHg) systolic pulmonary artery pressure.	46 (40-57)	65 (54-79)	0.003
VRT (m/seg). tricuspid regurgitation velocity.	3.1 (3.0-3.5)	3.5 (3.0-3.8)	0.798
Area AD (cm2). area of the right atrium.	20 (18-24)	26 (22-29)	0.008
TAPSE (mm). tricuspid annulus plane systolic displacement.	22 (17-24)	18 (13-22)	0.009
S-DTI (cm/seg). tricuspid tricuspid systolic wave by tissue Doppler.	11 (10-13)	11 (10-13)	0.810
DTDVD (mm). right ventricular end-diastolic diameter.	45 (40-47)	50 (44-53)	0.019
PAAT (ms). pulmonary artery acceleration time.	78 (69-100)	72 (62-93)	0.408
VAC (mm/mmHg). ventricle-arterial coupling.	0.45 (0.34-0.61)	0.25 (0.18 - 0.37)	0.002
ANALYTICAL CHARACTERISTICS	-	-	-
glomerular filtrate (ml/min)	69(36-85)	57 (39-84)	0.596
NT-proBNP (pg/ml)	361 (192-1680)	1514 (813 - 6039)	0.005
sSt2 (ng/ml)	25 (18-40)	58 (37-92)	<0.001
CA-125 (U/ml)	14 (10-20)	29 (15-79)	0.006

Table 1.

[Abstract:1645]

LOCALIZED INTRAVASCULAR COAGULATION AS A COMPLICATION OF VENOUS MALFORMATION: A CASE REPORT

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Case Presentation: A 29-year-old woman with exercise-induced right hip pain dating back to 1997 underwent a magnetic resonance imaging (MRI). It revealed a fibroadipose vascular anomaly (FAVA) affecting her right gluteus and the sciatic nerve

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and causing secondary lymphedema. Surgery was conducted, but her pain only worsened, which prompted consultation.

During the initial assessment, she described constant pain in the buttock, groin and hip, that intensified when standing, curtailing physical activity and proving unresponsive to analgesics. Physical examination indicated subtle hip asymmetry and changes in soft tissue density.

A lower limb MRI confirmed persistence of the venous vascular anomaly with muscular involvement, affecting the right supraacetabular bone and neural iliotibial tract, with an increase in size compared to the preoperative study. Blood tests revealed an elevated D-dimer level of 3900 ng/mL, with no fibrinogen consumption nor any other abnormalities.

Due to the suspicion of localized intravascular coagulation (LIC), treatment with low-molecular-weight heparin (LMWH) was followed for 10 days, resulting in improved clinical status and decreased D-dimer levels. Subsequent sirolimus therapy was introduced.

Discussion: LIC occurs in approximately 58% of patients with venous malformations. It is characterized by significant and prolonged pain, stagnation and swelling, rarely causing major bleeding or thrombosis. Risk factors include sclerotherapy, surgery, fractures, immobilization, pregnancy and sepsis.

Diagnosis involves clinical features, D-Dimer levels, and imaging examinations. MRI typically shows large venous pouches as hyperintense signals on T2WI with fat suppression. LMWH is the preferred anticoagulant therapy, and sirolimus might prevent further progression to disseminated intravascular coagulation.

Keywords: *localized intravascular coagulation, venous malformation, lymphedema*

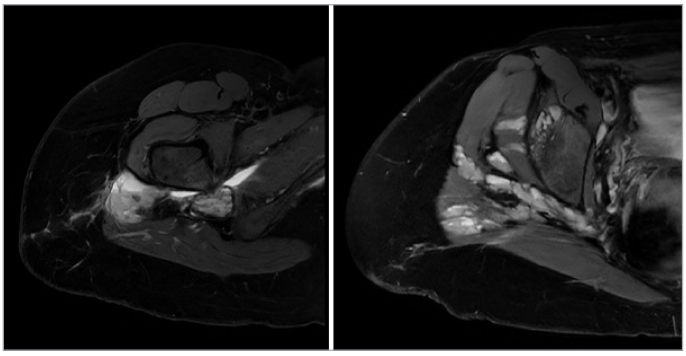

Figure 1. *MRI performed after surgery.*
It reveals a venous vascular anomaly involving muscle, impacting the right supraacetabular bone and neural iliotibial tract. Persistent edema around the bone component of the acetabulum and an increase in the size of the lesion are shown.

[Abstract:1700]

MULTIPLE PRIMARY MALIGNANCIES (MPMS): PRESENTATION OF A CASE WITH CONTEMPORARY ACUTE MYELOID LEUKEMIA, METASTATIC PROSTATE CANCER AND BASAL CELL CARCINOMA

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Introduction: MPMs involve the presence of two or more histopathologically distinct malignancies in one individual.

Case Presentation: An 88-year-old man with history of hypertension was admitted due to worsening peripheral oedemas, and urinary urgency. Physical examination revealed hepatosplenomegaly and a suspicious lesion on the upper left side of the nose. Laboratory tests revealed pancytopenia, and prominent monocytosis.

Further laboratory tests revealed a PSA level >100 ng/ml. Additionally, CT scans showed multiple intrabdominal conglomerate masses of lymph nodes, hepatosplenomegaly, and multiple sclerotic bone lesions. Nuclear bone scan showed high volume bony metastatic disease. Biopsy of the abdominal mass revealed metastatic infiltration from prostate adenocarcinoma. Bone marrow biopsy showed acute myeloid leukaemia (AML) and metastatic infiltration from prostate adenocarcinoma. Nasal skin biopsy revealed basal cell carcinoma.

Metastatic prostate cancer was treated with GnRH antagonist. During remission induction therapy for AML, the patient developed severe toxicity and after shared decision making, the patient entered palliative care facility.

Discussion: While the diagnosis of MPMs has significantly increased in recent years, the recognition of this term as a distinct clinical entity dates back a century. It is more than evident that a multidisciplinary team should decide on complex therapeutic dilemmas that often come up when the overall patient benefit is discussed.

Keywords: *multiple, neoplasms, elderly*

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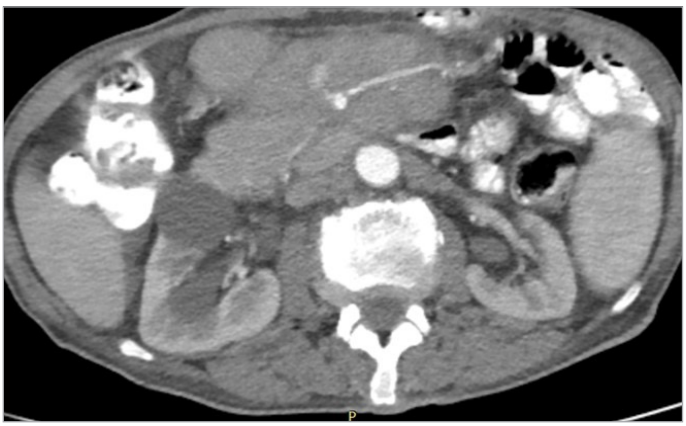

Figure 1. CT scan.
Intraabdominal masses of lymph nodes.

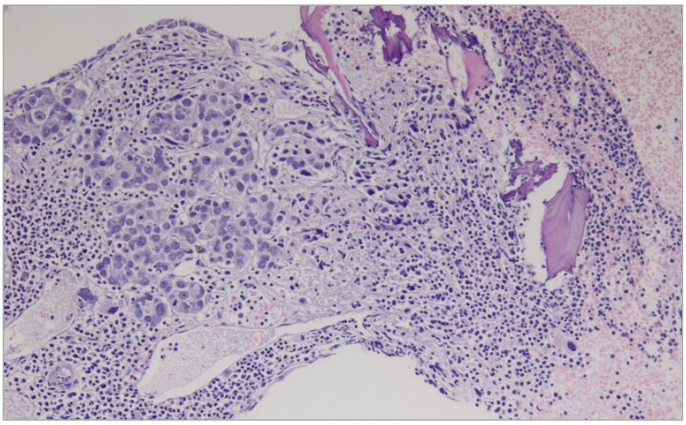

Figure 2. Histopathology.
Infiltration from blasts and malignant cells.

[Abstract:1745]

A CASE OF EARLY RENAL FAILURE, SPINA BIFIDA AND UNKNOWN PORPHYRIA

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Purpose: This case was decided to be written to raise awareness among physicians and present one of the complications of late diagnosis of porphyria.
Methods: In terms of methods, spot urine porphobilinogen test with Ehrlich Reactant was done to confirm diagnosis leading to 24-hour urine test to confirm the subtype of the disease. The patient's history and skin lesions also match the characteristics of porphyria.
Findings: We present a 33-year-old female patient. The patient presents with bullous lesions on her facial area, arms, and hands, forming right after sunlight contact. These bullous lesions happen to leave black scars and eventually become permanent white scars. The patient was diagnosed with meningomyelocele spina bifida at birth causing urine retention, which did not improve after surgery. At the age of 20, she began to require weekly dialysis due to the progression of stage 5 vesicourethral reflux. She had weekly dialysis for eight years, but as of today, since the age of 28, she requires it three times a week, done by herself at home. Although there are no comparable symptoms in her family history, her mother has congenital adrenal hyperplasia, and her father has been diagnosed with DM.
Conclusions: This case was determined to be presented because of a rare disease with incidental meningomyelocele history and complications. The patient has been experiencing renal failure since her 20s due to the severity and rarity of these two disorders.

Keywords: *porphyria, dialysis, renal failure*

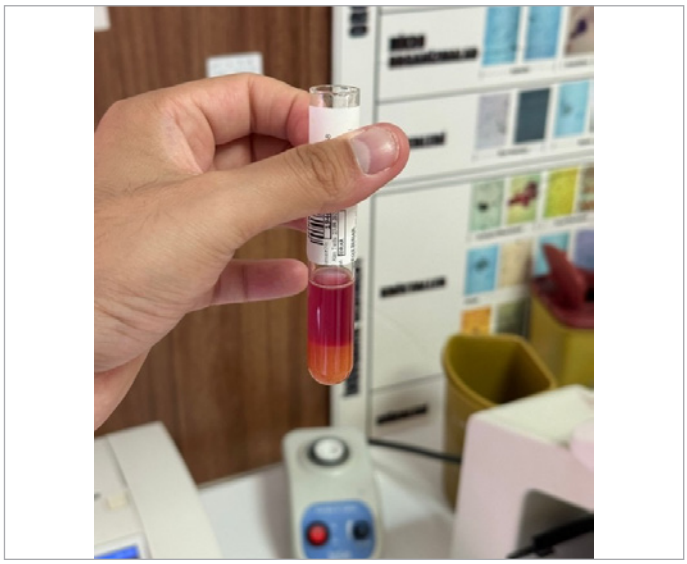

Figure 1. Ehrlich Reactant.
Spot Urine Test with Ehrlich Reactant.

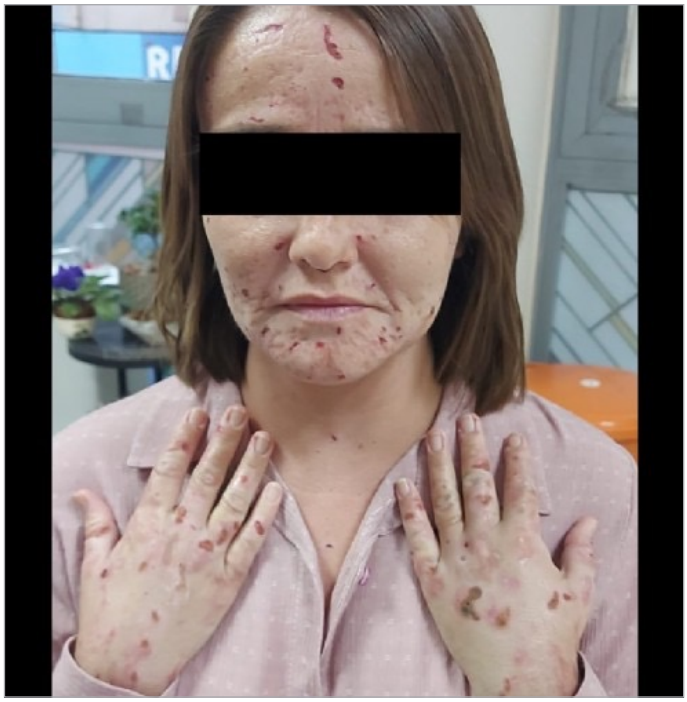

Figure 2. Face and Hand Lesions.
Lesions where sun seeing areas are affected.

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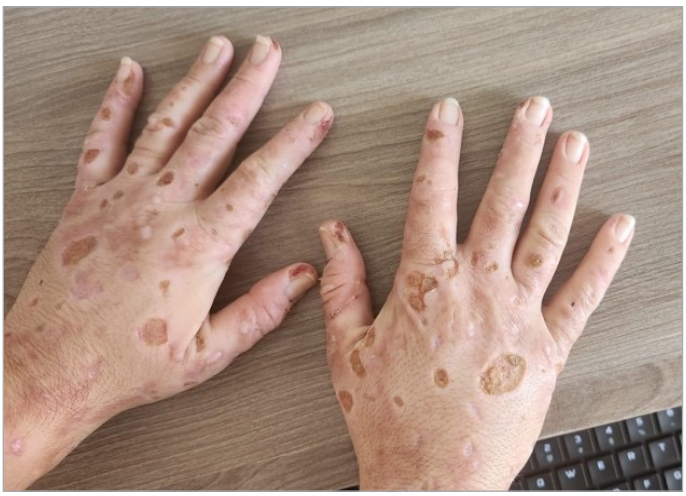

Figure 3. *Hand Lesions.*
Hand lesions with bullous lesions and cicatrice tissue.

[Abstract:1746]

HUMAN SYSTEMIC AMYLOIDOSIS: STILL HARDLY TRACTABLE BUT BECOMING CURABLE. A CHALLENGE FOR AN INTERNIST TO APPLY DIAGNOSIS AND TREATMENT

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Purpose: Primary systemic amyloidosis (PSA) is a rare plasma-cell dyscrasia characterized by monoclonal Ig protein overproduction and multisystem manifestations. PSA diagnosis is difficult due to overlapping symptoms with other more common conditions.
Methods: We report a case of a 59-year-old woman with a 2-month history of gastrointestinal symptoms presented at the Emergency Department due to elevated serum d-dimers and troponin levels. Physical examination showed peripheral oedema, symmetric peripheral sensory-motor polyneuropathy affecting the legs, carpal tunnel syndrome and non-blanching purpura, particularly evident in the lower extremities.
Findings: Laboratory evaluation revealed albuminuria (1200 mg/g creatinine) and persistently elevated cardiac troponin and d-dimers levels. Echocardiography of the heart revealed concentric left ventricular thickening (LVH) with evidence of heart failure with mildly reduced ejection fraction (EF 42%). We ruled out mesenteric or pulmonary embolism by CT angiography, but we found elevated serum monoclonal light (L) chains (680 mg/l), which could explain the abnormal findings from the physical and radiologic examination of the heart, gastrointestinal system, kidneys, and soft tissues. We proceeded with a rectal biopsy, revealing congo red and crystal violet stainings, which is attributed to amyloid deposition, thus confirming our suspicion of PSA.
Weekly treatment commenced with Daratumumab combined with Bortezomib, Cyclophosphamide, and Dexamethasone (Dara-VCD), with consideration for monoclonal antibody Birtamimab clinical trial enrolment. The patient has successfully responded with absence of symptoms and most of the signs.
Conclusions: This case emphasizes the diagnostic challenges and the multidisciplinary approach necessary for managing PSA, which was responded successfully following treatment.

Keywords: *amyloidosis (PSA), concentric LVH, dara-VCD*

[Abstract:1755]

MAY THURNER SYNDROME: A CASE REPORT

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A 35-year-old man presented with swelling in the left lower limb, without dyspnoea, chest pain or palpitations. He associated the onset of the symptoms with exercise and having been sitting while travelling in the previous days. No personal history of interest. Physical examination was normal except for swollen, reddened and painful left lower limb on palpation. Pulses were preserved. Hemodynamically stable and afebrile. Laboratory test D- dimer elevation, rest normal. A Doppler ultrasound of the lower limbs was performed, confirming thrombosis, and a CT scan with contrast of the abdomen was extended, leading to a diagnosis of left deep vein thrombosis (femoral-popliteal), May Turner syndrome.
It is an anatomically and pathologically variable condition leading to venous outflow obstruction due to compression of the left iliac vein between the right common iliac artery and the fifth lumbar vertebra, but there are others. It is especially seen in young women and most cases follow the classic left-sided description. Differential diagnosis should be made with pelvic mass, aortoiliac aneurysms, retroperitoneal fibrosis and osteophytes. Optimal treatment includes oral anticoagulation and local fibrinolysis, together with angioplasty and stenting if stenosis is present.
Suspect this syndrome in patients with risk factors and proximal venous involvement.

Keywords: *thrombosis, May Thurner, anticoagulation*

[Abstract:1777]

YOUNG MALE WITH SCANNING SPEECH

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We present a case of a 36-year-old male patient with a history of cervical lymph node tuberculosis treated 20 years ago without

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microbiological isolation and under follow-up by urology for erectile dysfunction in treatment with testosterone who was referred to Internal Medicine for dysarthria.
Active tuberculosis was ruled out with chest X-ray, PCR and culture. MRI (Magnetic Resonance Imaging) was requested to evaluate pituitary involvement as a cause of hypogonadism, showing nodular thickening of the tuber cinereum and pituitary stalk. On the other hand, MRI performed for gonalgia described an alteration of the signal intensity of the medulla in the distal femur. Additionally, he started with polyuria and polydipsia, together with persistent scanning speech and swallowing alteration deciding in that moment to hospitalize him to complete the study.
During admission, we confirmed the presence of central diabetes insipidus and the presence of hypogonadotropic hypogonadism without other hormonal alteration. The evaluation was completed with a CT (Computed Tomography) that showed an inflammation in the abdominal aorta, iliac and left femoral bifurcation. Bone biopsy was performed with non-specific chronic inflammation.
Due to the lack of diagnosis, we evaluated skin finding xanthomatous features on the torso. A skin biopsy was performed, and it was compatible with a xanthogranuloma in relation to non-Langerhans cell histiocytosis with positive BRAFV600E mutation. The patient was diagnosed of Erdheim-Chester disease with cerebellar, pituitary, bone, vascular and cutaneous involvement.

Keywords: *Erdheim–Chester disease, non-Langerhans cell histiocytosis, xanthogranuloma.*

[Abstract:1795]

SCIENTIFIC SCRUTINY OF SKELETAL BONE PAIN: A FORMAL EXAMINATION IN A UNIQUE CLINICAL CASE

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Male, 77 years old, followed in a general surgery appointment for 4 years because of abdominoperitoneal amputation due to rectal adenocarcinoma (T2N0M0). A follow-up abdominopelvic computed tomography (CT) was performed which revealed structural changes in the pelvis and iliac bones adjacent to the hip, pubis and ischion, suggestive of bone metastasis. The patient complained of anorexia and bone pain in his right leg. He denied weight loss. Analytically, he presented normocytic normochromic anaemia and an isolated increase in alkaline phosphatase (maximum value 244 (U/L). Bladder, prostate, and gastrointestinal cancer were excluded as primary tumour. The patient underwent bone scintigraphy which revealed that the lesions were not suggestive of metastasis, and the diagnostic hypothesis of non-langerhans cell histiocytosis was put forward. He underwent CT-guided bone biopsy in the region of the right femoral neck. The pathological results revealed the presence of a population of histiocytes, confirming the diagnostic hypothesis of Erdheim-Chester type histiocytic disease. Systemic involvement of the disease was excluded analytically and through thoracoabdominopelvic CT. The patient was referred to a haematology evaluation.

Keywords: *bone lesions, histiocytes, non-Langerhans cells, Erdheim-Chester disease*

[Abstract:1804]

A RARE CAUSE OF CHRONIC HEMATURIA: EOSINOPHILIC CYSTITIS

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Eosinophilic cystitis (EC) is a chronic cause of haematuria with unclarified aetiology which usually progresses with relapses. This disease is more common in allergic and atopic people. In Eosinophilic Cystitis histopathology; firstly inflammation dominated by eosinophilic infiltration, then fibrosis in the mucosa and finally necrosis in the muscle tissue can be observed. The most common symptoms are; increased urinary frequency, dysuria, haematuria and suprapubic pain. The diagnosis may be confused especially with lower urinary tract diseases. In this disease, there is a wide range of clinical symptoms from mild irritative symptoms to obstructive invasive bladder cancer imitations. Due to impossibility of diagnose by symptoms, signs and laboratory tests, it can only diagnosed by cystoscopy and biopsy.
In this case, we presented a 67-year-old female patient who has intermittent haematuria attacks that sometimes require transfusion for six years. During this time, our patient was investigated several times and received palliative treatment with short-term antibiotherapies.
We wanted to emphasize that the diagnosis of eosinophilic cystitis should be kept in mind in patients with chronic haematuria.

Keywords: *chronic hematuria, macroscopic hematuria, eosinophilic cystitis*

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[Abstract:1813]

BIOCHEMICAL MARKERS IN PREMATURE AGING IN CORNELIA DE LANGE SYNDROME

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[1] Royo Villanova Hospital, Zaragoza, Spain

[2] Ernest Lluch Martín Hospital, Calatayud, Spain

Purpose: To assess whether there is premature aging in patients with Cornelia de Lange syndrome (CdLS) through a study of biochemical parameters.

Methods: A retrospective study of 8 biochemical values was carried out in a Spanish cohort of 24 patients with Cornelia de Lange syndrome, 15 women and 9 men, aged between 2 and 37 years.

Results: In individuals with CdLS, there is no significant relationship between the values of the HOMA-IR index and age ($p = 0.1174$). However, it should be noted the 21.7% present a pathological HOMA index, and it is already observed in non-obese individuals less than 5 years of age. There is a decreasing trend in alkaline phosphatase concentrations in people with CdLS, although the relationship is statistically significant only in women (women, $p < 0.0005$; men, $p = 0.0823$), probably due to the smaller number of men analysed. A slight upward trend in PTH levels is observed in CdLS, without being significant ($p = 0.3352$). The 25(OH) vitamin D levels are below the lower limit of normality with a statistically significant downward trend ($p = 0.0438$). Both calcium and phosphorus have a marked, statistically significant downward trend (calcium, $p < 0.0001$; phosphorus, $p < 0.0001$), which coincides with the decrease in vitamin D. (Fig 1; Fig 2)

Conclusions: •It is observed that individuals with CdLS present a premature deterioration in carbohydrate and bone mineral metabolism.

•Specific clinical follow-up is recommended in these patients in order to prevent possible complications derived from the alteration of these axes.

Keywords: *Cornelia de Lange syndrome, premature aging, bone mineral metabolism, carbohydrate metabolism*

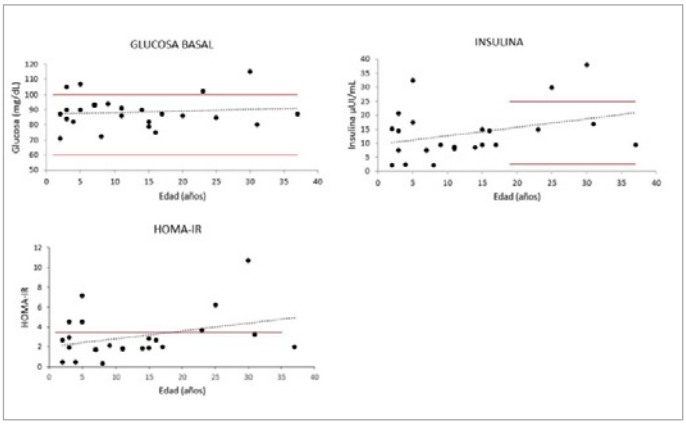

Figure 1. *Basal glucose, insulin and HOMA-IR levels in individuals with CdLS. Each point corresponds to an individual (glucose, n=24; insulin, n=23; HOMA-IR, n=23). The black dashed line shows the linear regression: glucose, p = 0.6174; insulin, p = 0.1224; HOMA-IR, p = 0.1174. The red lines indicate the upper and lower limits of a Spanish Hospital reference values for these parameters.*

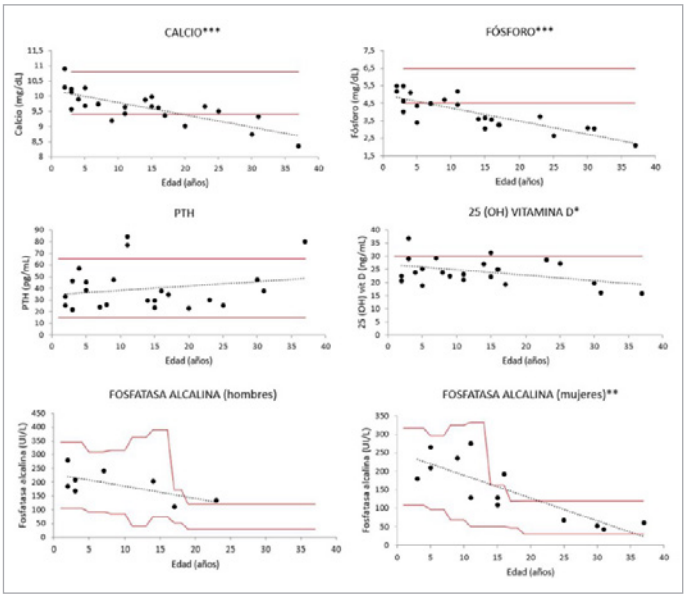

Figure 2. *Baseline levels of PTH, 25(OH)vitamin D, serum calcium, serum phosphorus and alkaline phosphatase in individuals with CdLS. Each point corresponds to an individual (PTH, n=24; 25 (OH) vitamin D, n=23; calcium, n=23; phosphorus, n=22; FA, n=21). The black dashed line shows the linear regression: PTH, p = 0.3352; 25 (OH) vitamin D, p = 0.0438; calcium, p < 0.0001; phosphorus, p < 0.0001; FA (men), p = 0.0823; FA (women), p = 0.0005. The red lines indicate the upper and lower limits of a Spanish Hospital reference values. * p < 0.05, ** p < 0.001, *** p < 0.0001.*

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[Abstract:1814]

FROM THE CLINIC TO THE IMAGE - HORSESHOE KIDNEY

Catarina Pinto Silva[1], *Rita. Sevivas*[1], *Flávia Fundora Ramos*[1], *Beatriz. Rosa*[1], *João Pedro Abreu*[1], *Carlos S. Oliveira*[1]

[1] ⚠ The authors did not provide affiliations upon requests from the event organizer

Horseshoe kidney is an anomaly of renal fusion that occurs in 0.25% of the general population. Most of the time it appears as an asymptomatic anomaly, however, affected individuals are more prone to a variety of complications, namely: renal lithiasis, obstruction of the ureteropelvic junction, trauma, infections and tumours. As a result of the abnormal anatomy, imaging findings and treatment vary greatly.

The present case portrays a 65-year-old man, with urinary complaints and a diagnosis of lower tract urinary tract infection, without changes in renal function or urinary output, with an incidental diagnosis of horseshoe kidney. He underwent treatment with ciprofloxacin and remains asymptomatic to date.

Keywords: *horseshoe kidney, anomaly of renal fusion, anatomical anomaly*

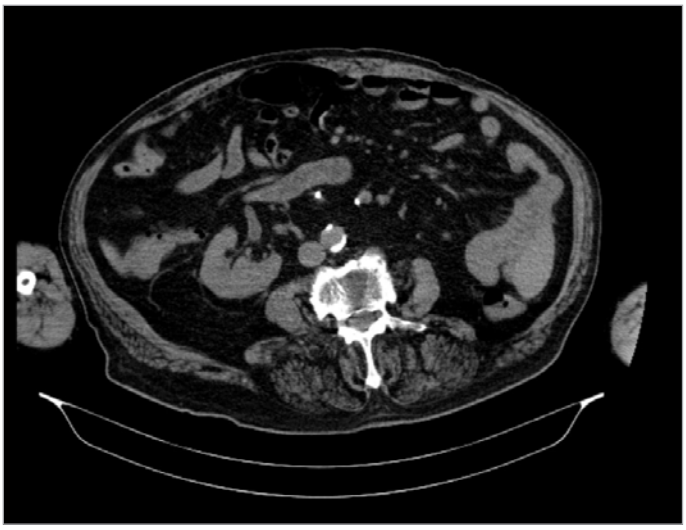

Figure 1.

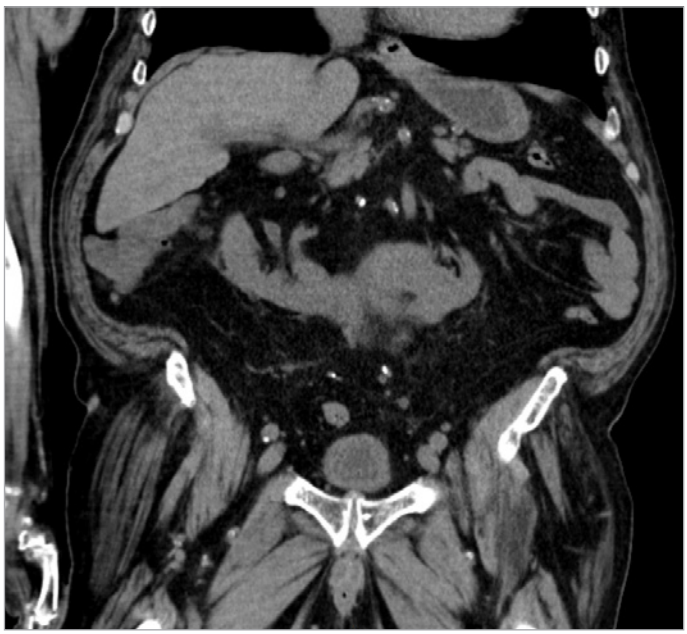

Figure 2.

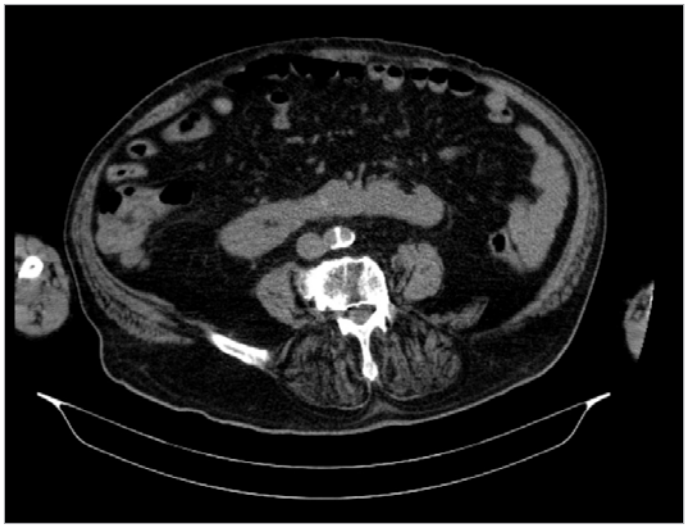

Figure 3.

[Abstract:1856]

KEEP IN MIND! A RARE CASE REPORT: ADULT OSTEOPETROSIS WITH DENTAL OSTEOMYELITIS

Mustafa Berkay Tastekin, *Oguz Abdullah Uyaroglu*, *Nursel Calik Basaran*, *Lale Ozisik*, *Gulay Sain Guven*

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Purpose: Osteopetrosis (OPT) is a rare inherited metabolic bone disorder characterized by extensive sclerosis of skeletons, visual and hearing impairment, dental problems, hepatosplenomegaly and anaemia. It has two major clinical forms: the autosomal dominant adult (benign) form is associated with milder symptoms often appearing in later childhood and adulthood whereas the autosomal recessive infantile (malignant) form has severe

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presentations appearing in very early childhood, if untreated, is typically fatal during infancy or early childhood.

Methods: Here we report a 36-year-old premenopausal women diagnosed with dental osteomyelitis who was consulted to our department by dentist for investigating the underlying etiology.

Findings: The patient didn't diagnosed with any other chronic disease and didn't on any treatment. The patients were found pale with poor nutritional status, short stature (height: 148 cm, and BMI: 21 kg/m^2). We didn't detect any pathological sign in her physical examination. The laboratory tests were all in normal limits except iron deficiency and insufficient vitamin D. In skeletal survey indicated diffuse medullary sclerosis of bones and had an atypical stress fracture in left femur shaft. In bone DXA scan of the skeleton revealed a Z-score of L1-L4 region 5.3, left neck of femur 3.3, total hip 4.4 incompatible with OPT. The patient was diagnosed with OPT based on her clinical and radiological findings, and close follow-up was planned for possible complications.

Conclusions: Diagnosis of OPT is mainly based on clinical and radiographic evaluation (typical generalized increase in bone density), confirmed by gene testing where applicable, and paves the way to understanding natural history, specific treatment where available, counselling regarding recurrence risks, and prenatal diagnosis in severe forms.

Keywords: *osteopetrosis, bone density, sclerosis*

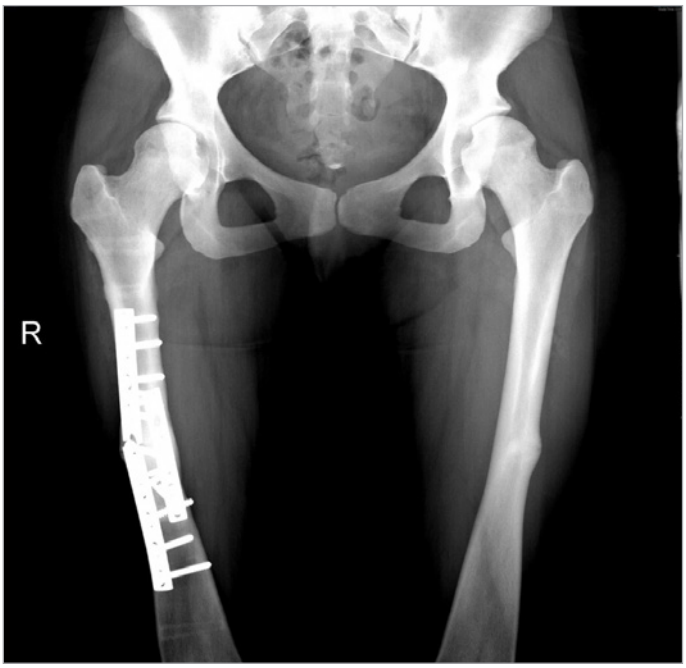

Figure 1. *Atypical stress fracture in left femur shaft.*

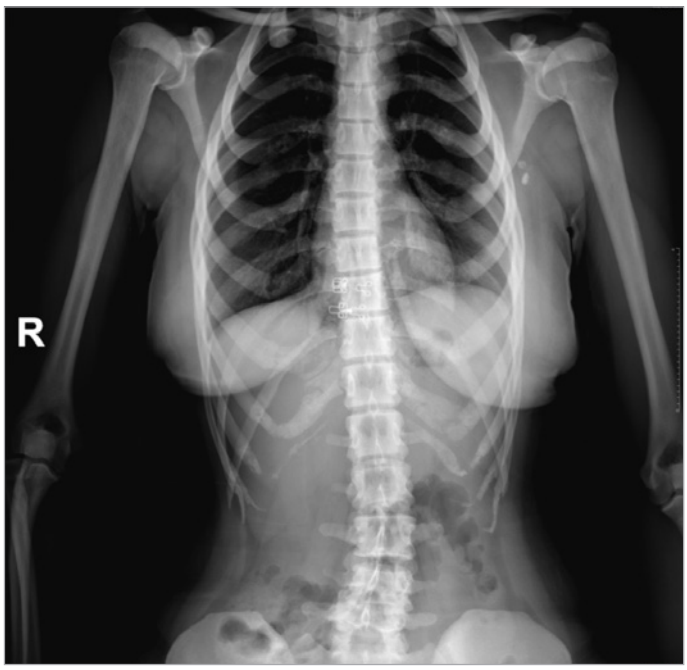

Figure 2. *Diffuse medullary sclerosis of bones.*

[Abstract:1927]

A CASE OF NEWLY DIAGNOSED CYSTIC FIBROSIS IN A 67-YEAR-OLD MAN

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Objective: Cystic fibrosis (CF) is a serious disease with an autosomal recessive inheritance pattern. Classic CF is characterized by frequent respiratory infections and pancreatic insufficiency and is typically diagnosed in childhood. Atypical CF, on the other hand, can present with bronchiectasis, pancreatic insufficiency, cholestasis, and infertility in adulthood, as the cystic fibrosis transmembrane regulator (CFTR) protein is able to function partially. We present this case to remind clinicians that CF should be considered in adult patients as well.

Case Presentation: A 66-year-old man with known diabetes and asthma presented to the chest clinic with hemoptysis. Sputum culture grew *Pseudomonas aeruginosa*, and the patient was admitted to the chest ward.

Chest imaging revealed cystic and bronchiectatic areas, dextrocardia, and consolidation. After treatment for pneumonia, the patient was referred to the internal medicine clinic for diabetes regulation. On presentation to our clinic, we noted that the patient had a history of frequent pneumonia, was childless, and had a pigeon chest appearance on physical examination. Due to the diagnosis of diabetes, we ordered an abdominal ultrasound. The ultrasound showed an atrophic appearance in the left lobe of the liver and pancreas. We suspected that the patient may have CF, and ordered genetic mutation testing.

The patient was found to have a heterozygous mutation with a CFTR protein activity of 42%, which was interpreted as a clinically

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insignificant variation. The patient's follow-up continues in our outpatient clinic.

Conclusions: It should not be forgotten that atypical CF patients may present with heterogeneous clinical findings in adulthood.

Keywords: *cystic fibrosis, pneumonia, infertility*

[Abstract:1950]

DIFFERENTIAL DIAGNOSIS OF "CAFÉ-AU-LAIT" LESIONS

Ana María Aldea Gamarra[1], *Ana Sofía Romero León*[1], *Olaya Huergo Fernández*[1], *Tatiana Paula Pire García*[1], *Samuel Díaz Planellas*[1], *Luis Antonio Álvarez Sala Walther*[1], *María Olmedo Samperio*[1], *Lucía Ordieres Ortega*[2]

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Case Description: A 37-year-old man arrived to the Rare Diseases Clinic with a clinical suspicion of Neurofibromatosis type 1 (NF1). He had a past history of an arteriovenous cerebral malformation treated with radiosurgery and a previously removed skin fibroma. His father also had 2 café-au-lait (CAL) macules with no other symptoms.

Physical examination showed ephelides on the trunk and face, four café-au-lait macules larger than 5 cm, xanthelasma in left eye and mild pectus excavatum. Ophthalmologic examination and blood tests were normal. Imaging tests of long bones and abdomen were also normal. A brain magnetic resonance imaging showed sequelae of radiosurgery (figure 1).

Clinical Hypothesis: Given the clinical findings we considered NF1 versus neurofibromatosis type 6 (NF6).

Diagnostic Pathways: Given the presence of café-au-lait macules without other criteria for NF1, a genetic test was performed, showing only a variant of uncertain meaning in NF1: c.6038C > T, p, Thr2013Ile.

Discussion and Learning Points: Although the preliminary suspicion was NF1, due to the lack of clinical confirmation, other diagnoses were considered. NF6 presents with multiple CAL spots alone. This syndrome is inherited in an autosomal dominant fashion, and our patient's father also presented CAL lesions. A close linkage to the NF1 gene has been described.

Keywords: *cafe-au-lait macules, neurofibromatosis type 1, neurofibromatosis type 6*

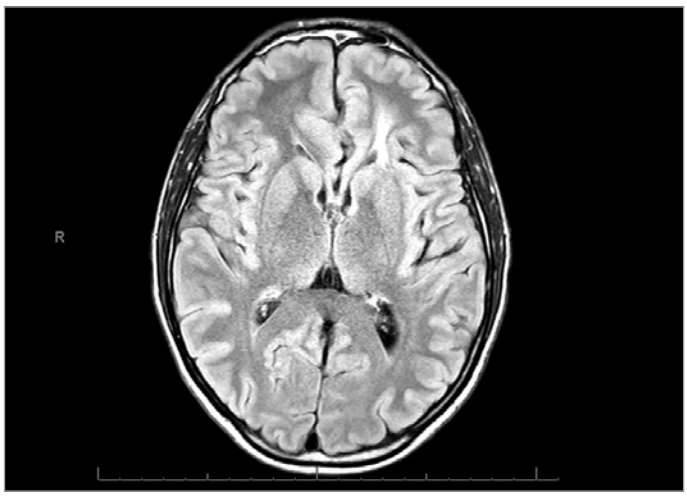

Figure 1. *Brain magnetic resonance imaging with sequelae of radiosurgery.*

[Abstract:2008]

A PARKINSONIAN SYNDROME REVEALING A FAHR SYNDROME: A CASE REPORT

Mesmous Wissame

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Introduction: Fahr syndrome is a rare anatomical-clinical entity characterized by bilateral and symmetrical intracerebral calcifications, localized in central grey nuclei, most often associated with phosphocalcium metabolism disorders. characterised by its clinical polymorphism.

Materials and Methods: Reporting to us the case of a woman 46 year-old known for type 1 diabetes Admitted to our level for the management of a trophy lesion of the right foot.

Results: Clinical examination: conscious patient, dysarthria for 2 years with a progressive installation, behavioural disorders, concentration and memory with intellectual decline. Neurological examination returning in favor of a walking disorder and balance at the origin of this trophic lesion on the right foot, a Parkinson's syndrome with tremors, muscle rigidity and akinesia. Radiology: cerebral MRI: large calcification ranges of central grey nuclei bilaterally and symmetrically evoking a Fahr syndrome. Biology: severe hypocalcaemia at 68.2 mg/l, hyperphosphoraemia at 57.3 mg/l, low PTH at 2.7 pg/ml, and 25 OH vitamin D collapsed at 9 µg/L. The diagnosis of Fahr Syndrome secondary to primary hypoparathyroidism was retained and a replacement treatment calcivitamine D was started in combination with neuropsychiatric management. The evolution was marked by the correction of phosphocalcium metabolism disorders and neuropsychiatric signs. The control TDM remained unchanged.

Conclusions: Fahr syndrome is generally difficult to suspect clinically as it can remain asymptomatic or result in polymorphic manifestations not corresponding to any specific table. Etiologist are dominated by dysparathyroids.

Keywords: *Fahr syndrome, Parkinson's syndrome, dysparathyroids*

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[Abstract:2066]

POSTERIOR MEDIASTIC MASS: DIAGNOSTIC AND ETIOLOGICAL CHALLENGE

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A 66-year-old woman with no relevant prior medical history was admitted due to fever and progressive dyspnoea lasting 2 days. The laboratory tests were unremarkable. In the study carried out during hospitalization, a tomography chest computed tomography followed by magnetic resonance imaging identification of a large mass in the posterior mediastinum in subcarinal topography. She underwent a biopsy via echobronchoscopy, without evidence of a lesional process, which is why she underwent right uniportal videothoracoscopy, whose histology revealed lymph nodes with a chronic granulomatous inflammatory process non-necrotizing of unclear aetiology. It is being studied at the Internal Medicine Consultation. In this clinical case, the challenge diagnosis and the relevance of differential diagnoses of mediastinal masses. Tissue biopsy for pathology, however, is necessary for final diagnosis. The establishment of a diagnosis should not be delayed, as mediastinal mass may be due to serious causes such as neoplastic disease or infection. Mediastinal granuloma is a rare but important to recognize cause for mediastinal mass. Monitoring these patients and investigating the different causes is of utmost importance in the management of these patients.

Keywords: *posterior mediastic mass, mediastinal granuloma, diagnostic challenge*

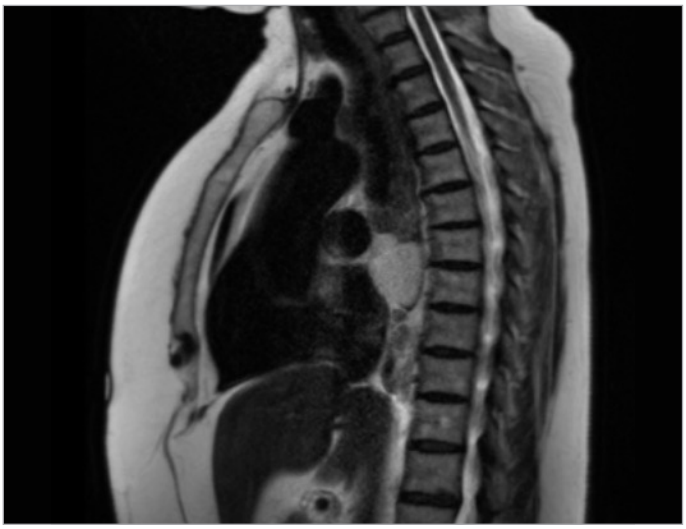

Figure 1. *Posterior mediastic mass.*

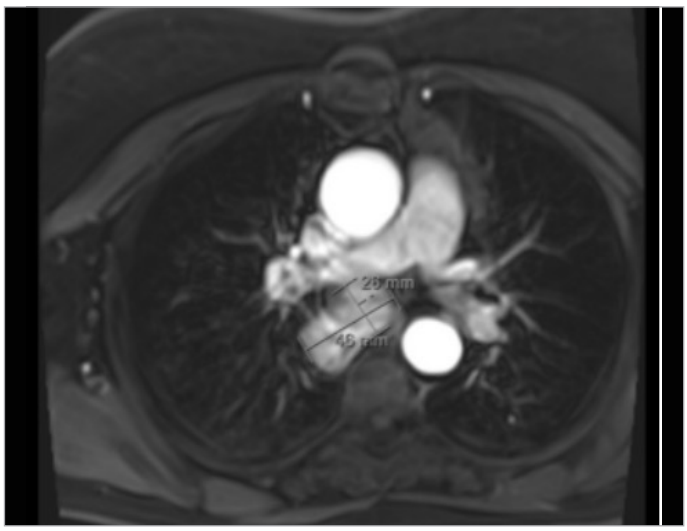

Figure 2. *Posterior mediastic mass.*

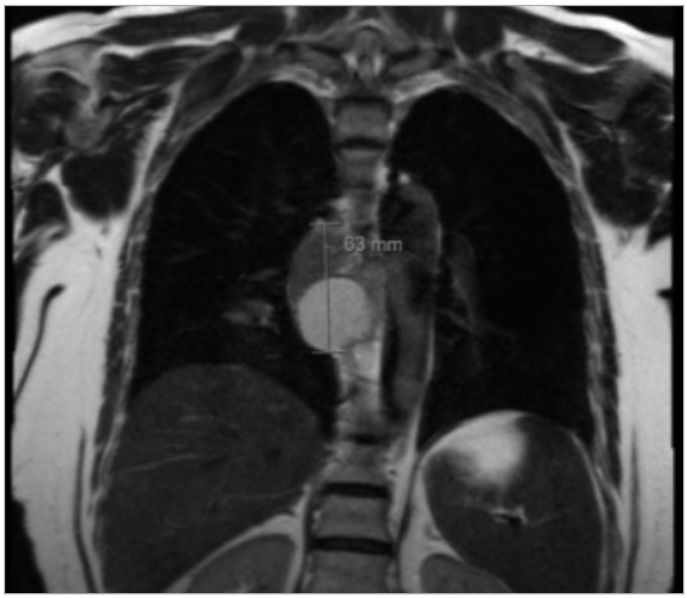

Figure 3. *Posterior mediastic mass.*

[Abstract:2067]

EMPHYSEMATOUS PYELONEPHRITIS IN A PATIENT WITH G6PC3 DEFICIENCY USING EMPAGLIFLOZIN TO RESTORE NEUTROPENIA: A CASE REPORT

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Case Description: A 29-year-old male patient with glucose-6-phosphatase catalytic subunit 3 (G6PC3) deficiency was admitted with fever, chills, and flank pain. The patient was previously

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admitted with episodes of urinary tract infections and pneumonia, with *E. coli* growth in urine and blood cultures, and had a history of broad-spectrum antibiotic use. He was being treated with weekly subcutaneous IGRT and G-CSF; he was started on empagliflozin for neutropenia three months before admission, and G-CSF requirement decreased. One week before admission, he was treated with three doses of fosfomycin, with no improvement in his symptoms.

Clinical Hypothesis: A presumptive diagnosis of complicated UTI was made.

Diagnostic Pathways: Urinalysis showed bacteriuria and pyuria; urine culture was positive for *Enterococcus faecium* and *E. coli*. CT urography showed right renal pelvicalyceal dilatation with gas collections, consistent with emphysematous pyelonephritis (Figure 1). After a urology consultation, decision was made to treat with intravenous antibiotics, reserving surgical intervention for unresponsiveness. Patient was started on imipenem, and after 14 days of treatment, control imaging showed resolution of emphysematous pyelonephritis (Figure 2). Empagliflozin was discontinued as a potential factor provoking complicated UTI, and G-CSF was restarted.

Discussion and Learning Points: Empagliflozin can increase neutrophil count and function in G6PC3 deficiency, even allowing termination of G-CSF and reducing its long-term adverse effects. However, SGLT2i treatment has considerable infectious side effects, so the risk-and-benefit ratio must be considered carefully when initiating SGLT2i in immunocompromised individuals at risk of severe infections.

Keywords: *empagliflozin, neutropenia, SGLT2 inhibitor*

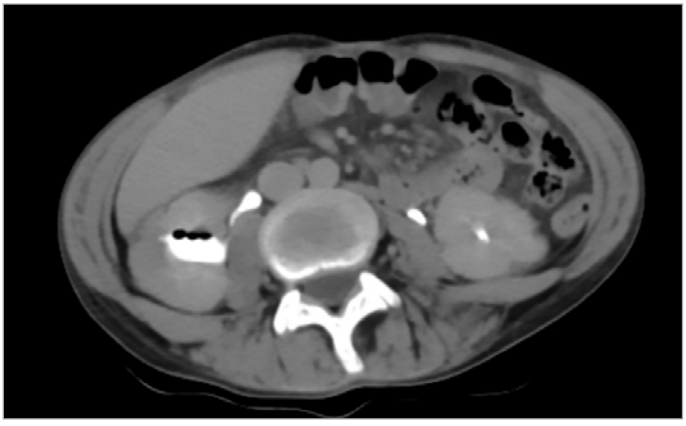

Figure 1.

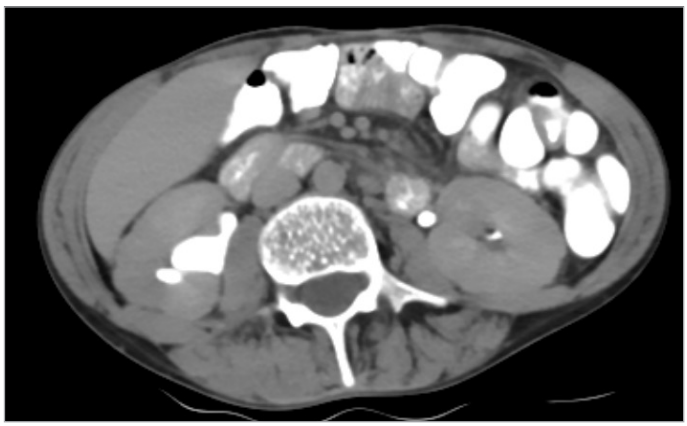

Figure 2.

[Abstract:2071]

TUBEROUS SCLEROSIS COMPLEX WITH DIFFUSE BONE OSTEOCONDENSATION: A CASE REPORT

Samar Derbal, Donia Chebbi, Olfa Hentati, Fatma Ben Dahmen, Yosra Cherif, Meya Abdallah

Internal Medecine department, Regional Hospital of Ben Arous, Tunis, Tunisia

Background: Tuberous sclerosis complex (TSC) is a rare autosomal dominant disorder. The most common reported symptoms are lesions of the skin, central nervous system, heart and renal angiomyolipoma. Skeletal lesions are rarely described in TSC in literature. We present a case of TSC diagnosed in an adult with multiple silent bone lesions.

Case Presentation: A 46-year-old women with a history of renal angiomyolipoma was hospitalized to the department of Internal Medicine. Physical examination showed multiple hypomelanotic macules and angiofibromas. The patient did not show any other abnormalities. Laboratory tests revealed an elevated creatinine at 130 µmol/l. The other serum tests were within the normal ranges. The chest X-rays was normal. In addition, le lumbar X-rays showed a diffuse bone condensation. Abdominal ultrasonography showed bilateral renal angiomyolipomas. Echo- cardiography was normal. Thoraco-abdominal scan ascertained the diagnosis of renal angiomyolipomas with bilateral pulmonary angiomyolipomas. Besides, it revealed multiple sclerotic bone lesions in the thoracic and lumba spine and ribs and sternum with an angiofibroma of the lumber vertebra. The patient was diagnosed with TSC.

Conclusions: The skeletal involvement in TSC is rare. This case reported multiple silent bone lesions in a patient with TSC. Their early diagnosis and management may avoid complications.

Keywords: *tuberous sclerosis, osteocondensation, skeletal*

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[Abstract:2075]

PRIMARY MEDIASTINAL SYNOVIAL SARCOMA: A RARE CASE REPORT

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Internal Medecine department, Regional Hospital of Ben Arous, Tunis, Tunisia

Background: Synovial sarcoma is a mesenchymal tissue cell tumour that exhibits epithelial differentiation. Most frequently, it arises in adolescents and young adults. Less than 20% of synovial sarcoma arise in extra extremity locations including the mediastinum.

Case Presentation: A 34-year-old man presented with retrosternal chest pain, shortness of breath on exertion for 6 month. He also complained of dysphagia and loss of weight. Physical examination was normal. The serum tests were within normal range. The tumour markers like alpha-fetoprotein, and human chorionic gonadotropin levels were within normal limits. The chest X-ray showed poorly homogeneous mediastinal opacity. Chest computed tomography revealed a 12x9x9 cm anterior mediastinal mass with peripheral calcifications repulsing the mediastinum and the thyroid with several parenchymal pulmonary nodules and vertebral body defects.

Histological examination revealed spindle cells and fibrillar or hyaline places with focal positivity for epithelial membrane antigen and Bcl2 on immunohistochemistry. The patient was diagnosed of a primary synovial sarcoma of the mediastinum and received chemotherapy. The evolution was marked by the tissue infiltration of the sub carinal region, pulmonary veins and compression of the left atrium with a 30% increase in pulmonary nodules. The patient died 7 months later.

Conclusions: Synovial sarcoma has been considered to have a poor prognosis. The lung is the most common site for metastasis followed by lymph nodes and bone. Our case seems interesting showing a rare localization of synovial sarcoma that can invade adjacent organs or give distant metastases.

Keywords: mediastinum, sarcoma, synovial

[Abstract:2081]

HYPERIMMUNOGLOBULIN D SYNDROME (HIDS)

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[1] Department of Internal Medicine, Marmara University, Istanbul, Turkey

[2] Department of Rheumatology, Marmara University, Istanbul, Turkey

Case Description: A 34-year-old male patient was referred to the rheumatology outpatient clinic due to bilateral macular itchy rashes on the legs consistent with leukocytoclastic vasculitis. His medical history included intermittent recurrent attacks of abdominal pain since childhood, a history of recurrent fever, and arthralgia. On physical examination, he had maculer rash on his ankles, axillary lymphadenopathy (LAP) and a palpable spleen.

Clinical Hypothesis: Causes of recurrent or periodic fever and abdominal pain; Familial Mediterranean fever, the autoinflammatory diseases, Lymphoma Diagnostic Path: Laboratory results showed leukocyte 2.5x10^3/µL, hgb 8.7g/dl, platelet 91x10^3/µL, with normal kidney and heart function tests. Viral serology was negative but there were elevated inflammatory parameters. There were no laboratory findings significant for vasculitis. The patient, who had LAP, splenomegaly and pancytopenia, was evaluated by haematology and a bone marrow biopsy was performed for the differential diagnosis of lymphoma and bone marrow infiltration, and positron emission computed tomography (PET-CT) was performed. There were no findings suggestive of lymphoma infiltration in the bone marrow biopsy. In the requested medical genetic tests, the missense variant in the MVK gene was detected as homozygous in the Severe Immunodeficiency Panel. He was diagnosed with HIDS after the MVK homozygous mutation.

Discussion and Learning Points: Hyperimmunoglobulin D syndrome is a rare, autosomal recessive genetic disease typically characterized by recurrent fever attacks associated with lymphadenopathy (LAP), abdominal pain, and high serum polyclonal immunoglobulin D (IgD) level. It should be considered in the differential diagnosis of rare hereditary diseases in patients with recurrent fever.

Keywords: recurrent fever, hyperimmunoglobulinemia D, abdominal pain

[Abstract:2086]

ACTIVATION OF INFLAMMATORY CASCADE IN FABRY DISEASE. OBSERVATIONAL STUDY

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[1] Department of Internal Medicine, Hospital Ramón y Cajal, IRYCIS, Madrid, Spain

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Aim: The aim of the study was to compare C3 and C4 complement component levels in patients with Fabry disease (FD) and healthy subjects. A single centre observational prospective study. Complement components C3 and C4 were measured in 16 patients with FD and 16 controls. Subjects were matched by age (±5 years) and sex. Those suffering from acute or chronic inflammation situations were excluded. Mann-Whitney U test was used for the analysis.

Findings: Median age was 44 years in FD group and 46 years in control group, with female sex predominance. The cardiovascular

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risk factors were evenly distributed between both groups (Table 1). C4 component was significantly elevated in FD group, whereas C3 showed the same tendency without reaching statistical significance.

Conclusions: FD is a multisystemic disease affecting main organs as heart, kidneys and brain. It is due to a deficient lysosomal a-galactosidase A activity which results in the accumulation of globotriaosylceramide (Gb3). The organ damage is not completely explained by this accumulation. It has been proposed that Gb3 acts as a damage-associated molecular pattern chronically activating the inflammatory cascade.

Previous studies had shown elevated C3 and C4 levels in patients with FD and their reduction with specific treatment. Our study shows a difference in C4 levels even if 8 patients were already under treatment. The absence of a statistically significant difference in C3 levels may be explained by reduced sample size.

These results support the hypothesis of an enhanced chronic inflammatory estate as a major physiopathologic mechanism in FD-organ damage.

Keywords: *fabry disease, complement, inflammation*

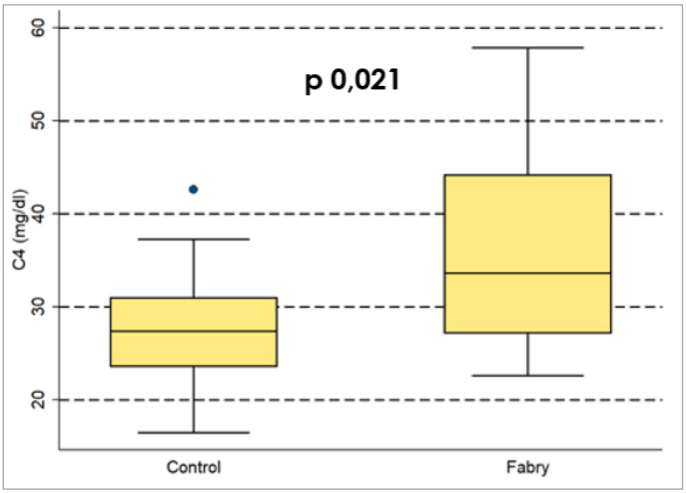

Figure 1. *C4 levels comparation.*

	Fabry Disease (n=16)	Control (n=16)
Age (years), median [IQR]	44,0 [19,0]	46,0 [21,0]
Female sex, n (%)	12 (75,0%)	12 (75,0%)
Cardiovascular risk factors, n (%)		
Arterial Hypertension	2 (12,5%)	1 (6,3%)
Diabetes mellitus	3 (18,8%)	2 (12,5%)
Dyslipidemia	5 (31,5%)	2 (12,5%)
Obesity (CMI ≥ 30 Kg/m2)	2 (12,5%)	1 (6,3%)
Cardiovascular disease, n (%)		
Acute myocardial infarction	0 (0,0%)	0 (0,0%)
Ictus	0 (0,0%)	1 (6,3%)

Figure 2. *Comparation of cardiovascular risk factors.*

	Fabry Disease(n=16)	Control (n=16)	p-valor
C3 complement factor, mg/dL	122.5 (104-164)	110.5 (84.3-158)	0,086
C4 complement factor, mg/dL	33.7 (23.9-57.9)	27.4 (16.5-42.6)	**0,021**

Median (IQR).

Figure 3. *Complement factor levels comparation.*

[Abstract:2097]

LYMPHANGITIC CARCINOMATOSIS: A CHALLENGING AND UNCOMMON DIAGNOSIS

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Lymphangitic carcinomatosis is considered an end-stage manifestation of malignancy. It accounts for less than 10% of all cases of metastatic lung cancers.

A 79-year-old male patient with Parkinson's disease was admitted to the hospital with subacute onset of malaise and progressive dyspnoea. He had no history of cough, fever, hemoptysis or weight loss. Family also reported impaired consciousness in the last few days. Laboratory tests had no relevant alterations, with negative inflammatory markers. A head computed tomography (CT) was performed, with no acute changes. Chest X-ray demonstrated multiple dispersed small sized hypotransparencies on both lungs. Blood gas analysis showed no respiratory failure at the time of hospitalization.

A few days after admission, level of consciousness started deteriorating, so the patient was admitted to intermediate care. Lumbar puncture was performed, which was negative, and

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an electroencephalogram was required, which also excluded epileptiform activity. Chest CT scan showed multiple nodular lesions diffusely in both lungs with areas of coalescence and a nodular lesion with irregular and spiculated contours in the upper segment of the left lower lobe, suggestive of neoformation. Angiotensin converting enzyme and adenosine deaminase were normal.

Based on the characteristics of these pulmonary lesions, the patient started dexamethasone assuming the diagnosis of lymphangitic carcinomatosis.

Although the patient never developed respiratory failure, neurological state kept on getting worse which ultimately led to death.

Lymphangitic carcinomatosis is associated with poor prognosis due to subtle presentation and challenging diagnosis. Consequently, the diagnosis is often delayed and not made until autopsy.

Keywords: *cancer, lung, carcinomatosis*

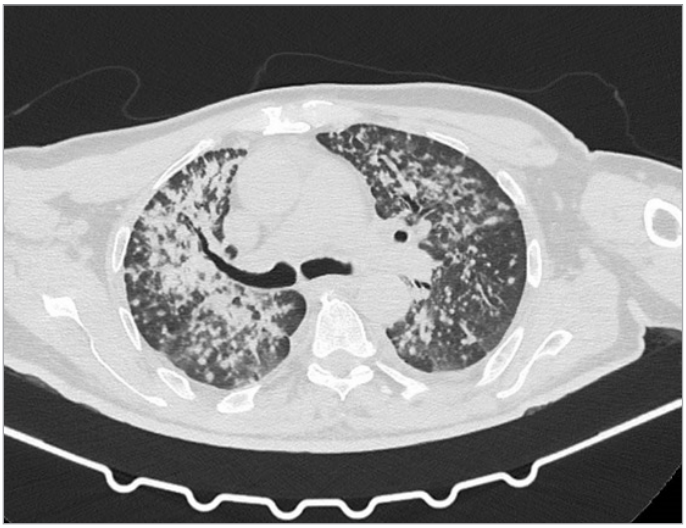

Figure 1. *Lymphangitic carcinomatosis in CT scan.*

[Abstract:2140]

GENERAL CHARACTERISTICS OF HEPATIC PORPHYRIA IN 36 PATIENTS: A NOVEL RESEARCH IN TURKEY

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[1] Maltepe University, Faculty of Medicine, Istanbul, Turkey

[2] Maltepe University, Department of Internal Medicine, Istanbul, Turkey

Purpose: This study was decided to be written to give a new perspective to physicians about the statistics of hepatic porphyria and show the common findings of this disease.

Methods: We have evaluated the data and anamnesis of 36 patients in our clinic. We assessed the age, gender, symptoms, spot urine porphobilinogen, the family history, and the general metabolic changes in these patients in terms of internal diseases between the years 2010 and 2023.

Findings: Out of 36 patients, 25 females and 11 males were evaluated. The average age of all the patients is 36.11 (SD: 16.174). Maximum age: 70, minimum: 8. Eight patients were reported to have first-degree relatives diagnosed with porphyria, and five patients had second-degree families as well. The most common symptom among the patients was abdominal pain in 18 patients, and the least common was dyspepsia in 1 patient. In 23 patients, the spot urine porphobilinogen was detected as positive, 4 patients were negative, and 9 patients were not tested. Out of 5 subtypes in hepatic porphyria, we report 20 with AIP, 7 with HCP, 6 with VP, and 1 with PCT, but no patients with the subtype ALAD. However, we report 1 patient with HEP, as hepatic symptoms are common in this type.

Conclusions: Spot urine porphobilinogen is the key to diagnosing porphyria. Knowing the symptoms is crucial to detecting these patients, and with early diagnosis and effective treatment, help prevent the major metabolic side effects as well as increase the life quality of the patients.

Keywords: *porphyria, hepatic porphyria, statistics*

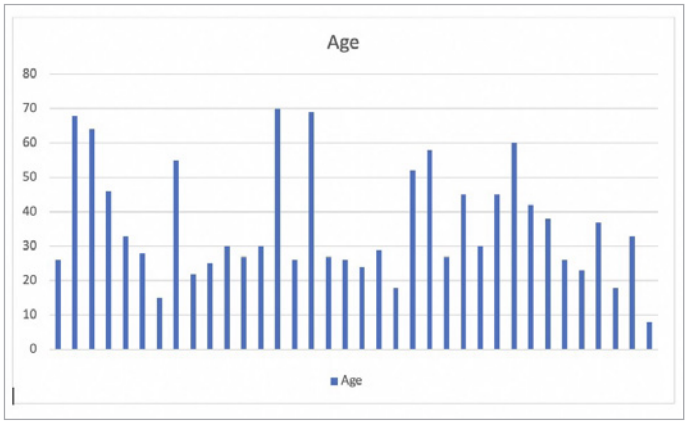

Figure 1. *Age Distribution.*

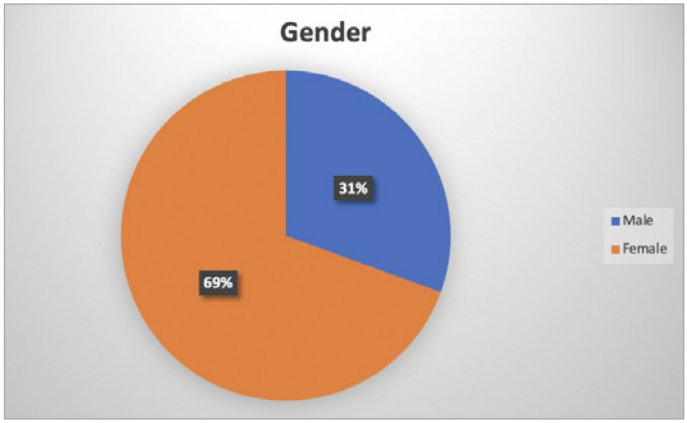

Figure 2. *Gender Distribution.*

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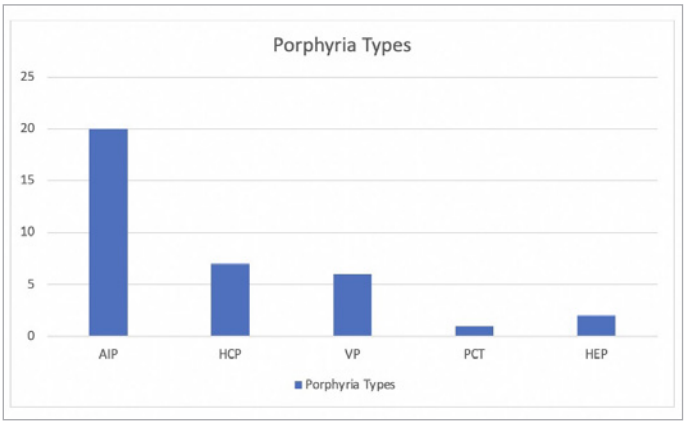

Figure 3. *Porphyria Subtypes.*

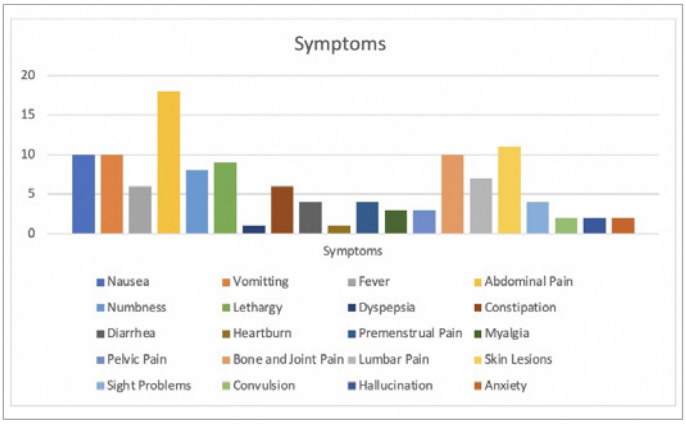

Figure 4. *Symptoms.*

[Abstract:2208]

INFLAMMATORY ORBITAL PSEUDOTUMOR REVEALING BEHCET'S DISEASE

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Objective: To provide an original observation of Behçet's disease revealed by an inflammatory pseudotumor of the orbit.
Methods: We report an observation of an inflammatory pseudotumor of the orbit revealing Behçet's Disease.
Results: Twenty-eight years old patient was admitted in internal medicine department for painful right eye oedema with headache and loss of visual acuity.
Ophthalmologic examination showed eye protrusion with conjunctival hyperaemia. Orbital MRI concluded that there was a periorbital inflammatory thickening associated with inflammatory myositis. The diagnosis of Behçet's disease was retained based on history of recurrent oral aphthous since childhood, pseudo folliculitis, pathergy test positivity and negativity of the rest of the aetiological investigations. The evolution was spectacular with boli methylprednisolone and colchicine prescription.
Conclusions: Although the association is rare, Behçet's disease should be included in the workup of inflammatory pseudotumor of the orbit.

Keywords: *Behçet's disease, inflammatory pseudotumor, corticosteroids*

[Abstract:2252]

UVEITIS AND MULTIPLE SCLEROSIS

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Introduction: The association of uveitis and multiple sclerosis is rarely described. The etiopathogenic mechanism is still unknown, for the clinical features, it can be widely various.
Methods: We report three original cases of uveitis associated to multiple sclerosis.
Results: Case 1: 18-year-old patient who presented an asymptomatic bilateral intermediate uveitis occurring during a relapse of multiple sclerosis. Treatment was with corticosteroids with clear improvement.
Case 2: 29-year-old patient who presented a unilateral panuveitis. Etiological assessment was negative and the patient was treated with oral corticosteroids with clear improvement
Case 3: 27 year old patient who presented with unilateral anterior uveitis. The patient received topical corticosteroids. The patient presented then recurrent bilateral intermediate uveitis. The corticosteroids were efficient at every episode.
Conclusions: Uveitis in multiple sclerosis occurs with different forms. Intermediate uveites and periphlebitis are the most common. We didn't find specific clinical or evolutionary features of multiple sclerosis or uveitis which could predict the evolution of both diseases but it is now confirmed that this association has a good visual prognosis.

Keywords: *multiple sclerosis, uveitis, ophthalmology*

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[Abstract:2300]

TAFRO SYNDROME; A SEVERE TYPE OF IDIOPATHIC MULTICENTRIC CASTLEMAN'S DISEASE; CASE REPORT

Abir Cherif, Mohamed Salah Hamdi, Meriem Jebri, Wiem Ben El Hadj, Samira Azzabi, Eya Cherif, Imen Boukhris, Ines Kechaou, Lamia Ben Hassine

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Background: TAFRO syndrome (thrombococytopenia, anasarca, fever, renal involvement, organomegaly) is a severe entity of idiopathic multicentric Castleman's disease (iMCD), which is rarely reported in literature. We herein present a case.

Case Presentation: A 61-year-old male with history of pernicious anaemia, gastric carcinoid tumour and pulmonary embolism, presented with fever, cough and dyspnoea. Physical examination revealed swollen cervical, supraclavicular, axillary, and inguinal lymph nodes, ascites and pitting oedema of the legs. Blood workup revealed elevated inflammatory markers, hypoalbuminemia, anaemia, thrombocytopenia, cholestasis, and elevated creatinine levels. Screening for Tuberculosis was negative on multiple occasions. Body Computed-Tomography (CT) Scan showed pleural, pericardial and abdominal effusion, hepatosplenomegaly and swollen mediastinal lymph nodes. Lymph node biopsies were consistent with Castleman's disease in its hyaline-vascular type. Kidney biopsy showed thrombotic microangiopathy, membranoproliferative glomerulonephritis and lesions of tubular necrosis. Therefore, the diagnosis of iMCD was established in its form TAFRO.

Patient was treated with furosemide and prednisone with no response. Hence the necessity of second-line treatment with Tocilizumab. Throughout the course of treatment, the swollen lymph nodes disappeared, and blood workup was close to normal. As the patient discontinued his treatment, polyserositis exacerbated uncontrollably. Patient was deceased within one year of the diagnosis.

Conclusions: In conclusion, due to its high mortality rate, all physicians and not only rheumatologists should be aware of the TAFRO syndrome, especially since a rapid diagnosis and early treatment are the key for survival.

Keywords: *idiopathic multicentric Castleman's disease, TAFRO, tocilizumab, polyserositis, polyadenopathy*

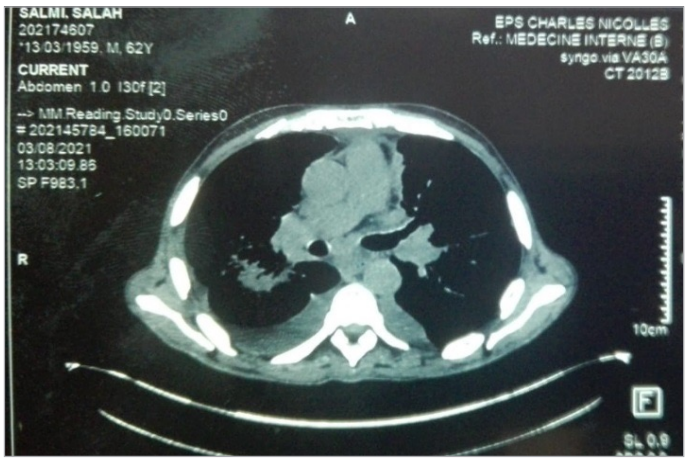

Figure 1. *Chest CT, mediastinal window. Mediastinal lymphadenopathies.*

[Abstract:2301]

IDIOPATHIC MULTICENTRIC CASTLEMAN DISEASE CO-EXISTING WITH ADULT ONSET STILL DISEASE: CASE REPORT

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Background: Multicentric Castleman's disease is a rare lymphoproliferative disorder. Depending on its presentation, it can mimic a myriad of other inflammatory diseases, making the diagnosis rather challenging. We herein present an example.

Case Presentation: A 16-year-old female with no medical history presented with fever, asthenia, weight loss and debilitating polyarthralgia. Physical examination revealed polyarthritis, diffuse enlarged lymph nodes, pharyngitis and a transient salmon-pink maculopapular rash. Blood workup showed elevated inflammatory markers and liver enzymes, severe anaemia, glycosylated ferritin of <20% and negative anti-nuclear antibodies and rheumatoid factor. Computed Tomography (CT) scan showed poly lymphadenopathy, hepatosplenomegaly and no mediastinal mass. Immunophenotyping test and bone marrow biopsy were normal. Systemic infections were ruled out as well.

The first lymph node biopsy was normal, raising the suspicion of adult onset still disease (AOSD). A second biopsy showed Castleman-like lesions. And a third biopsy concluded to Castleman's disease in its hyaline-vascular type. HIV test was negative, thus the confirmation of idiopathic multicentric Castleman's disease (iMCD).

According to the Yamaguchi diagnostic criteria of AOSD, inflammatory diseases, such as Castleman's disease, are a criterion of exclusion. On the other hand, our patient fills out all the criteria of Fautrel. Therefore, we considered that she had co-existing iMCD and AOSD. The patient didn't respond to steroids alone nor in association to methotrexate. Tocilizumab

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however, offered complete remission: fever, polyarthritis and poly-lymphadenopathy disappeared, and blood workup was close to normal.

Conclusions: There have been reported cases in literature of iMCD mimicking AOSD, but no co-existence was reported.

Keywords: idiopathic multicentric Castleman's disease, adult onset still disease, tocilizumab, polyadenopathy, polyarthritis, glycosylated ferritin

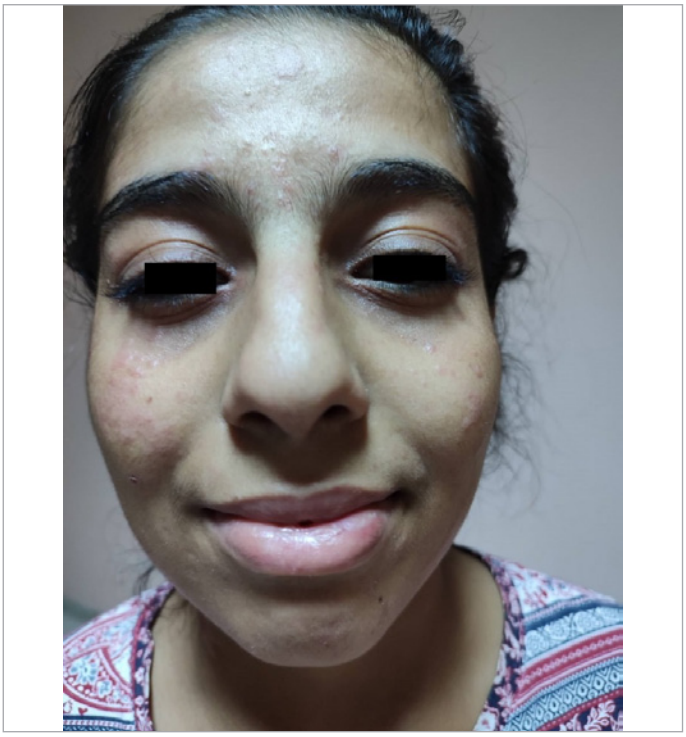

Figure 1. *Salmon-pink maculopapular rash.*

[Abstract:2307]

AN EXTENSIVE FORM OF EOSINOPHILIC FASCIITIS: A DIAGNOSTIC CHALLENGE

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Background: Diffuse fasciitis also known as eosinophilic fasciitis or Shulman Disease is a rare condition affecting of the fascia characterized by fibrosis and inflammation with frequent eosinophilia. We herein present a case of extensive eosinophilic fasciitis.

Case Presentation: A 71-year-old woman with no medical history presented with oedema of the limbs and face. Physical examination revealed diffuse palpable infiltration and induration of the subcutaneous tissue of the arms, legs, abdomen, and breasts with a shiny skin. Groove sign was present as she had a depression along the course of superficial veins of the arms and legs more marked on elevation of the limbs. She had pigmented skin lesions of irregular shape, and her joints movement were restricted. Eosinophil count was initially of 360/mm^3 and reached 1200/mm^3 a few months later. Immunology and radiology workup were normal.

Deep skin biopsy showed important fibrous thickening of the muscular fascia and inflammatory infiltrate largely made up of lymphocytes with presence of plasma cells and neutrophils, and absence of eosinophils. The patient was therefore diagnosed with Shulman's disease and was prescribed 30 mg per day of prednisone. Given the absence of response, the patient was started on Methotrexate at the dose of 15 mg per week. We observed partial relief of clinical symptoms within three months.

Conclusions: Shulman Disease manifests as diffuse fasciitis with or without eosinophilia. In either case, it presents with a bilateral sclerosing oedema of the limbs without symptoms of systemic sclerosis. It is clinically suspected and histologically confirmed.

Keywords: Shulman's disease, diffuse fasciitis with or without eosinophilia, methotrexate

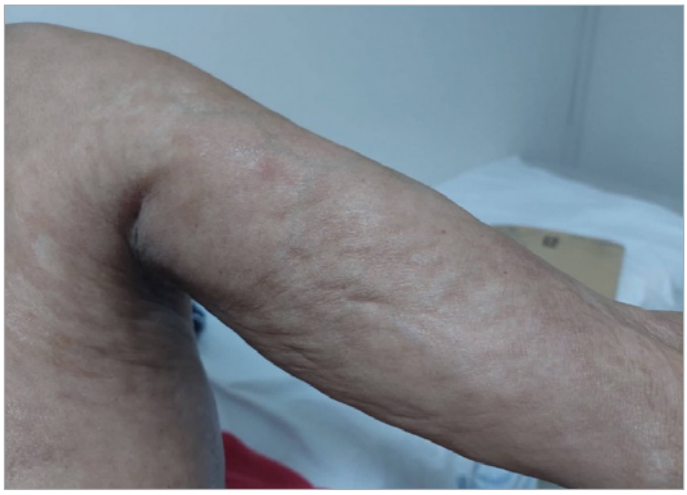

Figure 1. *Groove sign.*
Linear depression along the course of the veins on the arm, better visualized with the arm elevated.

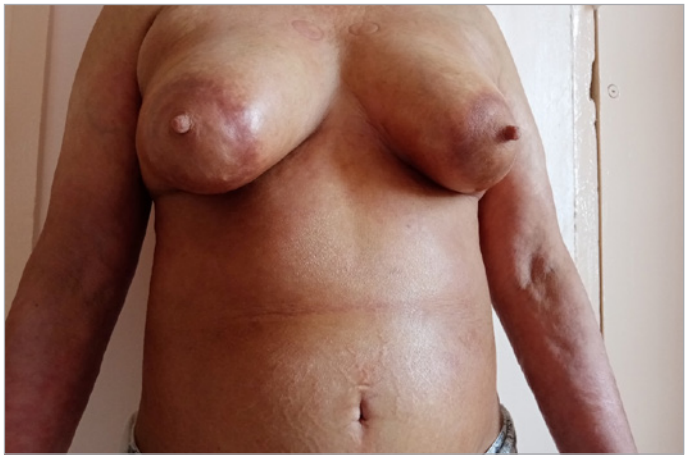

Figure 2. *Shulman's disease.*
Extensive induration and infiltration of the skin.

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[Abstract:2341]

RIFAXIMIN INDUCED STEVEN JOHNSON SYNDROME - FIRST CASE IN MIDDLE EAST

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Case Description: We present a case of Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) associated with Rifaximin use. This is the first case in the middle east and 3rd case in the world, based on our extensive search. Patient was a 55 year old female, known to have diabetes, hypertension and newly diagnosed liver failure due to NASH. She was started on Rifaximin, Furosemide, Spironolactone and lactulose for decompensated liver failure and prepared for liver transplant by her Gastroenterology team.

She developed erythematous rash localized to bilateral inner thighs one week after starting her medications. She was treated with topical and systemic steroid and discharged on topical steroid and topical zinc oxide. Rifaximin was continued during this time. Four weeks later patient was admitted to our hospital with diffuse skin rash with bullae involving mucosal surfaces.

Diagnostic Pathways: She underwent skin biopsy by dermatology that confirmed SJS/TEN. We reviewed all her medications and other potential exposures to identify the culprit trigger. After discussions with Dermatology and Pharmacology teams we identified that patient had never been exposed to rifaximin prior to recent initiation. She had used rest of her medications in the past without any side effects. Unfortunately, patient continued to deteriorate and passed away after two weeks of hospitalization.

Discussion and Learning Points: There is a paucity of data about rifaximin and SJS/TEN in cirrhotic patients. We report this case to increase the awareness about this association. SJS/TEN are lethal if not treated aggressively as soon as suspected.

Keywords: *Steven Johnson syndrome, rifaximin, toxic epidermal necrolysis*

[Abstract:2352]

THE IMPORTANCE OF HISTOPATHOLOGICAL DIAGNOSIS

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A 73-year-old woman with arterial hypertension, type 2 diabetes mellitus and dyslipidaemia, polymyalgia rheumatica and chronic idiopathic thrombopenia under follow-up by haematology and treatment with Romiplostim. He started with iron deficiency anaemia in transfusion range and constitutional syndrome, so abdominal CT scan was requested, describing pathological supra and infradiaphragmatic lymphadenopathies and splenomegaly of 17 cm with hypodense nodules. Screening for a possible hematologic origin (reticulocytes, coombs, haptoglobin, LDH, bilirubin, smear, proteinogram) was requested due to the suspicion of myeloproliferative syndrome, including splenic and bone marrow biopsy, both anodine, so EBUS was performed on the thoracic lymphadenopathies, which was negative. The clinical deterioration was progressive, added to the lack of results to guide the clinical picture. It was decided to extend the differential diagnosis and request tests to rule out autoimmune or infectious origin. Among them: autoimmunity study with ANA, ANCA, ENA; mycobacterial screening with Mantoux, QuantiFERON, Lowenstein culture, PCR in the biopsies performed; serology of hepatotropic viruses, cytomegalovirus, parvovirus, HIV; cat scratch disease, and leishmania. While awaiting the results, the anaemia and thrombopenia were accentuated, and data of non-immune haemolysis appeared, which were attributed to a possible splenic sequestration. In this context, haematology, Internal Medicine and Surgery met in a clinical committee and decided to perform a diagnostic and therapeutic splenectomy. Finally, the histopathological report revealed a diffuse proliferation of cells with abundant eosinophilic cytoplasm with vacuoles and nucleoli as well as occasional hemophagocytosis with immunhistochemical expression for CD68 and CD4, compatible with histiocytic sarcoma.

Keywords: *anaemia, splenomegaly, histiocytic sarcoma*

[Abstract:2357]

FOLLOWING THE CLUES UNTIL REACHING THE DIAGNOSIS: AN UNDERDIAGNOSED ETIOLOGY FOR CONGESTIVE HEART FAILURE

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Case Description: A 83-year-old female with a history of hypertension, type 2 diabetes mellitus, chronic heart failure (HF) with preserved ejection fraction and left ventricular hypertrophy (LVH) presented to Internal Medicine ward with signs of HF, new-onset atrial fibrillation, and orthostatic hypotension. The patient reported paresthesias in both hands. The chest X-ray revealed cardiomegaly. Laboratory results showed increased creatinine (1.8 mg/dL), NT-proBNP (2455 pg/mL), and troponins (112 ng/mL). EKG was on atrial fibrillation.

Clinical Hypothesis: Cardiac amyloidosis.

Diagnostic Pathways: Secondary AA and AL amyloidosis were reasonably ruled out thanks to directed blood tests. A whole-body scintigraphy with technetium-99 was consistent with a Perugini scale grade 3, highly suggestive of transthyretin amyloidosis (ATTR). Genetic testing was negative, indicating a wild-type variant.

Discussion and Learning Points: ATTR is an underdiagnosed condition with hereditary and wild-type variants, the latter one

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often overlooked. Essential diagnostic tools include a scintigraphy with technetium-99, demonstrating high negative predictive value via the Perugini scale. Early identification facilitates timely intervention, such as treatment with tafamidis. Key clinical indicators include bilateral carpal tunnel syndrome, unexplained chronic kidney disease, LVH in non-hypertensive patients, labile blood pressure, and orthostasis. Increased clinical suspicion could enhance the incidence and diagnosis of ATTR, leading to improved patient prognosis.

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1. Obi CA et al. ATTR Epidemiology, Genetics, and Prognostic Factors. Methodist Debakey Cardiovasc J. 2022 Mar 14;18(2):17-26.
2. Nativi-Nicolau JN et al. Screening for ATTR amyloidosis in the clinic: overlapping disorders, misdiagnosis, and multiorgan awareness. Heart Fail Rev. 2022 May;27(3):785-793.

Keywords: *heart failure with preserved ejection fraction, scintigraphy, amyloidosis*

[Abstract:2358]

FAMILIAL REPRESENTATION AND INHERITANCE OF PORPHYRIA CUTANEA TARDA

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Porphyria is a group of diseases that occur with a deficiency or mutations of the enzymes that synthesize heme. Porphyria cutanea tarda (PCT) occurs with heterozygosity in uroporphyrinogen decarboxylase (UROD) enzyme, and is also one of the most common subforms of the porphyria disease family. PCT presents generally as sporadic, but about 20–30% of patients have familial-PCT (F-PCT), and unlike sporadic, it concerns all tissues unlike sporadic PCT which only affects the liver. Cutaneous findings of sun sensitivity lesions, crust, milia, pigmentations, erosions, blisters, and hyperthyroidism are seen as symptoms in patients.

In this case report, we present two Azerbaijani siblings aged 2 and 8 that carry UROD gene mutation [c.536G>C (p.Arg179Pro)] and were consulted to us for clinical confirmation of PCT. The 8-year-old had scarring on cheeks and dyspigmentation on ears accompanied by nausea, headache and itching after sun exposure. He suffers from diarrhoea on a daily basis. The 2-year-old also complains from diarrhoea and periorbital erythema. Similarly, discolorations are present on face. Both tested positive for urine porphobilinogen.

This case report exhibits a familial representation of the mutated UROD gene with clinical exacerbations expected with PCT. Through this work, a clear representation of F-PCT is displayed to aid in clinical setting.

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Shah A, Bhatt H. Cutanea Tarda Porphyria. 2023 Apr 17. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: 33085356.
Frank J, Poblete-Gutiérrez P. Porphyria cutanea tarda--when skin meets liver. Best Pract Res Clin Gastroenterol. 2010 Oct;24(5):735-45. doi: 10.1016/j.bpg.2010.07.002. PMID: 20955974.

Keywords: *porphyria cutanea tarda, uroporphyrinogen decarboxylase, hepatoerythropoietic porphyria*

Figure 1. *A.A. age 2, left cheek.*
Scarring and dyspigmentation accompanied by erythematous rash on the left cheek and ear.

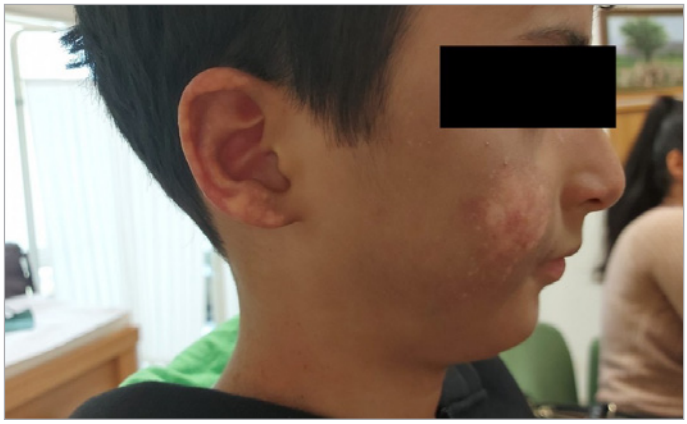

Figure 2. *Y.A. age 8, right cheek.*
Scarring and dyspigmentation on the cheek and ear accompanied by blisters and erythematous rash.

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[Abstract:2384]

WEAKNESS AND FATIGUE. IS IT ALWAYS THE MUSCLES?

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Case Description: A 40 year old female patient consulted in emergencies relating daily episodes of fatigue, weakness and dysphonia in the last five years, getting worse and worse in the last months. These episodes improved after resting, so she had given up progressively exercise first and her daily routine afterwards. She had no medical background. Physical examination revealed was normal. No abnormal findings were found in blood test.

Diagnostic Pathways: Multiple tests were performed in order to rule out endocrine diseases (thyroid function, urine catecolamines, plasma metanephrines, 24h urine cortisoluria, 5-hydroxyindole acetic acid), neurologic diseases (neurophysiological study, MRI, genetic tests) and neoplastic diseases (full body CT scan). After all these tests, the only abnormality found was a persistent low level of alkaline phosphatase. A genetic test revealed a pathogenic variant (c.1135C>A, p.H379N) in the ALPL gen, confirming the diagnosis of hypophosphatasia.

Discussion and Learning Points: Hypophosphatasia is an uncommon inborn metabolic disorder identified by reduced serum alkaline phosphatase activity resulting from loss-of-function mutations in the gene encoding the enzyme. In adults, hypophosphatasia may manifest through fractures, particularly in the metatarsal and femoral regions, as well as crystal-associated joint disorders. Nevertheless, it can also manifest as fatigue, weakness, and muscular symptoms that worsen with exertion. The patient began treatment with asfotase alfa, via subcutaneous administration. The progress was remarkable, showing improvement on all fronts, both subjectively and in terms of strength as demonstrated by dynamometry. Since then, she has regained her functionality and is able to perform her usual activities.

Keywords: *hypophosphatasia, weakness, fatigue*

[Abstract:2425]

LATE DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS IS STILL ENCOUNTERED: CASE REPORT

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We describe a case of systemic lupus erythematous in a young female, with atrophic-scarring lesions, and posterior ulcerations of the chest, abdomen, limbs, and hard palate, Raynaud syndrome and alopecia, evolving for more than 24 months. The blood results showed a mild inflammatory syndrome, leukopenia, thrombocytopenia, anaemic syndrome, nephrotic syndrome-proteinuria 4.5 g/24 hours, hypocomplementemia C3 of 10 mg/dL, electrophoresis of serum proteins with hypergammaglobulinemia, hyper IgG, kappa and lambda light chains and positive Coombs test. The lupus autoantibody panel was positive for ANA in a significant titer, for anti-dsDNA, anti-Sm, anti-SS-B and anti-SS-A antibodies—the skin biopsy described- discoid lupus-like lesions. Paraclinical examinations identified pleuritis, pericarditis and malignant arterial hypertension. Pulse therapy with methylprednisolone followed by Cyclophosphamide was prescribed. Later, Hydroxychloroquine and Mycophenolate Mofetil were added. Renal biopsy punction was postponed due to severe thrombocytopenia. Therefore, pulse therapy with Rituximab was initiated. Later the renal biopsy showed class IV lupus nephropathy (ISN/RPS 2003). The patient fulfilled the EULAR/ACR criteria 2019, severe active form with SELENA-SLEDAI of 24 points, and Damage Index SLICC/ACR of 13 points. The unfavourable evolution led to the initiation of Belimumab and the left kidney transplant.

Keywords: *systemic lupus erythematous, anti-dsDNA, anti-Sm, class IV lupus nephropathy*

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[Abstract:2453]

AUTOIMMUNE HEMOLYTIC ANAEMIA, SPLENOMEGALY AND FAMILY HISTORY: WHEN AUTOIMMUNE DISEASES AND GENETICS FIND EACH OTHER

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Case Description: We discuss the case of a 36-year-old female patient with past medical history of mixed-aetiology anaemia: pernicious anaemia, iron deficiency and autoimmune haemolytic anaemia (AIHA) with a positive direct Coombs test (DCT) for IgG and C3d. Besides a 20 cm splenomegaly, no other significant findings were noted in further investigations. Family history includes a twin sister with pernicious anaemia, positive DCT for IgG and C3d and splenomegaly; another brother with systemic lupus erythematosus (SLE), pernicious anaemia and splenomegaly; and the mother with pernicious anaemia and splenomegaly. Our patient experienced a third admission due to AIHA. Analytically, hypocomplementemia, C-reactive protein around 11 mg/L and positive antinuclear antibodies (ANA) at a titer of 1/160 (cytoplasmic pattern) with anti-U1-RNP and P-ribosomal specifies were found. Parenteral corticosteroid therapy was given followed by oral prednisone tapering to 30 mg daily.
Clinical Hypothesis: Autoimmune Lymphoproliferative Syndrome (ALPS).
Diagnostic Pathways: - T-cell immunophenotyping: 5.2% double-negative CD4-CD8 αβ T cells (DNT).
- Genetic study positive for p.Thr344Met variant in the FOXP3 gene, also found in patient's mother and sister.
Discussion and Learning Points: The typical presentation of ALPS involves autoimmune cytopenias and familial splenomegaly. Diagnosis involves demonstrating lymphocyte apoptosis impairment, DNT cell presence in immunophenotyping, and genetic studies detecting FAS gene mutations. Its association with systemic autoimmune diseases like SLE is exceptional. Literature review revealed a case associated with FOXP3 gene (p.Pro75Leu variant).

References:
Rais A et al. Case: FOXP3 Mutation in a Patient Presenting With ALPS. Front. Immunol. 2021; 12:692107.

Keywords: *systemic lupus erythematosus, autoimmune hemolytic anaemia, splenomegaly*

[Abstract:2456]

UNCOMMON PRESENTATION OF GASTROINTESTINAL SYMPTOMS: NAVIGATING THE DIAGNOSTIC CHALLENGE IN A CASE OF INFLAMMATORY DIARRHEA

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A 40-year-old male with a history of remission from diffuse B-lymphoma IIIS, presented with inflammatory diarrhoea accompanied by hematochezia, right hypochondrial pain, fever and rapid 10 kg weight loss over three weeks. The patient resided in Western Europe and had not travelled to tropical countries in recent years. Blood tests revealed elevated acute phase reactants and liver enzymes. The microbiological and serological studies were negative. Antibiotic therapy yielded no improvement. Computed tomography disclosed panproctocolitis with necrotic adenopathies, while colonoscopy identified punch ulcers in the colon. Biopsies of both the colon and ileocolic adenopathies confirmed infiltration by large B-cell lymphoma, germinal centre phenotype, indicative of a relapse of the prior lymphoma. The patient was promptly referred to Hematology, initiating chemotherapy.
In he realm of inflammatory diarrhoea, commonly attributed to infectious, inflammatory bowel disease, or ischemic colitis, a critical differential diagnosis was conducted, focusing on distinguishing between intestinal tuberculosis and a lymphoma relapse. Intestinal tuberculosis typically manifests with ileocecal involvement, abdominal pain, diarrhoea and lower gastrointestinal bleeding. Diagnostic confirmation involves visualizing the microorganism in intestinal biopsies or observing characteristic alterations in lymph node biopsies. Although gastrointestinal tract lymphomas are infrequent, the diffuse large cell type B predominates. Symptomatically mirroring intestinal tuberculosis, lymphoma diagnosis requires biopsy, as endoscopic imaging lacks specificity.
Given the rarity and severity of primary intestinal lymphomas, early diagnosis and treatment is imperative.

Keywords: *inflammatory diarrhoea, intestinal lymphoma, intestinal tuberculosis*

[Abstract:2461]

A RARE CAUSE OF CHRONIC DIARRHEA: VIPOMA

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Introduction: Pancreatic vasoactive intestinal peptide-producing tumour (VIPoma) is rarely observed. Typically, this syndrome is characterized by diarrhoea, hypokalemia, hypercalcemia, and

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achlorhydria/acidosis. Here, we will present a case of an individual who has been experiencing chronic diarrhoea for eight months and presented to the emergency department with a clinical picture of prerenal acute kidney injury.

Case Presentation: A 52-year-old female patient was brought to the emergency department with complaints of nausea, vomiting and 3-5 episodes of diarrhoea per day. Emergency department investigations revealed acidosis, hypokalemia, and hypercalcemia. The patient, evaluated as having a prerenal acute kidney injury secondary to diarrhoea, was admitted for further investigation and treatment. The patient had no known chronic illnesses or history of medication use in her medical background.

Clinical Progress: The prerenal acute kidney injury improved with intravenous fluid replacement. During follow-up, it was observed that the patient had persistent hypokalemia. Considering the patient's history, a 24-hour urine collection for 5-HIAA, VMA, HVA, and serum VIP levels was sent. The serum VIP level was >120 pmol/L. A Ga68-DOTATATE PET-CT was requested for the patient, revealing a 43x34 mm hypermetabolic lesion in the pancreatic body/tail.

Conclusions: The diagnosis of pancreatic neuroendocrine tumours, which are rare but significant aetiologies of chronic diarrhoea, is often challenging through routine investigations. Almost all patients require examination with Ga-68 dotatate PET-CT for the diagnosis of the disease. It is essential for this examination to be considered that the disease is included in the differential diagnosis through a detailed medical history.

Keywords: *diarrhoea, VIPoma, Ga-68 dotatate*

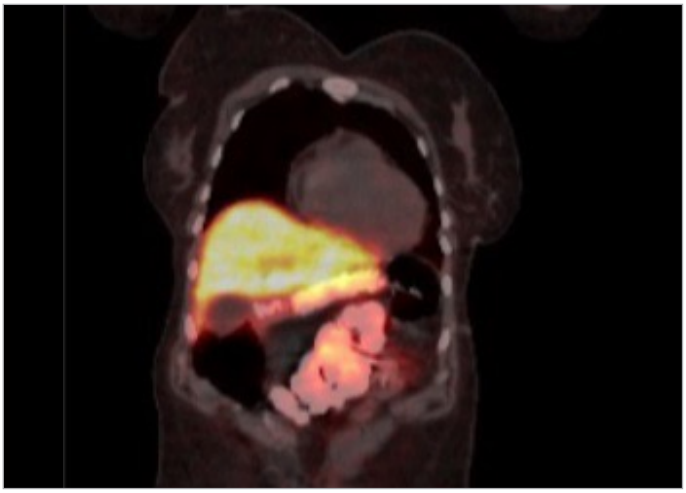

Figure 1. *Mass lesion observed at the pancreatic body/tail junction (SUVmax: 66).*

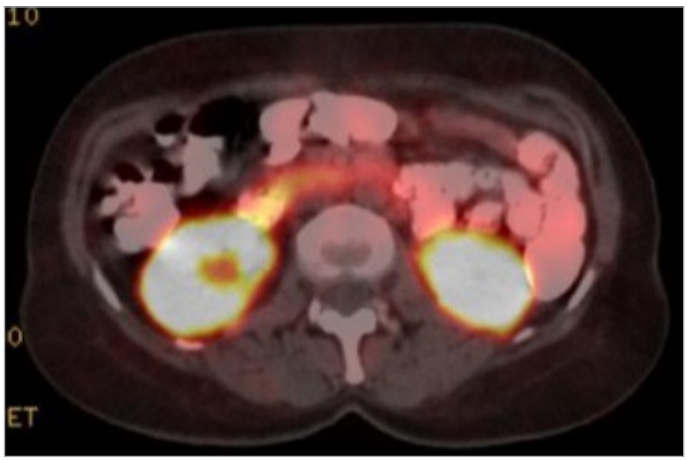

Figure 2. *Mass lesion observed at the pancreatic body/tail junction (SUVmax: 66).*

[Abstract:2467]

THE CLINICAL CHALLENGE OF LIVER INJURY IN A PATIENT WITH ANAEMIA AND EOSINOPHILIA

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A 36-year-old woman presented for evaluation of iron deficiency anaemia associated with fatigue, dizziness, abdominal pain, occasional itching, poor sleep and diarrhoea alternating with constipation. Her symptoms became worse in the last three months. The patient was known with anaemia and diabetes mellitus for seven years, both identified during pregnancy monitoring (HbA1C 6,5%%, Hb 7.7 g/dl) associated with eosinophilia (27%, 2520/µL) and thrombocytosis (620 x10^3/µL). She didn't receive any iron supplements for 2 years, and the serum iron (1.73 µmol/L) and ferritin (2.13 ng/ml) levels were low all these years. On sonography multiple, small, oval hypoechoic lesions in the liver parenchyma were identified, described as suggestive for liver metastasis. Standard gastrointestinal endoscopic study (upper endoscopy, colonoscopy) revealed no gastrointestinal lesions. The rapid urease test for H. pylori was negative. Serological tests were also negative for echinococcosis and giardiasis, but were strongly positive for toxocariasis (*Toxocara canis* Ig G) and ascariasis (Ascaris lumbricoides IgG). On MR imaging with contrast hepatic lesions were seen as multiple (12), ill-defined, oval lesions with a diameter of 0.6–1.5 cm in S4, S8, S7 segments, best seen on the portal venous phase (fig. 1).

Conclusion The imaging findings of toxocariasis may be similar to those of hepatic metastases, but they differ in that the hepatic

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nodules in toxocariasis have indistinct margins, are subtle, uniform in size, non-spherical in shape, and are best seen on MR images of the portal venous phase. Together with serological testing, this contributed to the accurate diagnosis in our case.

Keywords: *anaemia, iron-deficiency, eosinophilia, visceral larva*

[Abstract:2472]

LATE-ONSET VS LATE DIAGNOSIS OF CLASSIC HOMOCYSTINURIA

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A 50-year-old male presented with a holocranial headache, vomiting, and photophobia over the past 48 hours. Pain exacerbated by valsalva. No other associated clinical symptoms were observed. General and neurological examinations were normal.

An urgent brain CT revealed thrombosis of the right sinuses and the patient was admitted to the Neurology department and started on anticoagulation therapy.

He was a former smoker. Medical history included an unprovoked extensive deep vein thrombosis in February 2023, treated with Enoxaparin for 3 months. Additionally, the patient had undergone surgery for myopia magna 20 years ago and was under ophthalmological follow-up for bitemporal crystalline lens subluxation.

Family medical history was remarkable for an aortic aneurysm and a provoked pulmonary embolism in his father at the age of 70. Blood analysis revealed a mild vitamin B12 deficiency (112 pg/mL [normal range 150-800]) without methylmalonic acid alterations and severely elevated homocysteine (229 umol/L [normal range 0-15]), with no other significant findings. Further assessment revealed elevated plasma methionine (61 umol/L [normal range 20-37]) and small decreased cystine (28 umol/L [normal range 34-76]). Given the suspicion of classical homocystinuria, we started treatment with B12 vitamin supplementation, protein-restricted diet and betaine 2gr every 8 hours.

The patient was referred to a centre of expertise in rare diseases. Genetic testing for cystathionine beta synthase deficiency showed homozygous mutation for the c.1330G>A variant.

After diagnosis, treatment with pyridoxine and folate was added and successfully decreased homocysteine levels with no new symptoms.

Keywords: *inborn errors of metabolism, rare diseases, thrombosis*

[Abstract:2525]

CLINICAL PROFILE AND A ETIOLOGICAL FACTORS OF CHRONIC PULMONARY ARTERIAL HYPERTENSION IN AN INTERNAL MEDICINE DEPARTMENT

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Objective: Our aim is to determine the clinical characteristics, review the main an aetiologies and treatment modalities of patients with chronic thromboembolic pulmonary hypertension (CTEPH).

Methods: Prospective collection including patients newly diagnosed for CTEPH in internal medicine departments, over the last 7 years (2014-2022).The diagnosis of precapillary PH was confirmed by right heart catheterization, non-concordant perfusional defects on lung scintigraphy and chronic thromboembolic lesions on thoracic angioscanner. A deobstruction procedure couldn't be carried-out for patients who required it. They were instead offered a specific treatment for PH in addition to conventional treatment.

Results: Among 130 cases of PH of multiple causes, we identified 22 patients with CTEPH, with a median age of 43 years, sex ratio M/F=0.15. Half the cases had a history of chronic thromboembolic disease (CTED), with comorbidities in 20%. The most frequently identified thrombotic risk factor is the antiphospholipid antibody (36%), followed by the factor V Leiden mutation (9%) and protein S deficiency (5%). Symptoms are dominated by dyspnoea, with a reduction in 6 min walking test distance to under 250 m (20%).

Nearly half the patients presented with proximal involvement, bilateral location (32%), and severe haemodynamic parameters (35%). Specific treatment was initiated in all our patients with a fairly satisfying evolution and a death rate of 13% (3).

Conclusions: Delayed diagnosis of CTED exposes patients to the risk of developing CTEPH, whose prognosis is linked to the earliness and methods of management, including the development of vascular surgery dedicated to the lungs.

Keywords: *chronic thromboembolic pulmonary hypertension, pulmonary embolism, thromboembolic disease*

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[Abstract:2552]

DIAGNOSTIC CHALLENGES: JOURNEY INTO PROGESTERONE HYPERSENSITIVITY - AN INTRIGUING CLINICAL CASE OF RECURRENT CUTANEOUS LESIONS

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Case Presentation: A 30-year-old female, referred from Primary Care to Internal Medicine, presents with recurrent cutaneous lesions. No known drug allergies or significant medical history, except for adenoidectomy and tonsillectomy. An administrative professional residing in an urban setting, she previously used oral contraceptives. Symptoms initiated in 2020, comprising week-long episodes preceding menstruation, resolving with menstrual onset. Episodes involve asthenia, fever (up to 38°C), erythematous-edematous plaques on lower limbs (1-3 cm), painful with residual hyperpigmentation, and right iliac fossa pain. Despite evaluations by Gastroenterology, General Surgery, Pain Management, and Gynecology, a diagnosis proved elusive. Pain management with NSAIDs, Paracetamol, and topical Capsaicin was suboptimal. Imaging studies (abdominal ultrasound, CT, enteric resonance, and calprotectin assays) yielded no significant findings. Internal Medicine evaluation showed negative autoimmune tests but a notable erythrocyte sedimentation rate (ESR) of up to 97 mm/h during episodes. Biochemistry, complete blood count, coagulation, porphyrins, and proteinuria were normal. PET-CT revealed no pathology. Genetic testing for autoinflammatory diseases was negative. Skin biopsy suggested progesterone-induced autoimmune dermatitis.

Diagnostic Pathway: Progesterone hypersensitivity – a heterogeneous condition with cutaneous and/or systemic allergic reactions associated with exogenous and endogenous progesterone. Manifestations commonly cutaneous, but can include anaphylaxis and/or asthma. Treatment initiated with antihistamines showed partial improvement, followed by oral contraceptives with positive outcomes. This case highlights diagnostic challenges and underscores the complexity of progesterone-related hypersensitivity.

Keywords: *progesterone, hipersensitivity, rare diseases*

[Abstract:2561]

CARDIAC INVOLVEMENT IN HYPEREOSINOPHILIC SYNDROME: A CASE REPORT AND LITERATURE REVIEW

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Introduction: The hypereosinophilic syndromes (HES) are defined by the association of a sustained an absolute eosinophil count (AEC)> 1500/mm^3 over a month with eosinophil-mediated organ damage and/or dysfunction. Although the Cardiac involvement is rare, it is the leading cause of mortality. Thus all patients with HES should underwent cardiac screening.

Methods: We report a case of a 46-year-old woman who was admitted to our hospital due to hypereosinophilia.

Results: A 46-year-old woman who was admitted to our hospital due to a sustained major hypereosinophilia. Physical exam revealed a swollen face, oedema in four limbs and urticaria.

Laboratory findings showed hyperleucocytosis with hypereosinophilia, blood smear: EPN 32%.The diagnostic workup of the HE was negative. A cardiac MRI was performed objective a non-ischemic pattern myocardial fibrosis in the LV. The patient was started on oral glucocorticoids with significantly improve of her symptoms and rapid normalisation of the eosinophilic count.

Conclusions: Hypereosinophilia can affect any tissue individually or in combination, an investigation workup is essential to look for organ damage. Cardiac involvement should ruled out by performing an EKG, a TTE and if needed a cardiac MRI.

Keywords: *Gougerot-Sjogren, neurology, prognosis, inaugural*

[Abstract:2571]

VON RECKLINGHAUSEN'S DISEASE: A CASE REPORT AND LITERATURE REVIEW

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Introduction: Von Recklinghausen's disease is an autosomal dominant genodermatosis caused by a mutation in the NF1 gene encoding for Neurofibromin, affecting growth and differentiation. The disease has near-complete penetrance, but clinical expression varies widely.

Observation: Patient M.B, with unaffected parents, was diagnosed based on 04 out of 07 revised NIH criteria (2021): more than 06 café-au-lait spots measuring over 15 mm, lentigines in axillary and inguinal folds, more than 02 neurofibromas, and more than 02 Lisch nodules. Clinical evaluation, along with imaging studies (orbito-cerebral MRI, skeletal radiography, trans-thoracic ultrasound), aimed to identify disease complications. A suspicious subcutaneous neurofibroma measuring 3.5 cm, located near the

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dorsolumbar spine, warranted surgical excision. Orbito-cerebral MRI revealed 02 cerebral gliomas, with no evidence of optic pathway gliomas. Besides multiple cutaneous lesions causing aesthetic concerns, the patient experienced other complications, including facial dysmorphia with numerous microgeodes on radiography and thoracolumbar scoliosis.

Discussion: In 1882, Friedrich Daniel Von Recklinghausen first understood the origin of cutaneous tumours and named them neurofibromas. Precise diagnostic criteria enable early disease identification, facilitating proactive management and complication detection. Substantial progress has been made in understanding the genetic and molecular mechanisms underlying disease progression. Ongoing research aims to develop targeted treatments for specific manifestations, such as plexiform neurofibromas and gliomas.

Conclusions: Von Recklinghausen's disease is a rare genetic disorder with multisystemic manifestations that can significantly impact patients' quality of life. Although there is no curative treatment, early multidisciplinary intervention can help improve symptoms and quality of life.

Keywords: *Von Recklinghausen's disease, neurofibromin, café-au-lait spots*

[Abstract:2578]

MALAR RASH, FEVER, PANCYTOPENIA, ACUTE RENAL AND RESPIRATORY FAILURE: THE IMMUNE STORM

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Case Description: This case involves a 25-year-old woman with no prior medical history presenting with acute high fever after two months of fatigue, oral aphthosis, malar rash and arthralgia. Hepatosplenomegaly was found at physical examination and the patient developed oxygen dependence rapidly. Initial complementary tests showed increased serum creatinine levels (2.5 mg/dL) together with albuminuria (1 g/g) and abnormal urine sediment, high ferritin (5,000 ng/mL) and C-reactive protein values as well as hypocomplementemia. Pancytopenia was also present at the moment of admission. Since chest X-ray showed bilateral lung infiltrates, CT scan was performed leading to the suspicion of alveolar haemorrhage. Bronchoalveolar lavage confirmed this condition.

Clinical Hypothesis: Macrophage activation syndrome secondary to an autoimmune condition (systemic lupus erythematous, SLE).

Diagnostic Pathways: Antinuclear antibodies (ANA) were positive at a titer of 1/1280 with homogenous pattern. Anti-double stranded DNA levels were as high as 28000 units/L. Renal biopsy showed pathological changes consistent with lupus nephritis associated with thrombotic microangiopathy. Bone marrow aspiration did not find hemophagocytosis. Infectious as well as neoplastic diseases were excluded after a thorough study.

The patient received intensive treatment, including methylprednisolone, cyclophosphamide, rituximab and plasma exchange with IV immunoglobulins. Despite initial challenges, including intubation and refractory hypertension, the pathology was eventually controlled, leading to clinical and analytical improvement. Upon discharge, the patient continued with minimal corticosteroids, hydroxychloroquine and mycophenolate mofetil.

Discussion and Learning Points: This case emphasizes the importance of prompt treatment in SLE patients and highlights the potential for diverse renal involvement concurrent with lupus nephritis.

Keywords: *macrophage activation syndrome, systemic lupus erythematous, thrombotic microangiopathy*

[Abstract:2586]

CLINICAL CHARACTERISTICS AND OUTCOME OF PATIENTS WITH ADULT-ONSET STILL'S DISEASE: A 12-YEAR RETROSPECTIVE STUDY

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Background and Purpose: Adult-onset Still's disease (AoSD) is a rare systemic autoinflammatory disease of unknown aetiology, with a broad spectrum of clinical manifestations. The aim of this study was to describe the clinical features and outcomes of AoSD patients.

Methods: In this observational study, records of patients diagnosed with AoSD were reviewed. Inclusion criteria were patients over the age of 16 years fulfilling the Yamaguchi criteria and diagnosed over the period 2011–2022. Only the first disease episode was included in patients with polycyclic AOSD.

Findings: A total of 21 patients were included. There were 11 men and 10 women. Median age at diagnosis was 45 years (range: 16-60). Fever (n=21), arthralgia (n=20) and sore throat (n=13) were the most common symptoms. Median delay between onset of disease and diagnosis was 23 days (range: 12-120). At admission, eleven patients had a typical rash, five arthritis and three enlarged lymph nodes. Leucocytosis and elevated C-reactive protein were the commonest laboratory finding occurring in all cases followed by elevated ferritin level (19 cases). Acetylsalicylic acid was used as first-line treatment in 13 patients. Five patients received corticosteroids as second-line treatment due to insufficient response to acetylsalicyclic acid. The course of AOSD was monocyclic in 15 patients, polycyclic in five, and chronic in one.

Conclusions: The diagnosis of AOSD may be challenging given

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its non-specific clinical manifestations and laboratory features. Therefore, a high index of suspicion is necessary to ensure early diagnosis and prompt initiation of treatment.

Keywords: *adult-onset Still's disease, clinical characteristics, outcome*

[Abstract:2590]

A RARE COEXISTENCE: RETROPERITONEAL FIBROSIS AND TAKAYASU DISEASE IN A 54-YEAR-OLD FEMALE

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Introduction: Retroperitoneal fibrosis (RPF) and Takayasu disease (TD) are both uncommon autoimmune disorders with distinct pathophysiological mechanisms. The coexistence of these conditions in a single patient is a rare phenomenon, posing diagnostic challenges and complex therapeutic considerations.
Observation: We present the case of a 54-year-old female diagnosed with both RPF and TD, characterized by clinical symptoms including back pain, hypertension, tingling in the four limbs. Diagnostic imaging revealed characteristic features of RPF which were a fibrous retroperitoneal mass encasing the abdominal aorta and ureters, while the abdominal CT scan images were suggestive of RPF, the diagnosis of TD was posed with left upper extremity dysesthesia, blood pressure discrepancies, Aortic angiography showed evidence of typical inflammatory arteritis involvement, and positive inflammation markers. Management of this patient involved a multidisciplinary approach integrating corticosteroid therapy, immunosuppressive agents, a placement of double J catheters and a close monitoring of disease progression.
Conclusions: This case underscores the importance of considering overlapping autoimmune conditions in patients presenting with atypical clinical features and highlights the complexities of managing concurrent RPF and TD. Further research is warranted to elucidate the underlying mechanisms linking these two rare entities and to optimize therapeutic strategies for improved patient outcomes.

Keywords: *aortitis, retroperitoneal fibrosis, Takayasu's disease*

[Abstract:2623]

ATTR AMYLOIDOSIS IN PATIENT WITH REFRACTORY HEART FAILURE

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Purpose: Cardiac amyloidosis is a disorder caused by amyloid fibril deposition in the extracellular space of the heart. It can present with cardiac signs or symptoms or may be diagnosed as the result of screening in patients who manifest extracardiac signs of amyloidosis.
Methods: We present the case of a 73-year-old man with a history of IgM lambda monoclonal gammopathy, chronic renal disease with Bences jones proteinuria, sinus bradycardia and fibrosis of the corpus cavernosum, who came to hospital services for clinical manifestations compatible with heart failure with months of evolution, refractory to treatment. During his admission, the need for multiple diuretics in continuous perfusion to achieve minimal improvement in symptoms, sometimes hindered by hypotension, became apparent. Due the poor improvement, we decided to perform cardiac scintigraphy with diphosphonates, where uptake compatible with amyloidosis is manifested. Finally, myocardial biopsy confirmed ATTr deposit.
Conclusions: This case exemplifies that before a patient with an established diagnosis and that justifies the clinic, if the evolution is torpid, we must rethink the diagnosis and even repeat complementary studies, if necessary, to rule out alternate diagnoses.

Keywords: *amyloidosis, transthyretin, refractory heart failure*

[Abstract:2654]

A SPORADIC CASE OF LOEYS-DIETZ SYNDROME

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Loeyz-Dietz syndrome (LDS) is an autosomal dominant connective tissue disorder characterized by various clinical manifestations, most notably vasculopathies and skeletal abnormalities. Classically presenting with aortic root enlargement or aneurysms and craniofacial and skeletal abnormalities. The disease is rare, and it is associated with widespread familial arterial aneurysm and rupture.
A 39 year-old-male patient with a family history of aortic aneurysm disease and ex from cerebral haemorrhage secondary

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to cerebral aneurysm who presented with abdominal pain and constipation. Computed tomography (CT) of the thoracic and abdomen revealed thoracic hernia and diverticulitis. Although there were no signs of clinical appearance, considering the family history and CT findings, it was thought that it might be connective tissue disease. The genetics department was consulted. Genetic testing ultimately revealed a mutation in transforming growth factor beta receptor 2.This mutation was found to be associated with the Loey Dietz syndrome 2 phenotype.

Conclusions: We found a mutation in transforming growth factor beta receptor 2.This mutation occurs in type 2 Loey Dietz. Although the disease is not a significant case reported in the recent literature, we consider that the patient's diverticulitis and family history which started at a young age, is secondary to this mutation.

Keywords: *Loeys-Dietz syndrome, aortic aneurysm, transforming growth factor beta receptor*

[Abstract:2712]

A RARE CASE REPORT OF NEUROFIBROMATOSIS TYPE 1 IN A 45-YEAR-OLD MAN

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Introduction: Neurofibromatosis 1 (NF1) or Von Recklinghausen's disease is a rare autosomal dominant disorder that affects approximately 1 in 4,000 individuals. NF1 is characterized by the presence of pale tan or light brown discolorations (café-au-lait spots), multiple tumours of nerves and skin (neurofibromas), Lisch nodules, and by a predisposition to cancer. Here, we report a case of a 45-year-old man with NF1.

Observation: A 45-year-old man, admitted for etiological assessment of vertebral compression. He had no family history. The physical examination reveals a short man (150 cm), with hundreds of soft cutaneous neurofibromas, the largest amount being on the trunk and limbs, ranging from a few millimetres to several centimetres in diameter and multiple café-au-lait spots.

The standard laboratory tests values were in the normal range, apart from hypovitaminosis D at 17 ng/ml. Furthermore, the CT-scan of thoraco-lumbar spine showed vertebral compression of L4-L5-D7-D8. We completed with a full eye examination; Lisch's nodules on the iris of both eyes were without clinical visual involvement. The diagnosis of NF1 was made according to the presence of four of the seven diagnostic criteria of the National Institute of Health Consensus Development Conference: - café-au-lait spots,

-neurofibromas,

- Skeletal abnormalities (vertebral compression of L4-L5-D7-D8, short stature)

-Lisch nodules.

Conclusions: Neurofibromatosis type 1 is a rare genetic disorder characterized by the development of multiple non benign tumours of nerves and skin (neurofibromas).

Treatment for NF-1 is directed toward controlling symptoms and managing the complications.

Keywords: *Neurofibromatosis, neurofibromas, Lisch nodules*

[Abstract:2720]

FROM STROKE TO MELAS

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Purpose: To summarize the features of MELAS.

Methods: Case report.

Findings: 37-year-old woman with sensorineural hearing loss. She was admitted for presenting intermittent flashes of light and visual loss in the right temporal hemifield, disorientation, episode of visual hallucination and dysesthesia in the right arm. Physical examination showed temporal hemianopsia of the right eye with normal ophthalmologic examination. Hemogram and biochemistry within normality, including TSH, ESR, CRP, vitamin B12, folic acid, ANA, antiDNA, serology, immunoglobulins, proteinogram and thrombophilia studies. ECG, echocardiogram and echo-Doppler of TSA were normal. No oligoclonal bands were detected in cerebrospinal fluid. MRI revealed an image in the left occipital lobe suggestive of acute-subacute ischemic lesion. EEG showed acute waves in left parieto-occipito-temporal lobe. Patient was diagnosed of ischemic stroke in the left occipital lobe with status of symptomatic occipital simple partial seizures. 2 years later she was readmitted for photopsias, left temporal hemianopsia and self-limited prosopagnosia. MRI with mirror image with respect to the previous one. Muscle biopsy and genetic study were performed, confirming A3243G point mutation with 35% of heteroplasmy.

Conclusions: MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke) syndrome is the most common mitochondrial disease, that should be considered in those young patients diagnosed of acute stroke. It may present as epileptic seizures, migraine headache, vomiting, short stature, sensorineural hearing loss and ataxia. There is a correlation between heteroplasmy and symptomatic severity. Muscle biopsy and genetic testing establish the definitive diagnosis. Treatment consists of a combination of coenzyme Q-10, L-carnitine and other nutritional supplements.

Keywords: *acute stroke, young patient, mitochondrial myopathy, MELAS*

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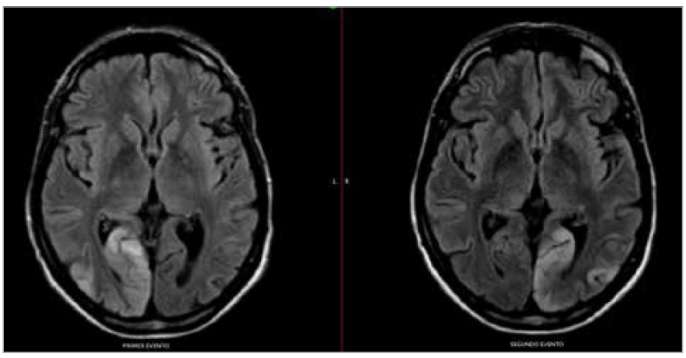

Figure 1.

[Abstract:2721]

TOXIC EPIDERMAL NECROLYSIS DUE TO LAMOTRIGINE

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Purpose: To describe the presentation of toxic epidermal necrolysis.

Methods: Case report.

Findings: 18-year-old female under treatment with valproic acid for absence seizures and generalized epilepsy, substituted by lamotrigine 3 weeks ago. She was admitted for patchy cutaneous eruption, progressively confluent, blisters and skin peeling predominantly on the upper extremities extending to the thorax, abdomen and lower extremities. In addition, peribuccal edema, conjunctival redness and odynophagia. Physical examination showed erythematous exanthema with bull's-eye lesions, denuded blisters on the lateral sides of the arms, Koebner's phenomenon in support áreas, erosions on lips and oropharyngeal mucosa and erythema on conjunctival and vulvar mucosa. Detachments around 20%. Lamotrigine was replaced by levetiracetam, associating oral corticosteroids and antihistamines, without improvement. Skin biopsy showed exanthema multiforme with associated histological signs of toxic epidermal necrolysis. Patient was referred to the Burn Unit for 3 weeks, receiving intensive fluid therapy, cyclosporine, topical anaesthetics, artificial tears, ophthalmic ointment and gynaecological ointments. Levetiracetam was maintained. On her return most of the lesions had epithelialized.

Conclusions: Stevens Johnson Syndrome is defined as a multiforme exanthema of the skin and other organs. It is considered the initial stage of a dermal reaction whose most severe form is Toxic Epidermal Necrolysis (TEN), characterized by intense pain and loss of the epithelial surface, compromise of the vital functions of the organism, hydroelectrolytic imbalance, renal and ocular involvement, great catabolism and potential risk of sepsis. Etiologically it is related to the use of drugs (60%), herpes simplex or mycoplasma infections and some genetic factors.

Keywords: *multiforme exanthema, toxic epidermal necrolysis (TEN), drugs*

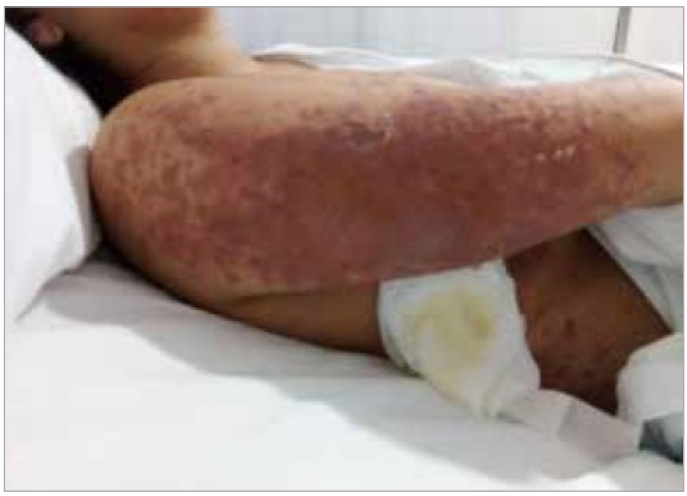

Figure 1.

[Abstract:2726]

SYSTEMIC SARCOIDOSIS WITH BONE AND BONE MARROW INVOLVEMENT: A CASE REPORT

Mohammed Ghazali, Hayat Bacha, Mohamed Lyes DJAMA, Malika Boucelma, Myalinda Sidi Said

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Introduction: Sarcoidosis is a multisystem disease often difficult to diagnose, its bone manifestations are not frequent and heterogeneous, which can lead to a potentially significant misdiagnosis.

Case Report: A 64-year-old female patient from Algeria was hospitalized in early 2020 for malignant hypercalcemia treated with hyperhydration, corticosteroids, and bisphosphonate with good progress. A year later the patient presented with mild thoracolumbar bone pain, an MRI carried out revealed (Fig 1): multiple layered multi-segmental geodes at the dorsal level with a gap in the L2 segment; serum protein electrophoresis was in favour of hyper-Beta2 globulin but the immunoglobulin, complement and immunophenotyping assays were negative. A bone biopsy showed bone marrow hypoplasia with the presence of a noncaseating granuloma formation. The CT scan showed lesions typical of stage 2 sarcoidosis and eliminated possible cancer in addition to digestive endoscopy. The diagnosis of systemic sarcoidosis with bone manifestations was retained. The laboratory tests were normal, notably the absence of cytopenia, leading to therapeutic absence and regular monitoring.

Discussion: Bone disease is only identified in 3–5% of sarcoidosis patients. Sarcoidosis lesions revealed on MRI in the axial skeleton and long bones resemble osseous metastases, as well as bone marrow lesions are rare and frequently accidental discoveries. Complicating the diagnosis or the need to formally eliminate neoplasia or malignant hemopathy like our case. The treatment is not codified let's go from simple monitoring to anti-TNF.

Conclusions: Bone sarcoidosis is an underestimated and cautious

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diagnosis based on several arguments and treatments discussed on a case-by-case basis.

Keywords: *bone lesions, sarcoidosis, hyperclacemia*

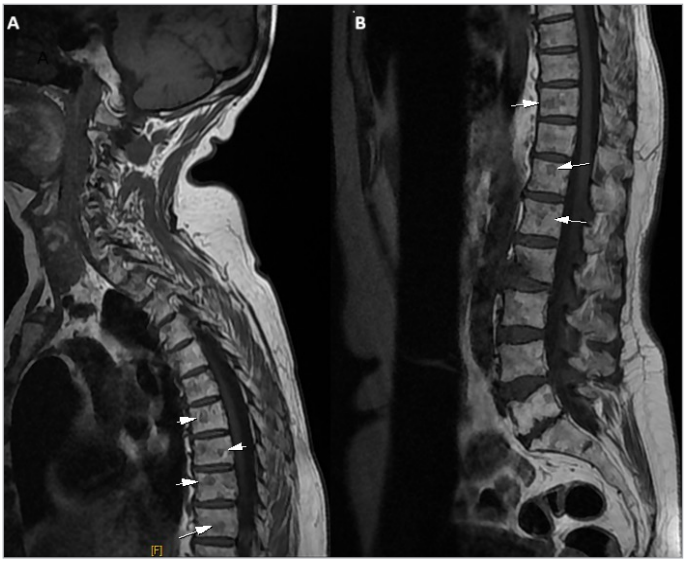

Figure 1. *MRI T2 sequence on the dorsocervical (A) and lumbosacral (B) spine reveals lacunar multisegmental "cutter" images (arrows) more marked in the dorsal region.*

[Abstract:2759]

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA IN ITS ISOLATED THROMBOTIC FORM: A CASE REPORT

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Introduction: Paroxysmal Nocturnal Hemoglobinuria (PNH) is a rare acquired clonal disease characterized by haemolysis, bone marrow failure, and thromboembolic complications.

Case Presentation: A 28-year-old patient from Algeria, with familial and personal history of unusual deep vein thromboses, was hospitalized for pyelonephritis and extensive ovarian thrombosis extending to the inferior vena cava, revealed by left lumbar pain and confirmed through angio-CT. Laboratory findings were normal. Thrombophilia investigations, both congenital and acquired, were negative. However, flow cytometry analysis identified glycosylphosphatidylinositol -deficient clones on two separate occasions. Unfortunately, treatment with enoxaparin and vitamin K antagonists proved ineffective, leading to recurrent episodes. Eculizumab was not available.

Discussion: The diagnosis of PNH is often considered in cases of hemolytic anaemia with negative Coombs test or in patients with aplastic anaemia or haemolysis associated with myeloid disorders. In our case, PNH was suspected due to recurrent thromboses at an early age in unusual locations. Thrombosis serves as an entry point to the disease in one out of ten patients. Recurrent thrombotic complications are the leading cause of mortality, and anticoagulant therapy does not provide protection against relapses. Hence, the significance of eculizumab, which reduces the risk of thrombotic recurrence by 85%.

Conclusions: PNH, though rare, may manifest solely through thrombotic events.

Keywords: *thrombosis, acquired thrombophilia, PNH, eculizumab*

[Abstract:2769]

PULMONARY HYPERTENSION AND ANTISYNTHETASE SYNDROME

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Introduction: Anti-synthetase syndrome (ASS) is characterized by an inflammatory myopathy, joint damage, Raynaud's phenomenon 'RP', skin lesions such as mechanic's hands, and rarely sclerodactyly. SAS is frequently associated with lung damage, especially parenchymal type Interstitial syndrome and more rarely vascular type pulmonary arterial Hypertension 'PAH', which determines the prognosis and requires emergency treatment.

Case Presentation: T.N, 36 years old woman complained of exertional dyspnoea and proximal myopathy. The clinical examination revealed dry crackles at the pulmonary bases, a burst of B2 at the pulmonary focus, inflammatory arthralgias, a proximal muscle deficit and muscle testing graded 2. We noted sclerodactyly, RP, fever of 38°C, deterioration in general condition, BMI at 18, HR at 100 batt/min, respiratory rate at 20 cycles/min, and oxygen saturation in ambient air at 98%. We observed an inflammatory syndrome ERS at 130, CRP at 60, albuminemia at 25g/l, AST and LDH levels at 3N, CPK at 7N. The anti-tRNA synthetase antibodies type anti JO1 were positive. The electroneuromyogram revealed severe myogenic damage and cardiac evaluation revealed a dilation of the right cavities with circumferential pericardial effusion and, PAPS at 53 mm Hg. Chest CT revealed an interstitial syndrome. Respiratory function exploration showed a severe restrictive syndrome.

Conclusions: The diagnosis of ASS associated with pulmonary hypertension 'PH' was made and referring to severe motor deficit, dyspnoea and cardiac damage corticosteroid and immunosuppressant were initiated. The clinical evolution was quickly favourable with normalization of the level of muscle enzymes and echocardiographic parameters and regression of inflammatory syndrome.

Keywords: *antisynthetases syndrome, pulmonary hypertension, myopathy*

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[Abstract:2773]

NOT SEEING THE WOOD FOR THE TREES: A CASE REPORT ON TRISOMY 18 WITH RARE FEATURES ASSOCIATED

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We present a child with plurimalformative syndrome to illustrate the importance for the diagnosis and investigation plan of interpreting clinical features together and not isolated.

Case Presentation: One month old child, third child of a young, healthy, unrelated couple, result of an uneventful pregnancy, but with reduced foetal movements. She was born at term, by caesarean section, Apgar score 3, Wt 2830 g, Ht 52 cm, HC 33 cm.

Physical Examination: Dysmorphic face (high forehead, absent eyebrows and eyelashes, thin lips, thick/abnormal ears), excess of skin on the neck, thorax with wide distance between nipples, evident blood vessels, hirsutism, hands with flexed/superposed fingers and small/narrow/thin nails, feet with ectrodactyly, bifid hallux and absent nail in the 4th toe, ambiguous external genitalia and systolic murmur at heart auscultation (complex heart defect identified by echocardiography). Due to the plurimalformative syndrome a MLPA test for subtelomeric rearrangements was indicated, but because ectrodactyly and digital anomalies seemed to be important diagnostic clues, a gene panel for skeletal dysplasia was performed. The result of the panel was normal, but MLPA test identified trisomy 18 (further confirmed by karyotype). After diagnosis, the child was sent for surgical correction of the heart defect. Trisomy 18 is a common chromosomal disorder usually characterized by growth deficit, craniofacial dysmorphy, flexed/superposed fingers, prominent heel and severe developmental delay. Ectrodactyly and bifid hallux are rarely associated.

In conclusion, for an efficient/economic investigation plan, the complete clinical evaluation is essential for the diagnosis, but the different birth defects should be interpreted in clinical context.

Keywords: *trisomy 18, ectrodactyly, rare disease*

[Abstract:2775]

A YOUNG MAN WITH A HEADACHE: UNRAVELLING A MYSTERY

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Vogt-Koyanagi-Harada syndrome (VKH) is an autoimmune disease with multisystem involvement with tinnitus, dizziness, headache, panuveitis and cutaneous manifestation.

A 24-year-old male presented with fever and headache for 10 days. His physical examination was normal with no signs of meningism. His white cells were 14.8x10^{9}/L with 84% neutrophils and CRP was 10 mg/dL. Treatment initiated as sinusitis. On day three, as his headache persisted with photophobia, brain imaging and lumbar puncture were arranged. His cerebrospinal fluid (CSF) showed protein 260 mg/dL, glucose 38 mg/dL (Random blood sugar 120 mg/dL), total cell counts 620/mm (Lymphocyte 95%, neutrophils 5%). His contrast CT brain followed by MRI was normal. Cytology confirmed the lymphocytosis. CSF TB PCR was negative. ACE levels, calcium and LDH were normal.

He was immediately started treatment as partially treated pyogenic meningitis/encephalitis (intravenous meropenem, vancomycin and acyclovir).

On day 16 of illness, he complained of bilateral tinnitus and vertigo (vancomycin was withheld). His audiogram showed bilateral mild to moderate sensory neural deafness. On day 21 of illness, he developed left lower motor neuron facial palsy and day 22, bilateral red eyes. Ophthalmology examination confirmed the uveitis and papiloedema. Then the diagnosis of VKH syndrome was made and started on intravenous methylprednisolone pulses for three days followed by prednisolone, while continuing same antibiotics and antivirals for 21 days. The patient made a remarkable improvement with normal vision.

Clinicians should be alert on rare causes of headache and diversity of clinical manifestation of VKH syndrome to avoid delaying diagnosis and treatment.

Keywords: *Vogt-Koyanagi-Harada syndrome (VKH), meningitis, uveitis*

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[Abstract:2812]

FABRY DISEASE (FD) CHARACTERISTICS IN ADULT PATIENTS FOLLOWED IN INTERNAL MEDICINE: A REPORT OF NINE CASES

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Introduction: Fabry Disease (FD) is a lysosomal disorder linked to the X chromosome, resulting from a deficiency in alpha-galactosidase A. Characterized by systemic vasculopathy and pro-fibrotic processes.

Case Presentation: This series includes nine patients from two different Algerian families with a history of sudden death and end-stage renal failure in first-degree parents. The average age is 46.87 ± 3.74 years, 95% CL [38.14-55.41], M/F sex ratio: 3.2. The average diagnostic delay is 22.75 ± 6.58 years, 95% CL [7.18-38.31]. Six are symptomatic: anhidrosis and hypertrophic cardiomyopathy (5), acroparesthesia, renal failure, and conduction disorder (4), angiokeratoma (3), cornea verticillata, and deafness (2), arrhythmia, lower limb arterial occlusive disease, and stroke (1). Two are associated with arterial hypertension and one with scleroderma (SSc). Diagnosis relied on genetic study and enzymatic assay. Five received beta-galactosidase supplementation. Evolution was marked by three deaths under treatment: two due to vascular involvement and one due to cranial trauma.

Discussion: Our series highlighted the issue of diagnostic delay, the predominance of cutaneous and neurological phenotypes. The cardiovascular and renal manifestations, which constitute the submerged part of the disease but are the leading cause of mortality despite replacement therapy. The association of FD and SSc is rarer, and both have a vascular tropism, exposing the patient to an added risk.

Conclusions: FD is multisystemic, underdiagnosed, progressive, and debilitating. Clinical manifestations are polymorphic. Family investigation is necessary for early diagnosis and treatment.

Keywords: *fabry, vascular disease, renal failure*

[Abstract:2819]

THE IMPORTANCE OF THE HEART DEFECT TYPE FOR THE DIAGNOSIS IN RARE DISEASES: A CASE REPORT ON FAMILIAL WILLIAMS SYNDROME

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Williams syndrome (WS) is caused by a microdeletion of chromosome 7q. Characteristic features include a distinct facial appearance, cardiac anomalies (most frequently supravalvular aortic stenosis), intellectual disability (ID), and connective tissue abnormalities. We present a family with three cases diagnosed with WS to illustrate the importance of the type of heart defect for directing the investigations and diagnosis.

Case 1: 14-year-old girl, followed for 10 years in different services (Paediatrics, Cardiology, Genetics) for short stature, microcephaly, heart defect and ID. Family history positive for heart defects (sister, mother, three siblings of the mother). She is the result of an uneventful twin pregnancy (sister died soon after birth) and preterm natural birth. Postnatal: developmental delay, supravalvular aortic stenosis (surgically corrected) and pituitary dwarfism. Physical examination: mild dysmorphic face, sloping shoulders, narrow thorax, moderate ID. Karyotype, subtelomeric MLPA: normal;

Case 2: older sister of case 1, result of an uneventful pregnancy and natural, full-term birth. Postnatal: developmental delay, short stature, microcephaly; diagnosed with severe supravalvular aortic stenosis (surgically corrected). Physical examination: mild dysmorphic face, sloping shoulders, narrow thorax, psoriasis, mild ID. Karyotype, subtelomeric MLPA: normal;

Case 3: mother of the girls, presenting mild dysmorphic face, systolic murmur and borderline intellect.

Due to the type of heart defect MLPA for microdeletions was performed and established the diagnosis of WS (confirmed by follow-up MLPA). This changed management plan (Nephrology, Endocrinology follow-up and Psychiatric support specific for personality).

In conclusion, the type of heart defect is essential for diagnosis in rare disorders.

Keywords: *Williams syndrome, supravalvular aortic stenosis, rare disorder, MLPA*

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[Abstract:2840]

SKELETAL ASPECTS OF GAUCHER DISEASE: CASE REPORT

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Introduction: Gaucher disease (GD) is a rare multisystem disease caused by a deficiency in the activity of the enzyme acid β-glucosidase (GBA), provoking an accumulation of glucocerebroside in the lysosomes of different cells, causing cytopenia, hepatosplenomegaly, changes in the central nervous system (CNS) and skeletal manifestations. It is the most common lysosomal storage disease.

Case Presentation: The patient was a 23-year-old man, issued from a consanguineous marriage, admitted for etiological assessment of normocytic normochromic anaemia (level of haemoglobin at 3.7 g/dl) with thrombocytopenia at 29,000 mm^3. He had a history of recurrent bone pain with a surgical drainage procedure for a subperiosteal hematoma two years before his admission. In order to explore bicytopenia, a myelogram was done and showed the presence of Gaucher cells. The GBA enzyme activity was determined in leukocytes by spectrofluorometry and found to be at 0 nmol/mg/h; and The molecular genetic study is in progress. Radiography revealed bone lesions, Erlenmeyer flask deformity associated with femoral, subperiosteal detachment, Osteonecrosis of the hip, confirmed on the CT scan. Furthermore, bone density showed spine and wrist osteoporosis, with femoral osteopenia. The patient received Blood transfusions, Vitamin D supplements, bisphosphonates, and enzyme replacement therapy was indicated.

Discussion and Conclusions: Involvement of the skeleton is one of the most prevalent aspects of GD and a major cause of pain, disability, and reduced quality of life. Prompt initiation of specific therapy for GD is crucial to optimizing outcomes and preventing irreversible skeletal complications.

Keywords: Gaucher, lysosomal disease, skeletal manifestations

[Abstract:2899]

NON-INFECTIOUS FEVER. ABOUT A CASE

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62-year-old woman. No allergic drug reactions. No cardiovascular risk factors or previous diseases except tonsillectomy in childhood. Ex-alcoholism 1 year ago, ex-smoking (25 packs/year). Home treatment: allopurinol 300 mg, metamizole 575 mg Baseline situation: Independent.

She went to the emergency system due to a 10-day history of fever (does not calm with paracetamol) and neck pain (which he attributed to swollen lymph nodes at that level). Due to the last blood tests, her doctor has said "she has a bad liver". In the last 2 days, she began with skin rash on trunk and lower limbs. No other symptoms. She lives in a little village. No pets except a canary. No insect bites. No recent trips. Does not report risky sexual relations. Physical examination: Skin rash on the trunk in the form of confluent maculo-papules, pruritic, disappears on pressure. Cervical lymphadenopathy. Abdomen with right hypochondrium pain. Complementary tests: Creatinine 1'13, GFR 49, LDH 434, AST 101, ALT 159. CRP 46'1, procalcitonin 1'3. Eosinophils 8.7%.

Liver MRI with contrast and abdominal ultrasound: Geographic hepatic steatosis with LOE of 6 mm of low suspicion in segment VII with the aforementioned considerations. The rest of the findings together + the clinical context suggests the possibility of liver toxicity.

In conclusion, taking into account clinical evolution, previous drugs (allopurinol), positive complementary tests and the rest of the negative study, the patient was diagnosed with DRESS due to allopurinol. She started taking corticosteroids (prednisone) 1 mg/kg/day with big improvement.

Keywords: DRESS, fever, skin, rash

[Abstract:2903]

TUBEROUS SCLEROSIS COMPLEX (BOURNEVILLE DISEASE): A CASE REPORT

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Tuberous sclerosis complex (TSC), also known as Bourneville disease is an inherited neurocutaneous disorder that is characterized by pleomorphic features involving many organ systems, including multiple benign hamartomas of the brain, eyes, heart, lung, liver, kidney, and skin. The expression of the disease varies substantially. The diagnosis of TSC can be made clinically or through genetic testing. Mutations in the TSC1 or TSC2 genes (which encode hamartin and tuberin proteins) are the culprits behind mTOR overactivation, the main mechanism driving the pathogenesis of the condition. Here we present a case report of a 34-year-old female with an unremarkable medical history who presented to the hospital reporting recurrent severe abdominal pain, originating in the left lower quadrant and umbilical area, associated with nausea and vomiting. On a physical exam cutaneous angiofibromas in her nose and cheeks, as well as hypopigmented spotting lesions on bilateral lower extremities were noted. The patient's current presentation raised concerns about the possibility of TSC. Further imaging studies revealed an enlarged pelvic mass, renal angiomyolipomas, lymphangioleiomyomatosis in the lung, calcified cerebral subependymal nodules and multiple sclerotic bone lesions. Based on the diagnostic criteria from the International Tuberous Sclerosis Complex Consensus patient has definite TSC, patient met (4) major clinical features (angiofibromas

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+ subependymal nodules + lymphangioleiomyomatosis + >2 angiomyolipomas) and (1) minor clinical feature (sclerotic bone lesions). This case emphasizes the importance in recognizing the diverse clinical presentations of TSC, the challenges in diagnosis and the need for appropriate follow-up and management.

Keywords: *angiofibromas, subependymal nodules, angiomyolipomas*

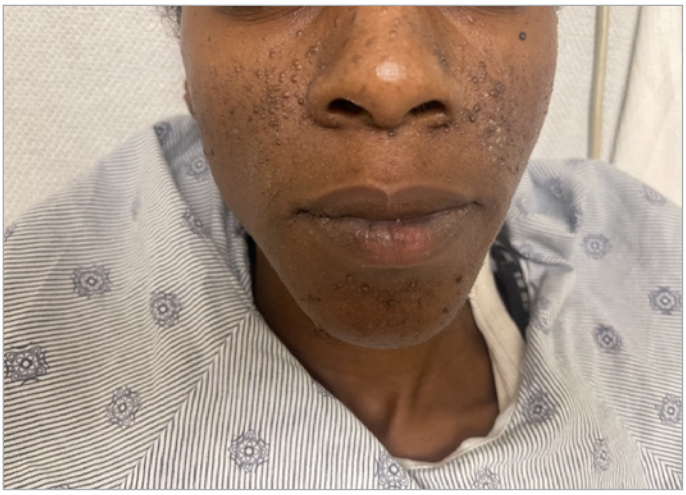

Figure 1. *Facial angiofibromas are the most visible and unsightly of all the cutaneous manifestations of tuberous sclerosis (TSC).*

[Abstract:2949]

INTERSECTION OF RARE DISORDERS: PORPHYRIA CUTANEA TARDA, CHRONIC LYMPHOCYTIC LEUKEMIA, POLYCYTHEMIA VERA, AND FCAS SYNDROME IN A 42-YEAR-OLD MALE PATIENT

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This article delves into the intricate case of a 42-year-old male patient presenting with diarrhea and abdominal pain. Diagnostic investigations led to the identification of a positive urine porphobilinogen test, ultimately confirming the diagnosis of PCT. Notably, a mutation in the UROD gene solidifies the PCT diagnosis. The patient also harbours an autosomal dominant mutation in the NLRP12 gene, leading to the manifestation of the rare disease known as FCAS.

The patient's complex medical history begins at the age of 16, when liver enzymes began escalating. Subsequent years saw the emergence of diabetes mellitus (DM), with a persistently elevated haemoglobin A1C of 10.20. At age 23, a liver biopsy, a bone marrow biopsy, and a series of additional tests were administered. Immunohistochemical tests revealed positive markers for CD5, CD20, and Bcl-2.

He was further diagnosed with non-alcoholic steatohepatitis (NASH), polycythemia vera, chronic lymphocytic leukaemia (CLL), and hypertension (HT). The patient underwent cholecystectomy, gynecomastia surgery, and appendectomy at the age of 39.

The identification of the NLRP12 gene mutation sheds light on the patient's susceptibility to autoimmune phenomena, contributing to a broader understanding of the underlying mechanisms that may play a role in the development of coexisting conditions. The coexistence of PCT with CLL and PV further underscores the complexity of this case. Importantly, the article sheds light on the underdiagnosis of porphyria, which can have serious consequences. This rarity gains significance as increased liver enzymes should prompt consideration of porphyria, yet the condition often goes undiagnosed due to its infrequency.

Keywords: *PV, PCT, FCAS, CLL*

[Abstract:2959]

CLINICAL CARE IN THE CONSULTATION OF RARE DISEASES IN A TERTIARY HOSPITAL, A DESCRIPTIVE STUDY

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Objectives: Know the different pathologies that have been evaluated and followed up by the unit in the first 14 months of the start of rare disease consultation in a tertiary level hospital.

Methods: Retrospective observational descriptive study that included patients evaluated in the rare diseases consultation from its beginning on 03/10/2022 to 05/25/2023. The analysed data were main pathologies, family association, the services that carried out the consultation and the genetic tests performed.

Results: Of the 56 patients analysed, 20 had a diagnosis of primary immunodeficiencies (common variable immunodeficiency being the most prevalent 55%), 12 of hereditary haemorrhagic telangiectasia (HHT), 3 of connective tissue diseases, 3 of metabolic diseases, 3. of autoinflammatory syndromes, 2 of Von Hipple Lindau Syndrome and another 13 of various pathologies classified as rare diseases. The main referral services were, in order, Hematology (37.5%), Internal Medicine (32.14%), Primary Care 14.28%), Pulmonology (5.35%), Pediatrics (3.57%) and others (7.14%). Of the 56 patients analysed, 27 had a genetic study performed or corroborated in our centre, the other 29 were pending or had made a clinical diagnosis of their pathology.

Conclusions: During 14 months, a total of 56 patients have been evaluated, with the most prevalent pathologies in the consultation being primary immunodeficiencies (35.71%) and hereditary haemorrhagic telangiectasia (21.42%) (results table 1). The main referral services were Hematology (37.5%) and Internal Medicine (32.14%). The results presented in similar studies in reference centres showed a similar prevalence in relation to the main pathologies and referral services (results table 2).

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Keywords: *rare diseases, consultation follow-up, internal medicine*

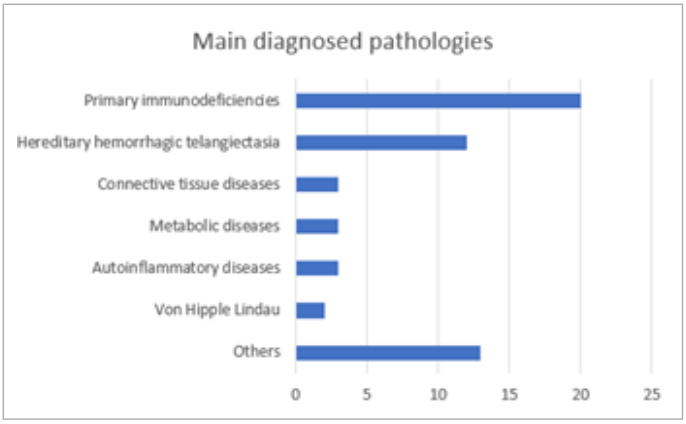

Figure 1. *Main pathologies diagnosed in the rare diseases consultation.*

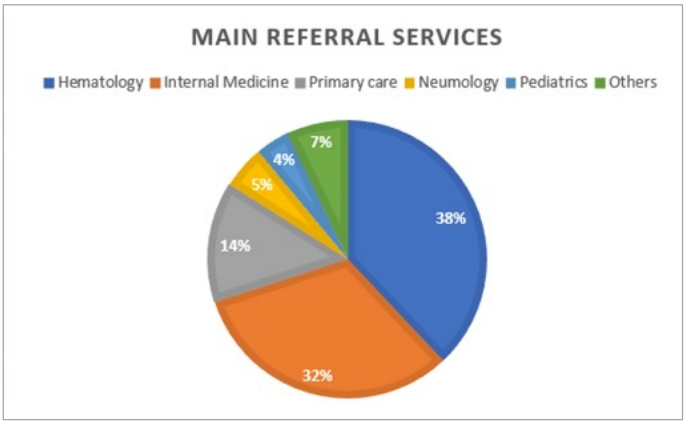

Figure 2. *Main referral services for consultation of rare diseases.*

[Abstract:2977]

MALIGNANT PLEURAL MESOTHELIOMA WITH ATYPICAL ONSET IN A PATIENT WITH TB MICRONODULAR SEQUELLAE

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A case report is presented of a patient aged 60 years, chronic smoker, with a personal history of long-term exposure to asbestos, known with personal history of pulmonary tuberculosis, presenting for repeated haemoptysis, dyspnoea at rest with orthopnoea, marked fatigability, altered general state, symptomatology with onset one week ago, currently exacerbated.

Computer Tomography showed massive right pleurisy, inhomogeneous condensation processes in Middle Lobe and Right Lower Lobe with imaging features of malignancy, pulmonary micronodules Left Upper Lobe and Left lower lobe and Pulmonary embolism apical and posterior subsegmental branches, segmental and subsegmental anterior branch Upper Right Lobe.

Emergency anticoagulant treatment is initiated, diagnostic and evacuatory thoracocentesis is performed, then in the next 24 hours the pleural effusion is rapidly restored, requiring the introduction of pleural drainage tube, then repeat chest CT with CT scan and angio CT pulmonary arteries raising suspicion of pleural mesothelioma and concluding remission of pulmonary embolism. Three weeks after the acute episode of pulmonary embolism, the patient underwent a diagnostic thoracoscopy with a biopsy from the right parietal pleura, confirming histopathologically the presence of right pleural malignant mesothelioma. The patient is admitted to the oncology ward with an altered general condition and a poor prognosis and chemotherapy treatment is started.

Discussion: Mesothelioma cells secrete procoagulant factors and interleukin 6, which can enhance platelet function and thrombosis and may promote inhibition of fibrinolysis, leading to pulmonary embolism. The incidence of pulmonary embolism combined with MPM is very low and the prognosis is extremely poor.

Keywords: *malignant pleural mesothelioma, pleural effusion, pulmonary embolism*

[Abstract:3004]

COWDEN SYNDROME: A CASE REPORT

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Case Presentation: A 45 year old woman, with a family history of a father diagnosed with Cowden syndrome. Diagnosed with Cowden Syndrome in 2010.

Clinical Hypothesis: Hamartomas, in a patient with a previous diagnosis of Cowden's disease.

Diagnostic Pathways: The diagnostic of an individual is made if he has three or more major criteria, and one of this has to be macrocephaly, Lhermitte-Duclos disease (LDD) or gastrointestinal hamartomas, or in the presence of a combination of two major and three minor criteria.

Discussion and Learning Points: Cowden syndrome (CS) or multiple hamartoma syndrome is a rare disease containing a germline mutation in PTEN which is located on chromosome 10q 23.3. It is an autosomal dominant disorder in which there is a mutation in the phosphatase and tensin gene that can develop multisystem hamartomas. That syndrome is typical in young adults: between the second and third decade of life 99% (range 4-75 years). Typical lesions present in the form of mucocutaneous lesions: oral papillomas, trichilemmomas and acral keratosis.

Keywords: *Cowden syndrome, hamartoma, PTEN gene*

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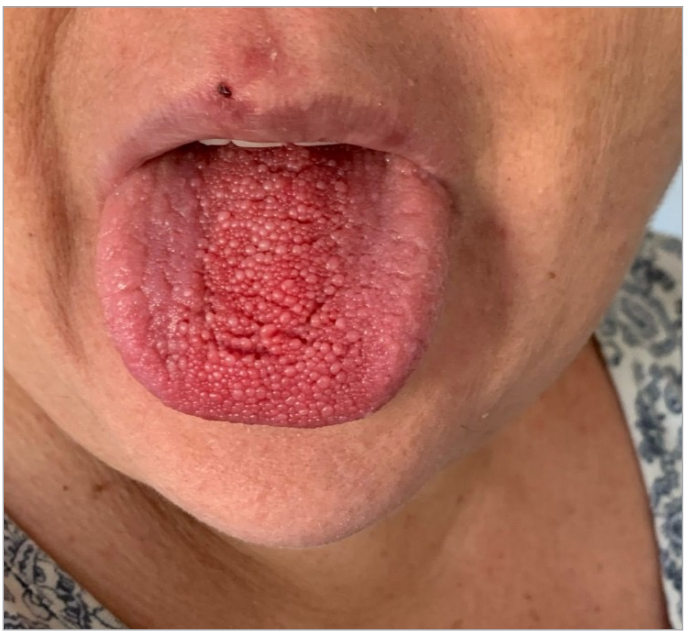

Figure 1. Mucocutaneous papillomatosis.

[Abstract:3007]

A CONFOUNDING BESIDES THE PROTOCOL SYSTEMIC DISEASE

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Summary: 65 years old female patient, with medical history of hypertension, pulmonary fibrosis and rheumatoid polyarthritis-treated with Adalimumabum.

Purpose: The patient supposed to present a myocarditis, associated with hepatic cytolysis and a computer-tomography (CT) with an unspecific bilateral apically pulmonary infiltration aspect.

Methods: Physical examination – significant revealed: altered general condition, plethoric facies, high temperature of the skin and mucosa, hypotonic with major hypokinetic muscular system and typically modification of polyarthritis.

Findings: Laboratory investigations - thrombocytopenia, a high level of Erythrocytes Sedimentation Rate(E.S.R.), cytolysis hepatic enzymes, negative hepatic viral panel and non-suggestive tumor markers. The abdominal ultrasound and head CT–normal features. RT-PCR SARS-CoV-2 – negative results. Cardiology consult – unspecific modification – a suspicion of systemic manifestations. In evolution, the patient presented proximal myopathy phenomena, fever (≤41°C), a continuous increased of cytholysis enzymes and ESR We remarked the appearance of the cholestathic syndrome. ANA-extins Blot – negative result and positive for gp210 antibodies. Cerebrospinal fluid, QuantiFERON, acute viral hepatitis, tests for zoonosis and mononucleosis syndromes – normal results. In nine days after admission, patient presented Acute Respiratory Distress and a spontaneous parasternocleidomastoidian hematoma, the C.T. scan being suggestive for Milliary Pulmonary Tuberculosis. Also, positive Gen-Xpert test and P/Q and N-type calcium channel antibodies-present. The patient has been admitted in Intensive Care Unit. After three days, the patient presented aspects suggestive for lymphohistiocytosis and infausto evolution after 2 days.

Conclusions: Pulmonary tuberculosis is an immunosuppressive disease, which could be associated with a proof prognostic, especially in association with others immuno-mediated diseases.

Keywords: *pulmonary tuberculosis, Eaton-Lambert Syndrome, lymphohistiocytosis*

[Abstract:3074]

LARYNGEAL EDEMA-RELATED MORTALITY IN HEREDITARY ANGIOEDEMA PATIENTS: INSIGHTS FROM VERBAL AUTOPSY FINDINGS OBTAINED FROM RELATIVES

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Hereditary angioedema (HAE) is a rare genetic disorder characterized by sudden and often unprovoked episodes of swelling that can be potentially life-threatening. In our study, verbal autopsy findings from relatives of HAE patients who were potentially lost due to laryngeal oedema have been elucidated. We analysed 80 families, involving a total of 156 individuals diagnosed with HAE. We reached out to 22 out of a total of 30 families and recorded verbal autopsy findings related to the individuals who died through a questionnaire. The questionnaire contained socio-demographic information of individuals who died from laryngeal edema, detailed information about fatal laryngeal attacks, and whether there were lifelong angioedema attacks. Of those who died, 14 were male and 8 were female, with an median age of 34. In individuals who died due to a fatal laryngeal attack, 45.5% experienced swelling simultaneously in the tongue-lip-face, while 18.2% simultaneously had swelling in the hands and feet. The median time from the onset of symptoms to the moment of death was 3.5 hours. Of the individuals, 40.9% died at home,40.9% died in the hospital, and the remaining 18.2%died in their own vehicle. In 20 individuals who died before the fatal laryngeal oedema attack, there was a history of recurrent angioedema attacks suggestive of HAE throughout their lives. The individuals who died; 40.9% had previously sought medical

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attention due to HAE symptoms but did not receive an accurate diagnosis, 50% had never sought medical care for this purpose. Defined as a verbal autopsy, our study revealed that individuals who died were mostly symptomatic before the fatal attack, and approximately half of them sought medical attention for an angioedema attack without receiving an accurate diagnosis.

Keywords: *angioedema, allergy diagnosis, laryngeal edema*

Demographic and Clinical Characteristics	Percentage	Details
Degree of Relatives (for Verbal Autopsy)	6 (27.3%)	1st (mother, father, child)
	12 (54.5%)	2nd (grandma, grandpa, brother, sister)
	3 (13.6%)	3rd (uncle, aunt)
	1 (4.5%)	4th (cosuin)
Age	34 ± 17	(year ± SD)
Gender n, (%)	14/22 (63%)	Male
	8/22 (37%)	Female
Marital Status n, (%)	16/22(72.7%)	Married
	8/22 (27.3%)	Single (n;7) or Divorced (n;1)
Having at least one child n, (%)	15/22 (68.2%)	Boy or girl
Laryngeal Edema with Simultaneous	10/22 (45.5%)	Swelling in Tongue-Lips-Face
Angioedema n, (%)	4/22 (18.2%)	Swelling in Hands-Feet
Duration from Symptom Onset to Death	3.5± 9	(mean hours ± SD)
Place of Death n, (%)	9/22 (40.9%)	Home
	9/22 (40.9%)	Hospital
	4/22 (18.2%)	Private vehicle or ambulance
Lifetime Presence of HAE Symptoms n, (%)	20/22 (90.9%)	-
Medical Care Seeking for HAE Symptoms n, (%)	9/22 (40.9%)	Previously Visited Healthcare
	11/22 (50%)	Never Visited Healthcare
	2/22 (9.1%)	Died After Diagnosis

Table 1. *Demographic and Clinical Characteristics.*

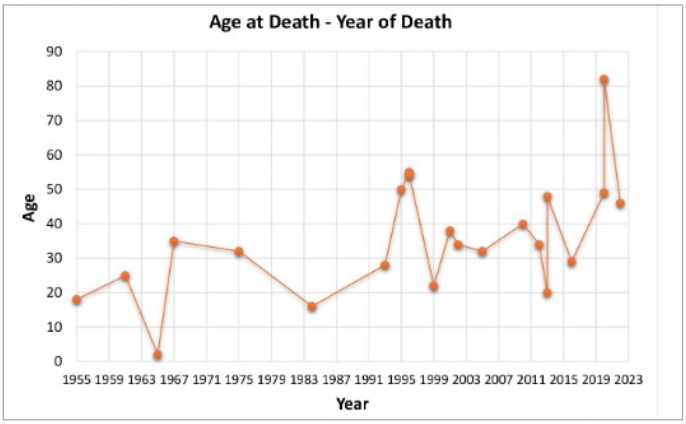

Figure 1. *The age and year of death for the 22 individuals who died due to laryngeal edema.*

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