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Paediatric Inflammatory Multisystem Syndrome: A Diagnostic Challenge in a COVID-19-Negative Patient

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ABSTRACT

Paediatric inflammatory multisystem syndrome (PIMS) is associated with SARS-CoV-2 infection in patients aged 19 years or below according to World Health Organization (WHO) criteria. The condition is characterised by fever, inflammation and organ dysfunction. PIMS mimics Kawasaki disease or toxic shock syndrome. As SARS-CoV-2 infection is a global pandemic, clinicians need to be aware of the conditions associated with it.

We present the case of 18-year-old woman who was admitted with multi-organ failure requiring admission to the intensive care unit. The differential diagnosis included toxic shock syndrome, Kawasaki disease and PIMS. The overall picture fit the criteria for PIMS but the patient had a negative polymerase chain reaction (PCR) test for SARS-CoV-2, which presented additional diagnostic difficulties. As the PCR test was negative, IgG antibodies against SARS-CoV-2 were measured to detect past infection and tested positive. The patient was diagnosed with PIMS as she met the WHO criteria after other differential diagnoses were excluded. She was successfully treated with methylprednisolone and intravenous immunoglobulin (IVIG).

KEYWORDS

COVID-19, SARS-CoV-2, toxic shock syndrome, Kawasaki disease, intensive care unit, IgG antibodies

LEARNING POINTS

- Paediatric inflammatory multisystem syndrome (PIMS) can also occur in young adults as clinical improvement was observed in a young woman after the administration of methylprednisolone and intravenous immunoglobulin (IVIG).
- Multidisciplinary care is important for the diagnosis and management of PIMS.
- The presentation of PIMS has a lot of similarities with Kawasaki disease and toxic shock syndrome.

BACKGROUND

Paediatric inflammatory multisystem syndrome (PIMS) has been observed in children and adolescents since the start of the SARS-CoV-2 pandemic [1]. PIMS occurs in patients who have had SARS-CoV-2 infection in the previous 4–6 weeks [2]. Early diagnosis and treatment reduce morbidity and mortality in patients with PIMS.

CASE DESCRIPTION

An 18-year-old woman presented to the emergency department with a 2-day history of a sore throat and flu-like illness. She had been treated with antibiotics by her general practitioner but had progressively deteriorated.

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On initial assessment, she had subconjunctival haemorrhage with tender cervical lymphadenopathy. On abdominal examination, she had a macular rash and generalized abdominal tenderness. She was admitted for further investigations.

On the first day of admission, she became hypotensive within a few hours of presentation. She was treated with aggressive fluid resuscitation and broad-spectrum antibiotics for possible septic shock. As her hypotension did not improve, she was started on vasopressors and transferred to the intensive care unit.

She had a history of thalassemia minor and medical termination of a pregnancy about 6 months previously. Her medication history included the progesterone only pill. Her family history was not significant and she had no relevant travel history in the last 6 months.

Her clinical condition deteriorated the following day as her vasopressor requirement increased and she needed non-invasive ventilation. She was investigated for sepsis, but all results were negative. A uterine ultrasound did not show any retained products of pregnancy.

The working diagnosis at the time was toxic shock syndrome, Kawasaki disease or PIMS. However, the history and investigations did not fit the criteria for toxic shock syndrome [3] or Kawasaki disease [4]. On the other hand, the patient was meeting the criteria for PIMS, but she had not had SARS-CoV-2 infection in the past and was not vaccinated at that time. Infectious diseases colleagues were consulted and recommended that IgG antibodies against SARS-CoV-2 should be checked to identify previous infection. The results indicated recent infection (most likely asymptomatic), in view of which the final diagnosis was PIMS.

Investigations

A complete blood count showed leucocytosis of 35.44×10^9/l (normal 3.9–11.19/l) and lymphopenia 0.71×10^9/l (normal 1.0–3.29/l), neutrophilia 33.9×10^9/l (normal 1.7–6.1×10^9/l), haemoglobin 6.7 g/dl (normal 11.8–15 g/dl), MCV 66.3 fl (normal 76–96 fl), MCH 17.2 pg (normal 27–33 pg) and MCHC 25.9 g/dl (normal 31–36.9 g/dl). The platelet count was normal. A comprehensive metabolic panel showed raised urea 13.0 mmol/l (normal 2.5–7.8 mmol/l), creatinine 347 µmol/l (normal 45–84 µmol/l), troponin 77 ng/l (normal 0–9 ng/l) and elevated hepatic enzymes: bilirubin 102 µmol/l (normal 3–21 µmol/l), ALP 101 U/l (normal 45–87 U/l) and GGT 79 U/l (normal 6–42 U/l). Inflammatory markers were elevated including a C-reactive protein of 358 mg/l (normal 0–5 mg/l), ferritin 967 ng/ml (normal 6.9–282.5 ng/ml), D-dimer 3.88 µg/ml (normal 0.01–0.50 µg/ml), procalcitonin 21.10 µg/l (normal 0.0–0.06 µg/l), interlukin-6 of 1910 ng/l (normal 0–7 ng/l) and B-type natriuretic peptide 30,180 ng/l (normal <125 ng/l). Bacterial blood cultures were negative.

Chest x-ray showed bilateral patchy infiltrates (*Fig. 1*). A CT pulmonary angiogram was negative for pulmonary embolus but showed airspace consolidation and lower lobe effusions (*Fig. 2*). An electrocardiogram and transthoracic echocardiogram were normal even though pro-BNP was elevated.

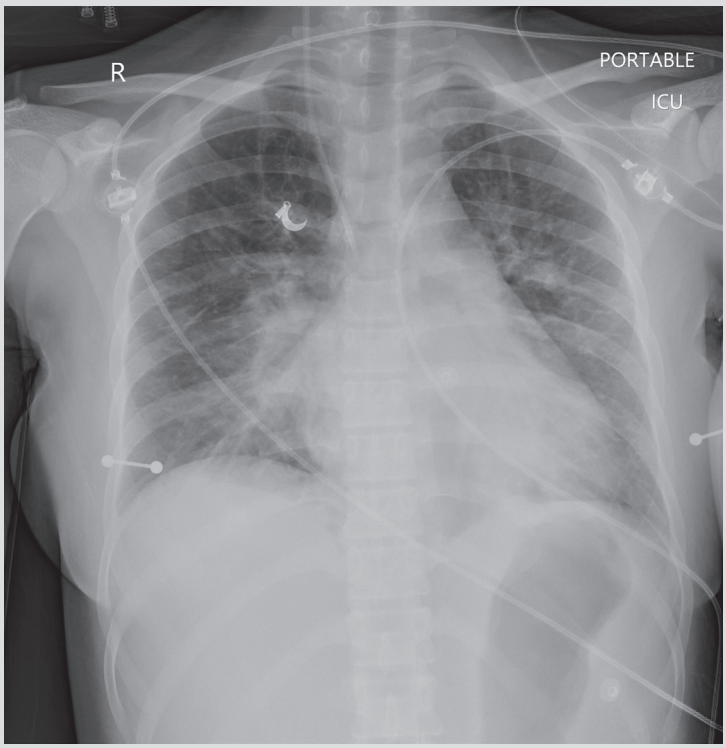

Figure 1. Chest x-ray showing bilateral patchy infiltrates

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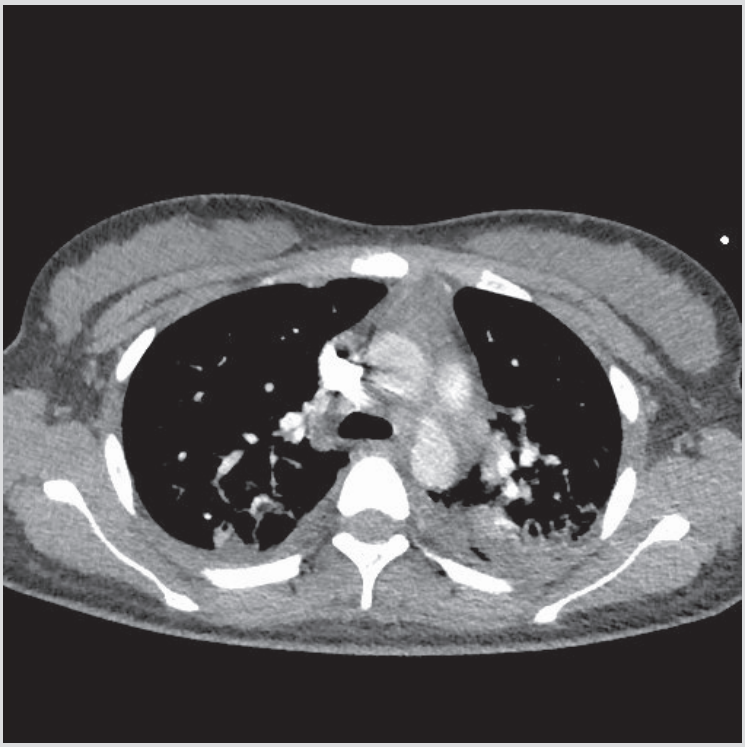

Figure 2. CT pulmonary angiogram showing infiltrates bilaterally with small pleural effusions

Differential diagnosis

The differential diagnosis included sepsis, toxic shock syndrome, Kawasaki syndrome and SARS-CoV-2 infection.

Treatment

The patient was initially given broad-spectrum antibiotics to cover for infection, but continued to deteriorate. During the initial period of admission, investigations were carried out to exclude other conditions (i.e., sepsis, toxic shock syndrome, SARS-CoV-2). On day 3 she was commenced on treatment for PIMS (methylprednisolone and IVIG) and had started to improve by day 4. She received 3 days of methylprednisolone and IVIG and a tapering dose of steroids.

Outcome and follow-up

The patient was diagnosed with PIMS based on WHO criteria [1,5]. Her clinical condition improved within 24 hours of starting methylprednisolone and IVIG. She was discharged from hospital after 10 days. She was well at a follow-up clinic 4 weeks after discharge.

DISCUSSION

PIMS is a difficult condition to diagnose in those patients who have a negative PCR test for SARS-CoV-2 and are unaware of previous infection. Presentation varies but typically includes shock, dyspnoea, abdominal pain, elevated inflammatory markers, and raised D-dimers and interlukin-6 [2]. Early diagnosis is unusual as symptoms are non-specific.

The WHO criteria [1] for the diagnosis of PIMS include more than 3 days of fever and two of the following:

1. Rash or bilateral non-purulent conjunctivitis or signs of mucocutaneous inflammation
2. Hypotension or shock
3. Features of myocardial dysfunction
4. Evidence of coagulopathy
5. Acute gastrointestinal problems.

In addition, the following features should be present to meet the criteria for PIMS: elevated inflammatory markers, no obvious cause of inflammation, and evidence of SARS-CoV-2 infection or contact with a patient with SARS-CoV-2 infection.

The pathophysiology of PMIS in both children and adults is unknown, although hyperinflammation and extrapulmonary organ dysfunction have been described in hospitalized patients with severe SARS-CoV-2.

PIMS usually occurs between 4 and 6 weeks after the patient has been diagnosed with SARS-CoV-2 infection [2]. The presentation can be similar to cytokine storm which is a serious and fatal complication of SARS-CoV-2 infection in adults. As in cytokine storm, IL-6 plays a key role in PIMS: it interacts with the cytokine and STAT3, and produces a complex panel of cytokines which are responsible for PIMS activation[6]. The European Centre for Disease Prevention and Control (ECDC) released a publication on 15 May 2020 stating that there had been five deaths among 250 cases of PIMS [7]. When PIMS is suspected, a multi-disciplinary approach and the involvement of the relevant specialities is important.

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