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CONCURRENT IDIOPATHIC MULTICENTRIC CASTLEMAN DISEASE WITH TAFRO AND SJÖGREN'S SYNDROME IN A YOUNG PATIENT: A CHALLENGING DIAGNOSTIC OVERLAP

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ABSTRACT

Background: Idiopathic multicentric Castleman disease (iMCD) with TAFRO syndrome (characterized by thrombocytopenia, anasarca, fever, reticulin fibrosis/renal failure, organomegaly) is a recently described disorder. The diagnostic criteria for iMCD-TAFRO exclude patients with concomitant autoimmune diseases such as primary Sjögren's syndrome. However, recent case reports suggest that although rare, these conditions may coexist.

Case report: We report the case of a 37-year-old woman who presented with escalating systemic inflammation, cytopenias, anasarca, renal dysfunction and organomegaly, with lymph node biopsy suggestive of Castleman disease. Simultaneously, dense lacrimal gland hyperplasia with histopathology demonstrating lymphoepithelial sialadenitis and strongly positive anti-Ro52 antibodies led to a diagnosis of Sjögren's syndrome. Given the rapid clinical deterioration and marked hyperinflammation, corticosteroid therapy and tocilizumab were implemented, leading to sustained remission.

Conclusion: This case illustrates the diagnostic complexity posed by overlapping features of Idiopathic multicentric Castleman disease with TAFRO syndrome and Sjögren's syndrome and reinforces the need to reconsider existing diagnostic criteria to ensure timely diagnosis and effective treatment. Epidemiologically, this is also a rare case of iMCD with TAFRO syndrome in a patient of African descent, contrasting with previous reports predominantly involving Asian individuals.

KEYWORDS

Multicentric Castleman disease, TAFRO syndrome, Sjögren's syndrome, hyperinflammation

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LEARNING POINTS

- Idiopathic multicentric Castleman disease (iMCD) with TAFRO syndrome (thrombocytopenia, anasarca, fever, reticulin fibrosis/renal failure, organomegaly) (iMCD-TAFRO) is a rare, life-threatening disorder marked by severe systemic inflammation and multiorgan failure, and early recognition and timely initiation of immunomodulatory therapy are critical for positive outcomes.
- Although current diagnostic criteria for iMCD-TAFRO exclude patients with concomitant autoimmune diseases such as Sjögren's syndrome, an increasing number of case reports suggest that these conditions may coexist, challenging existing definitions and suggesting a potential physiopathological overlap.
- This case highlights the diagnostic challenge posed by the coexistence of these conditions and underscores the need for an individualized assessment integrating clinical, laboratory, and immunological findings.

INTRODUCTION

Multicentric Castleman disease (MCD) encompasses a rare and heterogenous group of lymphoproliferative disorders characterized by lymphadenopathies with distinctive histological features and, occasionally, severe systemic inflammation that can become life-threatening. MCD is classified into cases associated with human herpesvirus eight (HHV8) infection — typically occurring in patients with human immunodeficiency virus (HIV) — and idiopathic MCD (iMCD)[1]. Based on clinical phenotypes, iMCD is further subdivided into iMCD-TAFRO (thrombocytopenia, anasarca, fever, reticulin fibrosis/renal failure and organomegaly), iMCD-IPL (idiopathic plasmacytic lymphadenopathy) and iMCD-NOS (not otherwise specified). Another subtype is POEMS-MCD, which occurs in the context of POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes)[1,2].

In iMCD, a hyperinflammatory state is driven by an over-production of cytokines – primarily interleukin-6 (IL-6), which in turn stimulates the secretion of vascular endothelial growth factor (VEGF). The trigger for this systemic inflammatory response remains unknown, but current hypotheses suggest that genetic predisposition, viral infections and immunological disturbances may play a role[1,2].

The most severe iMCD subtype is iMCD-TAFRO, and timely diagnosis and treatment can be lifesaving. The most recently proposed diagnostic criteria *(Table 1)* require the presence of multicentric lymphadenopathy and lymph node histopathology consistent with iMCD, along with thrombocytopenia, anasarca, fever or a hyperinflammatory state, and organomegaly[3,4]. Additional criteria include renal dysfunction, reticulin fibrosis on bone marrow biopsy, isolated elevation of serum alkaline phosphatase, and the absence of polyclonal hypergammaglobulinemia[3,5]. Although autoimmune diseases are considered an exclusion criterion, several reports have described iMCD-TAFRO patients with positive antinuclear antibodies (ANA), rheumatoid factor, anti-SSA and SSB antibodies in the absence of a clear autoimmune diagnosis[3]. Moreover, some case reports have documented concurrent iMCD-TAFRO and Sjögren's syndrome (SjS)[6]. Here, we report the case of a 37-year-old African woman who presented with iMCD-TAFRO and SjS.

CASE DESCRIPTION

A 37-year-old woman from Guinea Bissau, with no known prior medical history, presented to our hospital with a 5-month history of bilateral palpebral oedema, xerostomia, anorexia, fever, weight loss and episodes of epistaxis. On physical examination, there were upper palpebral hard tumefaction *(Fig. 1)*, as well as decreased breath sounds bilaterally on pulmonary auscultation. She also had palpable lymph nodes bilaterally in the cervical, axillary, and inguinal regions. Initial workup revealed anaemia and thrombocytopenia (haemoglobin of 6.5 g/dl and platelets of 136,000 $\times 10^9$/l), an acute kidney injury (creatinine of 2.12 mg/dl) and increased inflammatory markers, with a C-reactive protein of 22.48 mg/dl, erythrocyte sedimentation rate of 141 mm and ferritin of 714 ng/dl.

A computed tomography (CT) scan showed bilateral pleural effusion and ascites, hepatosplenomegaly and multiple lymphadenopathies, above and below the diaphragm. Further laboratory workup is summarized in *Table 2*. Importantly, extensive infections screening was negative including HIV serology and autoimmune workup was positive for ANA (titer of 1:320), with strongly positive anti-Ro52 antibodies and a polyclonal hypergammaglobulinemia. Orbital magnetic resonance imaging showed a marked thickening of the lacrimal glands, and a biopsy was compatible with lymphoepithelial sialadenitis, with a focus score>1, suggestive of SjS. Diagnostic paracentesis showed a lymphocytic predominance, with negative polymerase chain reaction testing for Mycobacterium tuberculosis and no malignant cells on cytology. A myelogram and a bone marrow biopsy showed slight stromal fibrosis and an otherwise hypercellular bone marrow, with reactive changes and increased megakaryocytes. During this workup, the patient's condition deteriorated quickly, with worsening cytopenias (nadir haemoglobin and platelet counts of 6.2 g/dl and 4,000 $\times 10^9$/l, respectively), accompanied by multiple episodes of epistaxis requiring red blood cell and platelet

Clinical criteria – all required:	
Thrombocytopenia	Nadir platelet level ≤100 ×10^9/l
Anasarca	Pleural effusions, ascites or subcutaneous oedema
Fever	>38°C
Organomegaly	Small volume lymphadenopathy in two or more regions, hepatomegaly or splenomegaly
Pathological criteria – required:	
Lymph node excisional biopsy	Consistent with iMCD
HHV8	Negative testing
Additional criteria – at least one required:	
Renal insufficiency or renal failure	Requiring haemodialysis
Bone marrow with reticulin fibrosis or megakaryocytic hyperplasia	Without evidence of an alternative diagnosis
Polyclonal hypergammaglobulinemia	Absence
Elevated ALP	With mild to no elevation of bilirubin or transaminases
Exclusion criteria – must rule out the following diseases:	
Infectious	HHV8, EBV, HIV, tuberculosis
Autoimmune	SLE, RA, SjS, Adult-onset Still disease, Juvenile idiopathic arthritis, primary hemophagocytic lymphohistiocytosis
Malignancy	Lymphoma, multiple myeloma, POEMS, metastatic cancer
Probable iMCD-TAFRO: all four clinical criteria and additional criteria are met, but pathological criteria are not able to be assessed.	

Table 1. *Diagnostic criteria for iMCD-TAFRO, according to Nishimura et al[3].*
Abbreviations: iMCD, idiopathic multicentric Castleman disease; TAFRO, thrombocytopenia, anasarca, reticulin fibrosis/renal disfunction, organomegaly; ALP, alkaline phosphatase; HHV8, human herpes virus 8; EBV, Epstein-Barr virus; HIV, human immunodeficiency virus; SLE, systemic lupus erythematosus; RA, rheumatoid arthritis; SjS, Sjögren's Syndrome; POEMS, polyneuropathy, organomegaly, endocrinopathy, monoclonal paraprotein, skin changes.

transfusions. Kidney function also declined (peak creatinine 5.79 mg/dl), with refractory hyperkalaemia requiring one session of haemodialysis. Along with a marked increase in inflammatory markers (peak ferritin 2,613 ng/ml) and persistent fever, the patient had a worsening neurological status characterized by hyperactive delirium. Due to this decline, she was started on high-dose corticosteroid therapy (5 days of 500 mg/day of methylprednisolone, followed by 1 mg/kg/day of oral prednisolone), resulting in a remarkable clinical improvement. Subsequently, the result of an excisional inguinal lymph node biopsy was suggestive of Castleman disease – showcasing lymphoid hyperplasia and proliferation of plasma cells, with no evidence of Immunoglobulin G4 (IgG4) infiltration, HHV8 infection or neoplastic cells and the diagnosis of iMCD-TAFRO was made. Since siltuximab was not readily available, the patient was started on tocilizumab (8 mg/kg every 2 weeks) and corticosteroid tapering was initiated. She was discharged after 28 days of hospitalization. After 4 months, due to sustained clinical response, the dosing interval of tocilizumab was increased to every 4 weeks, and prednisolone has been tapered to 5 mg/day. Currently, more than 6 months after the diagnosis, the patient remains in clinical remission, with complete resolution of the cytopenias and kidney injury, normalized inflammatory markers, and with a follow-up CT scan showing resolution of ascites, pleural effusion, and hepatomegaly, as well as a marked reduction in splenomegaly (from 13 to 10.5 cm) and lymphadenopathies *(Fig. 2)*.

DISCUSSION

SjS is a systemic, chronic autoimmune disease characterized by xerophthalmia and xerostomia resulting from lymphocytic infiltration and subsequent destruction of the lacrimal and salivary glands. Its pathophysiology is not yet fully understood, but one of the mechanisms implicated is the presence of autoreactive B lymphocytes, which leads to the production of autoantibodies (primarily anti-Ro/SSA and anti-La/SSB), along with increased levels of inflammatory cytokines such as IL-6[7]. Due to this persistent B-cell activation, lymphoma is a well-recognized complication of SjS, developing in approximately 5% of

Analysis	Value
Hemoglobin (g/dl)	7.7
Platelets (×10⁹/l)	82,000
Creatinine (mg/dl)	3.04
C-reactive protein (mg/dl)	30.84
Ferritin (ng/dl)	903
AST (U/l)	29
ALT (U/l)	10
Serum alkaline phosphatase (U/l)	299.25
Total bilirubin (mg/dl)	1.38
Lactate dehydrogenase (U/l)	342
Beta2-microglobulin (mg/dl)	19.06
Immunoglobulin G (mg/dl)	2566
Immunoglobulin G4 (mg/dl)	21.20
Serum protein electrophoresis with immunofixation	Polyclonal hypergammaglobulinemia, with no monoclonal component
Antinuclear antibody	Positive at a titer of 1:320
Rheumatoid factor (UI/l)	12
Anti-dsDNA, SSA and SSB antibodies	Negative
Anti-gp210 and anti-Ro52 antibodies	Strongly positive
C3 (mg/dl)	119
C4 (mg/dl)	22.9
HIV antibody and antigen	Negative
Urine and blood cultures	Negative
IGRA test for Mycobacterium tuberculosis	Negative
PCR testing for *Mycobacterium tuberculosis* in ascitic fluid	Negative
Urine protein (mg/dl)	97.81
Peripheral blood flow cytometry	B-cell population with no monoclonal features
Bone marrow biopsy	Hypercellular, with increased megakaryocytes. Slight stromal fibrosis (MF:1). No signs of malignant cells.

Table 2. *Initial findings.*
Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; dsDNA, double stranded DNA; IGRA, interferon gamma release assay; PCR, polymerase chain reaction; MF, myelofibrosis.

patients — mostly as indolent subtypes. This sustained immune activation in SjS, with a potential overlap with the pathophysiology of iMCD, may act as a trigger for iMCD by increasing lymph node hyperplasia in the setting of chronic inflammation[8].

It is also noteworthy that both iMCD-TAFRO and SjS typically occur in older adults, most often in the fifth decade of life, whereas our patient was only 37 years old. Recent case reports describing concurrent iMCD-TAFRO and SjS also involve patients in their fourth decade, which may support the hypothesis that an underlying autoimmune disease could accelerate the onset of MCD[6,8]. Epidemiologically, this is also a rare, reported case of iMCD-TAFRO in a patient of African descent, as the vast majority of cases have been described in Asian patients, with only a small minority reported in Caucasian and Hispanic individuals[1,6].

Extraglandular manifestations of SjS can occur in around 10-20% of patients and present in a wide range of clinical features. These may include general constitutional symptoms; respiratory manifestations such as chronic dry cough, lymphocytic interstitial lung disease or bronchiolitis; renal with tubulointerstitial nephritis or cryoglobulinaemic-related glomerulonephritis; and even peripheral nervous system involvement[7]. While frequent, cytopenias in SjS are usually mild and have no significant clinical repercussions[6]. Assuming that the presence of SjS does indeed exclude a diagnosis of iMCD-TAFRO, several clinical features described in this case – and in others that consider a possible overlap between iMCD-TAFRO and SjS –, such as ascites, pleural effusion, non-tubular renal involvement or cytopenia secondary to myelofibrosis – are notably rare in SjS. Conversely, if one assumes that the primary diagnosis in this case is iMCD-TAFRO and that the positive autoantibodies are merely incidental findings, the presence of lacrimal gland hyperplasia with lymphoepithelial sialadenitis remains difficult to explain. Another important finding was the presence of polyclonal hypergammaglobulinemia, which is commonly observed in other subtypes of iMCD (particularly in iMCD-IPL) but is notably rare in iMCD-TAFRO[7]. Once again, the overlap with SjS provides a plausible explanation for this finding, as polyclonal hypergammaglobulinemia is a typical laboratory abnormality in SjS[7].

In iMCD-TAFRO, the recommended first-line treatment is siltuximab, an anti-IL-6 monoclonal antibody and the only drug approved for this purpose in the United States and Europe. Tocilizumab or rituximab are also important therapeutic options[9]. Tocilizumab, a monoclonal antibody targeting the IL-6 receptor, is approved in Japan for the treatment of iMCD, and is widely used off-label elsewhere, with small case series and case reports demonstrating efficacy and safety profiles comparable to those of siltuximab[10]. Rituximab, an anti-CD20 monoclonal antibody, is also considered an option for induction therapy and most experience comes from HIV-associated



Figure 1. Bilateral thickening of the patient's lacrimal glands.

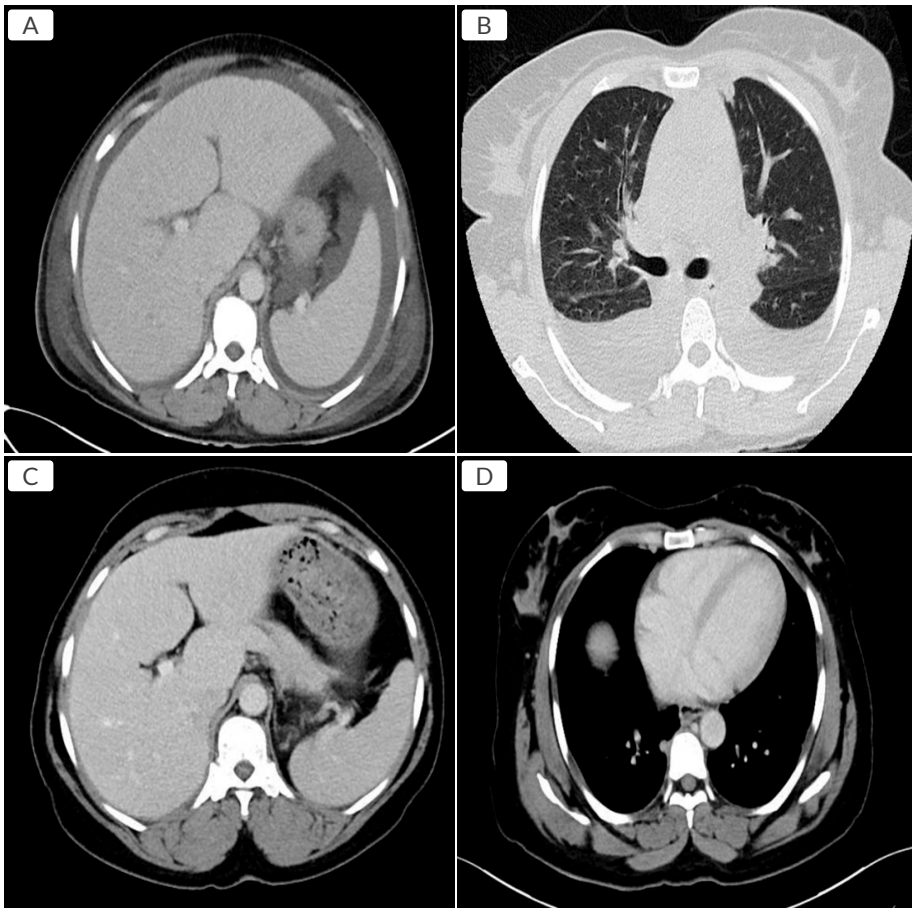


Figure 2. A, B) Initial computed tomography (CT) scans showing ascites, hepatosplenomegaly and pleural effusions; C, D) Follow-up CT scans 5 months later showing resolution of fluid overload and improvement of organomegaly.

MCD[9]. In addition to monoclonal antibody-based therapy, corticosteroids are often required, sometimes in high doses, to suppress the hyperinflammatory process[9,10]. There is currently no clear consensus regarding the optimal treatment of iMCD in the presence of concomitant autoimmune diseases. In this case, the option of starting rituximab was considered since it could be a means to treat both iMCD and SjS. However, tocilizumab was chosen due to the patient's clinical deterioration and escalating systemic hyperinflammation, and remission has been sustained to date without the need to switch biologic therapy. iMCD-TAFRO is a recently recognized disease, and its definition and pathophysiology are still under revision. Although current diagnostic criteria list autoimmune disorders such as SjS as exclusion criteria, this case report — along with several others published recently — challenges that notion, providing growing evidence that these conditions may coexist.

REFERENCES

1. Dispenzieri A, Fajgenbaum DC. Overview of Castleman disease. *Blood* 2020;**135**:1353-1364. doi: 10.1182/blood.2019000931
2. Dirnhofer S, Nishimura Y, Dispenzieri A. Non-Clonal Lymphoproliferative Diseases. *Hematol Oncol* 2025;**43**:e70065. doi: 10.1002/hon.70065
3. Nishimura Y, Fajgenbaum DC, Pierson SK, Iwaki N, Nishikori A, Kawano M, et al. Validated international definition of the thrombocytopenia, anasarca, fever, reticulin fibrosis, renal insufficiency, and organomegaly clinical subtype (TAFRO) of idiopathic multicentric Castleman disease. *Am J Hematol* 2021;**96**:1241-1252. doi: 10.1002/ajh.26292
4. Fajgenbaum DC, Uldrick TS, Bagg A, Frank D, Wu D, Srkalovic G, et al. International, evidence-based consensus diagnostic criteria for HHV-8-negative/idiopathic multicentric Castleman disease. *Blood* 2017;**129**:1646-1657. doi: 10.1182/blood-2016-10-746933
5. Kakutani T, Kamada R, Tamai Y. Pathophysiology, Treatment, and Prognosis of Thrombocytopenia, Anasarca, Fever, Reticulin Fibrosis/ Renal Failure, and Organomegaly (TAFRO) Syndrome: A Review. *Curr Issues Mol Biol* 2024;**46**:11255-11269. doi: 10.3390/cimb46100668
6. Li ZY, Kim S, Huang S, Mian R. Multicentric Castleman disease with TAFRO syndrome and Sjögren's. *Clin Case Rep* 2019;7:2388-2392. doi: 10.1002/ccr3.2502
7. Tromby F, Manfrè V, Chatzis LG, Arends S, Tzioufas AG, Bootsma H, et al. Clinical manifestations, imaging and treatment of Sjögren's disease: one year in review 2024. *Clin Exp Rheumatol* 2024;**42**:2322-2335. doi: 10.55563/clinexprheumatol/5xq3fb
8. Grange L, Chalayer E, Boutboul D, Paul S, Galicier L, Gramont B, et al. TAFRO syndrome: A severe manifestation of Sjögren's syndrome? A systematic review. *Autoimmun Rev* 2022;**21**:103137. doi: 10.1016/j. autrev.2022.103137
9. Van Rhee F, Voorhees P, Dispenzieri A, Fossa A, Srkalovi G, Ide M, et al. International, evidence-based consensus treatment guidelines for idiopathic multicentric Castleman disease. *Blood* 2018;132:2115-2124. doi: 10.1182/blood-2018-07-862334
10. Nashimoto N, Kanakura Y, Aozasa K, Johkoh T, Nakamura M, Nakano S, et al. Humanized anti-interleukin-6 receptor antibody treatment of multicentric Castleman disease. *Blood* 2005;**106**:2627-2632. doi: 10.1182/blood-2004-12-4602