

Case Study

Kawasaki-like Presentation in A Child with Multisystem Inflammatory Syndrome in Children and Adolescents (MIS-C)

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Background: SARS-CoV-2 infection appears mild in most children. However, multisystem inflammatory syndrome (MIS-C) is more commonly seen in children and adolescents.

Aims: We aim to report a pediatric patient with MIS-C which was misdiagnosed as an upper respiratory tract infection.

Case Description: A 5-year-old boy presented to casualty with fever and rhinorrhoea, associated with cough for 2 weeks. He had multiple visits to the general practitioners but his symptoms did not improve despite antibiotics. He developed rash over his face, trunk and limbs one day prior to admission. He had a high spike fever and vomiting as well. Upon examination, the boy was lethargic and had a coated tongue. There were polymorphic macules and papules over the limbs and trunks. His lips were reddish and there were sub-centimeter bilateral cervical lymph nodes. The child developed multiple spikes of temperature in the ward. His blood investigations showed lymphocytosis. Echocardiography showed a small pericardial effusion of 3mm. He had raised inflammatory markers. He had a negative RT-PCR test for SARS-CoV-2 but showed positive serology test for IgG to SARS-CoV-2. He was treated as MIS-C and given intravenous immunoglobulin (IVIG) at 1g/kg. A skin biopsy was done and revealed vacuolar interface dermatitis. He recovered well and was discharged on day 4 of admission.

Conclusion: MIS-C is a potentially life-threatening complication among children with SARS-CoV-2 infections. A high index of suspicion is paramount for early diagnosis and treatment of MIS-C to reduce its mortalities.

Keywords: Multisystem Inflammatory Syndrome in Children and Adolescents (MIS-C), pediatric dermatology, COVID-19

Introduction

WHO declared severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) a global pandemic in March 2020. According to the COVID-19 dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU), as of 5 May 2022, there were about 515 million confirmed cases of covid-19 resulting in more than 6.2 million death worldwide.¹ Contrary to adults, most children with SARS-CoV-2 infection have mild symptoms.² In April 2020, there were unprecedented clusters of children and adolescents from North America and Europe, presented with multisystem inflammatory condition and mimicked toxic shock syndrome and Kawasaki Disease.³ These cases presented with acute illness leading to a hyperinflammatory syndrome which resulted in multiorgan failure and had a temporal and geographical relationship with the COVID-19 outbreak. Subsequently, World Health Organisation (WHO) developed a preliminary case definition and case report form for multisystem inflammatory disorder in children and adolescents (MIS-C) as summarised

in Figure 1.⁴ We report a case of MIS-C fulfilling WHO criteria who was initially referred to our dermatology clinic for a Kawasaki-like illness.

History

A 5-year-old boy, previously well with vaccinations up to his age, presented to casualty with fever, rhinorrhoea, and cough for 2 weeks. These were accompanied by a poor appetite. Prior to his presentation to the hospital, he had multiple visits to the general practitioners and was started on oral Amoxicillin/clavulanic acid 20mg/kg for 12 days. However, his symptoms did not improve, and he became lethargic for the past six days. He also developed a rash one day prior to admission. The rash was described as erythematous patches over the face then spreading to limbs and trunk within a day. He then started to have a high spiking fever (38.2°C) and three episodes of vomiting on the day of admission, prompting his parent to bring him to the hospital. Among his family member, his uncle had fever and cough as well. His last contact with his uncle was four days prior to his illness. Other family members were well.

Upon examination, the child was lethargic looking with coated tongue. There were polymorphic macules and papules over the limbs and trunks, involving palms and soles. His lips were reddish. (Figure 2) Examination of the neck revealed sub-centimeter lymph nodes in the bilateral cervical region. His conjunctiva and groin were unremarkable. Admitting diagnosis was Kawasaki-like disease and further assessment and management was planned.

In the ward, he had multiple spikes of fever up to 39°C. Otherwise, his vitals were stable. His laboratory investigations showed leukocytosis (20.6X10³/ul) with predominantly lymphocytes (57%). There were no blast cells seen on the peripheral blood film. His renal function and liver profile were within the normal range. Echocardiography showed good contractility with a small pericardial effusion of 3mm. He had raised inflammatory markers, with C-Reactive Protein of 111.4 nmol/L (<47.6), and Erythrocyte sedimentation rate (ESR) of 29 mm/hour (<10). Autoimmune workup including antinuclear antibody (ANA) and anti-double stranded DNA (dsDNA) was negative and the complement C3 and C4 levels were within normal range. His coagulation profile was normal. D-dimer was raised at 0.460 ug/ml. (<0.25). His blood culture showed no growth after 5 days. He had a negative RT-PCR test for SARS-CoV-2. However, his SARS-CoV-2 serology test had positive IgG and Negative IgM. He was subsequently treated as MIS-C. A single dose of Intravenous immunoglobulin (IVIG) at 1g/kg was given. A skin biopsy was done which later revealed vacuolar interface dermatitis. There were no features of leukocytoclastic vasculitis. (Figure 3-4) Immunofluorescence studies were negative for IgG, IgM, IgA, C3 and C1q. His fever settled after the IVIG, and the rash faded in 2-3 days. He was discharged well on day 4 of admission. Upon our last review in the dermatology clinic one month later, he was well and didn't experience significant sequelae. Repeated echocardiography after one month showed resolved pericardial effusion.

Discussion

MIS-C is believed to be resulted from the dysregulated immune system toward SARS-CoV-2 infection as opposed to direct cellular injury from viral infection.⁵ Patient may present with multisystemic inflammation mimicking toxic shock syndrome and Kawasaki disease.³ Clinical manifestations of MIS-C such as fever, gastrointestinal symptoms, and rash, are commonly seen in many systemic infections among the paediatric population.⁶ Therefore, it remains a diagnosis of exclusion.

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| <p>Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19 Preliminary case definition [4]</p> <p>Children and adolescents 0–19 years of age with fever ≥ 3 days.</p> <p>AND two of the following:</p> <ol style="list-style-type: none"> 1. Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands or feet). 2. Hypotension or shock. 3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP). 4. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers). 5. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain). <p>AND.</p> <p>Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin.</p> <p>AND.</p> <p>No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.</p> <p>AND.</p> <p>Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.</p> |
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Figure 1: Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19 Preliminary case definition

RT-PCR and serology tests for SARS-CoV-2 were positive in 32-59% and 87% of MIS-C cases, respectively.⁶⁻⁷ Our case fulfilled the WHO criteria for MIS-C as he presented with 2 weeks of fever, associated with Kawasaki-like features such as polymorphic rash and cervical lymph nodes, evidence of pericardial effusion from echocardiography and acute gastrointestinal symptoms. His blood investigations also showed elevated inflammatory markers and no evidence of bacterial infections. Finally, his COVID-19 serology showed positive IgG, indicating past SARS-CoV-2 infection. A systemic review by Trisha Radia et al reported that patients with MIS-C have a high frequency of gastrointestinal symptoms such as vomiting, diarrhea, and abdominal pain.⁷ Rashes of varying descriptions had been reported in 42-75% of MIS-C cases. These include urticarial, morbilliform, livedoid rash, and purpura.⁶⁻⁷ Skin lesions were commonly seen over the lower limbs, chest and

upper limbs, including palms and soles.⁷ Skin biopsies of patients with MIS-C may present two different patterns: leukocytoclastic vasculitis or erythema multiforme-like.⁸ The histologic findings in our case were in favour of the erythema multiforme-like pattern.

Kawasaki-like MIS-C had been frequently reported in paediatric patients with SARS-CoV-2 infection. From previous case series, few distinguishing features differ from classic Kawasaki Disease. Kawasaki-like MIS-C affects the elder paediatric population (4-17 years), more likely to have gastrointestinal symptoms, a higher risk of shock syndrome, myocarditis, lymphopenia and is more likely to require intensive care support.⁹⁻¹⁰ They tend to have the incomplete form of Kawasaki disease (2 or 3 principal clinical criteria of Kawasaki disease, and echocardiography or laboratory finding similar to Kawasaki disease).⁹ Clinicians should be aware of this cluster of presentations with a high index of suspicion. All children and adolescents present with Kawasaki-like illness should have RT PCR and serology tests for SARS-CoV-2 done.



Figure 2: Clinical photos showing polymorphic macules and papules over the face, limbs, and trunks. The lesions also involved his palms and soles.

Current management of MIS-C is mainly following the guidelines for the management of Kawasaki Disease. Aggressive and prompt management is recommended. This includes the use of IVIg with or without corticosteroids.^{6,11} Between 30-80% of patients may require adjunctive immunomodulatory therapy such as methylprednisolone, anakinra, tocilizumab and infliximab may be required to control inflammation. According to Trisha Radi et al, up to 68% of cases of MIS-C require critical care admission. The mortality rate of MIS-C remains low (1.5%) with prompt management and critical care support.⁷

Conclusion

Children with SARS-CoV-2 infections usually have mild symptoms. Nonetheless, MIS-C is an uncommon but potentially life-threatening complication. Familiarity with the presenting features of MIS-C such as Kawasaki-like illness and a high index of suspicion is paramount for early diagnosis. Prompt treatments of MIS-C is essential to reduce its morbidities and mortalities.

Acknowledgement

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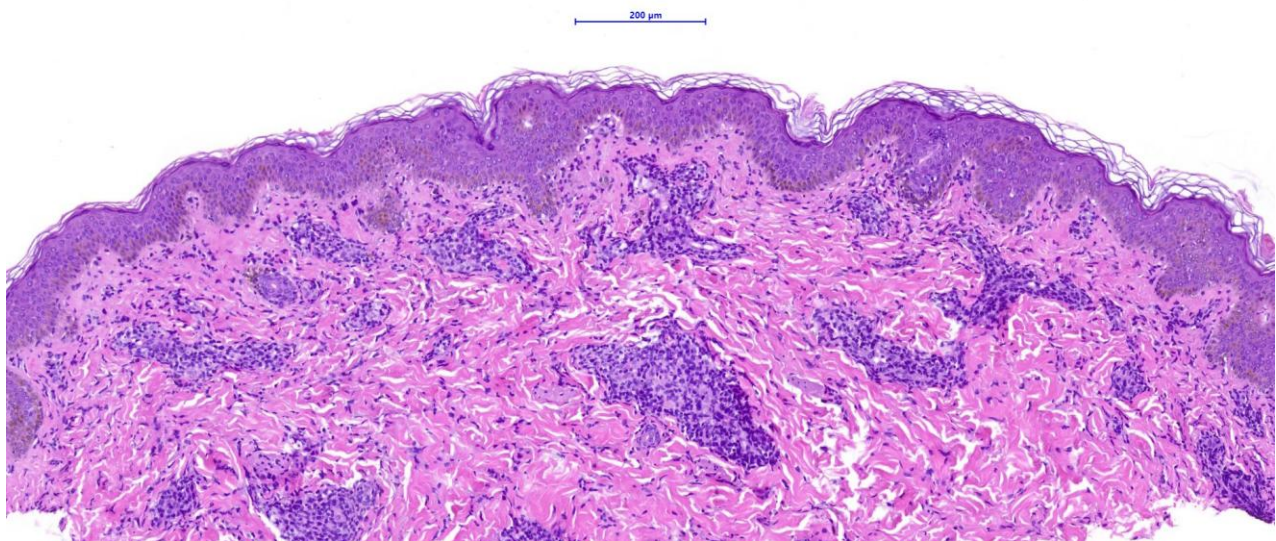


Figure 3: Low power view showing skin tissue with mild irregular acanthosis, densely collagenous dermis and mild to moderate inflammatory cells infiltration with perivascular aggregates.

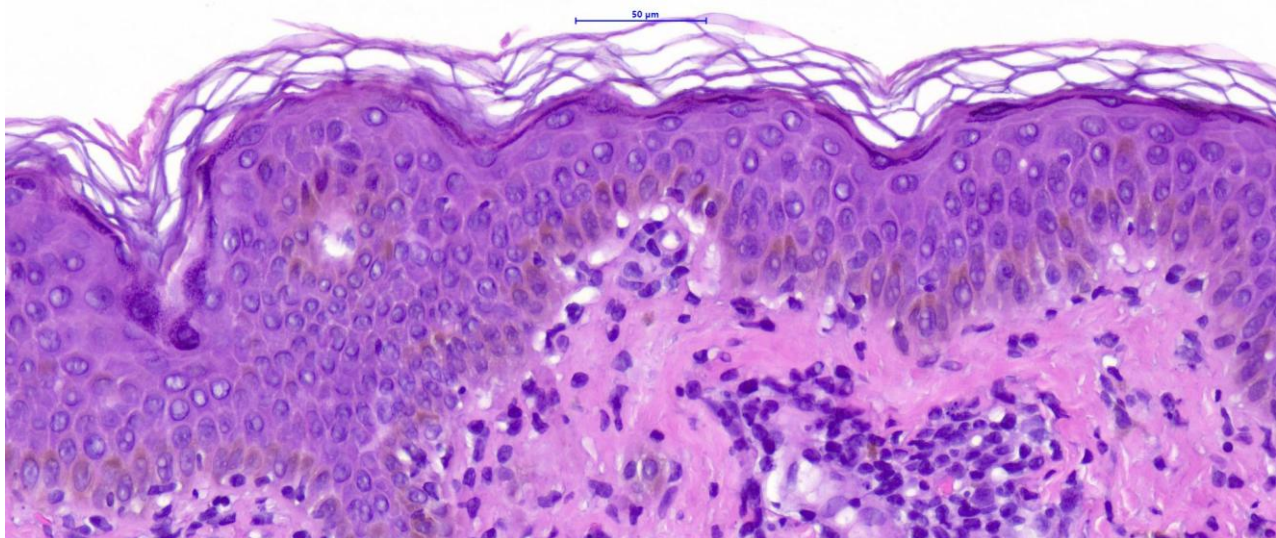


Figure 4: High power view showing focal lymphocytes infiltration in the dermo-epidermal junction with basal vacuolar changes.

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