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CASE REPORT

A Case of Steroid-Responsive Multisystem Inflammatory Syndrome in Adults With SARS-CoV-2

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Abstract

While the COVID-19 pandemic continues to evolve, different phenotypic variants of the disease are being recognized. Multisystem inflammatory syndrome in adults is an emerging entity that has yet to be fully characterized. The syndrome involves extrapulmonary multiorgan failure with hyperinflammation that typically affects young healthy males, approximately 2 to 12 weeks after infection with SARS-CoV-2. There are no formal guidelines for management, although the syndrome appears responsive to immunomodulators and supportive care. Clinicians should be aware of this unusual and severe clinical entity and the general principles of its management.

Background

Despite many advances in prevention and management, SARS-CoV-2 infections remain a major cause of morbidity and mortality worldwide. Reports on multisystem inflammatory syndrome in adults (MIS-A) suggest a mortality rate of 11% (1). With each wave of infections, new clinical phenotypes have emerged (1–5). Most physicians have become accustomed to recognizing COVID-19 hyperinflammatory syndrome, the most common severe presentation of illness caused by SARS-CoV-2; however, other emerging rare clinical phenotypes may go unrecognized.

Objective

Multisystem inflammatory syndrome in children (MIS-C) has been well characterized in the guidelines published by the American College of Rheumatology (ACR) for management (6). A similar syndrome has since been recognized in adults, MIS-A, and is under active characterization by the Centers for Disease Control and Prevention (CDC) (Table 1) (7). Given its rarity, incomplete characterization, severity, and reported responsiveness to immunomodulating therapies, MIS-A presents a difficult but important diagnosis. We report a case of MIS-A in a previously healthy young man who responded to oral dexamethasone.

Case Report

A 33-year-old Black man with no prior medical illness presented for cardiogenic shock. He was diagnosed with mild COVID-19 infection 4 weeks previously after developing symptoms of mild cough and dyspnea with chest tightness. He worked as a barber and often was not wearing a mask and felt the COVID-19 vaccination was not necessary. He quarantined at home for 1 week and his symptoms improved. For approximately 2 weeks he felt well, but then developed dyspnea and chest tightness again in addition to fevers, myalgias, fatigue, and abdominal pain (Figure 1). He initially presented to an outside institution where he was noted to be febrile (39 °C), tachycardic, hypotensive, hypoxic, and encephalopathic. Nasopharyngeal swabs samples tested for SARS-CoV-2 via polymerase chain reaction yielded negative results. Physical examination revealed normal heart sounds, but a jugular venous pressure of 15 cm. He had rales in the bases of both lungs and diffuse abdominal tenderness. Laboratory results were notable for white blood cell count of 27×10^9 cells/L, platelets of 252×10^9 K/L, creatinine level of 460 µmol/L, troponin level of 0.25 µg/L, pro-brain natriuretic peptide level of 1719 ng/L, lactic acid level of 5.4 mmol/L, aspartate aminotransferase level of

Table 1. **CDC Case Definition for MIS-A**

A patient aged ≥21 years hospitalized for ≥24 hours, or with an illness resulting in death, who meets the following clinical and laboratory criteria. The patient should not have a more likely alternative diagnosis for the illness (eg, bacterial sepsis, exacerbation of a chronic medical condition).
I. Clinical Criteria
Subjective fever or documented fever (≥38.0 °C) for ≥24 hours before hospitalization or within the first 3 days of hospitalization* and at least 3 of the following clinical criteria occurring before hospitalization or within the first 3 days of hospitalization.* At least 1 must be a primary clinical criterion.
A. Primary clinical criteria 1. Severe cardiac illness: Includes myocarditis, pericarditis, coronary artery dilatation/aneurysm, or new-onset right or left ventricular dysfunction (left ventricular ejection fraction <50%), second/third-degree A-V block, or ventricular tachycardia (note: cardiac arrest alone does not meet this criterion) 2. Rash AND nonpurulent conjunctivitis B. Secondary clinical criteria 1. New-onset neurologic signs and symptoms: Includes encephalopathy in a patient without prior cognitive impairment, seizures, meningeal signs, or peripheral neuropathy (including Guillain-Barré syndrome) 2. Shock or hypotension not attributable to medical therapy (eg, sedation, renal replacement therapy) 3. Abdominal pain, vomiting, or diarrhea 4. Thrombocytopenia (platelet count $<150 \times 10^9$ L)
I. Laboratory evidence
The presence of laboratory evidence of inflammation AND SARS-CoV-2 infection. A. Elevated levels of at least 2 of the following: C-reactive protein, ferritin, interleukin-6, erythrocyte sedimentation rate, procalcitonin B. A positive SARS-CoV-2 test for current or recent infection by reverse transcriptase polymerase chain reaction, serology, or antigen detection

Adapted from Multisystem Inflammatory Syndrome in Adults (MIS-A) Case Definition Information for Healthcare Providers. Accessed at https://www.cdc.gov/mis/mis-a/hcp.html on 12 January 2022.

* These criteria must be met by the end of hospital day 3, where the date of hospital admission ins hospital day 0.

45.9 µkat/L, and alanine aminotransferase level of 33.5 µkat/L. A chest radiograph showed minimal right basilar opacities, but no frank pneumonia. An electrocardiogram revealed diffuse ST elevations. Transthoracic echocardiogram revealed global hypokinesis with an ejection fraction of 20%. Because of concerns for worsening shock while the patient was receiving vasopressors and dobutamine, he was administered piperacillin-tazobactam and transferred to the cardiac intensive care unit at our institution. A right-heart catheterization was performed on day 6 of admission, revealing elevated right atrial pressure with normal heart pressures and cardiac index. By day 7 of admission, pressors and inotropes had been withdrawn and a repeat transthoracic echocardiogram showed improved ejection fraction of 40%. However, on day 9, he developed headaches, photophobia, and eye pain, and had persistent encephalopathy. Inflammatory makers noted

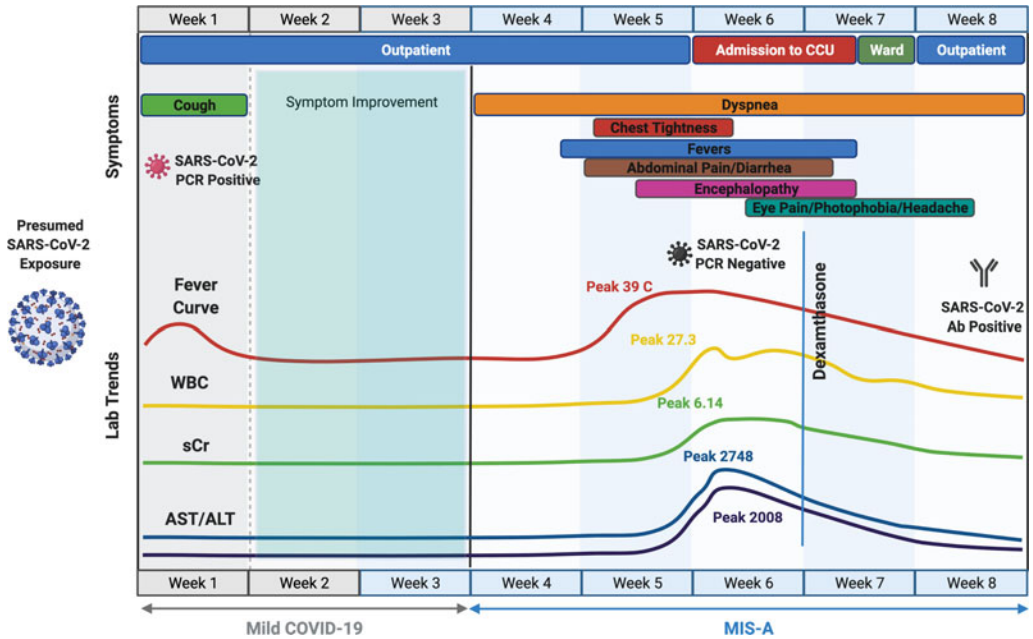

Figure 1. **Time course of MIS-A from SARS-CoV-2. The time from onset through symptom resolution and laboratory study normalization is approximately 8 weeks. The patient was polymerase chain reaction positive for COVID-19 at initial presentation, but negative at presentation from relapse. On outpatient follow-up, the patient was found to have positive SARS-CoV-2 antibodies. The figure is based on data obtained during outpatient visits and inpatient admission. For periods without data, the figure was completed with approximated values based on the clinical course. The full data set of values is available on request. This figure was created with BioRender.com. ALT = alanine aminotransferase; AST = aspartate aminotransferase; MIS-A = multisystem inflammatory syndrome in adults; sCr = serum creatinine; WBC = white blood cell.**

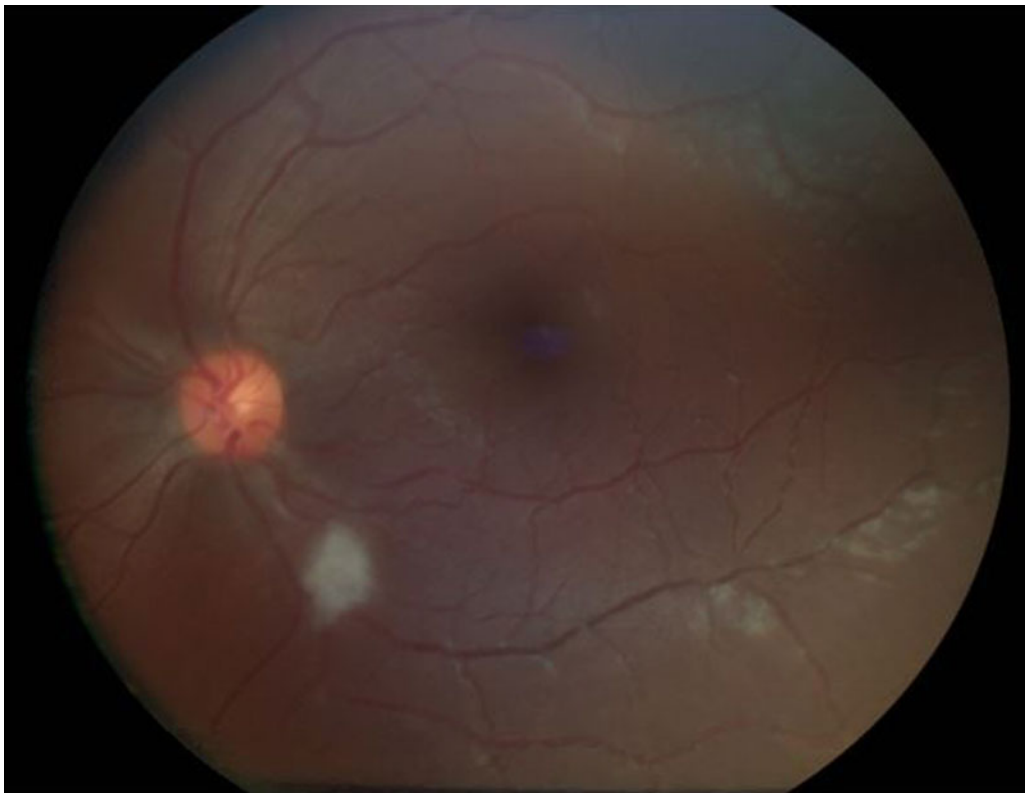

Figure 2. **Color fundus photograph of left eye demonstrating cotton wool spot and vessel tortuosity.**

to be elevated: D-dimer level of more than 20 000 ng/mL, sedimentation rate of 100 mm/h, C-reactive protein level of 29.7 mg/dL, and ferritin level of 2312 ng/mL. Magnetic resonance imaging of the brain showed no acute pathology. The ophthalmologic assessment was consistent with episcleritis, whereas dilated fundus examination revealed bilateral vascular tortuosity and a single cotton wool spot in the left eye (Figure 2). He was administered oral dexamethasone 6 mg daily for a planned 10-day course after a continued systemic inflammatory state with multiorgan involvement was recognized. The patient experienced immediate improvement of his symptoms when receiving dexamethasone, including complete resolution of episcleritis within 24 hours. His liver function tests and renal function normalized, his inflammatory markers decreased, and his vision improved. By day 14 of admission, his mental status had returned to baseline and he was discharged to complete the dexamethasone course at home. In a follow-up outpatient visit on day 28 after admission, the patient continued to have clinical improvement. Unfortunately, however, the patient was lost to follow-up.

Discussion

Multisystem inflammatory syndrome in adults is a rare and serious post-COVID-19 sequela with high morbidity and mortality. MIS-A generally presents 2 to 5 weeks after initial infection with SARS-CoV-2 but can also present up to 12 weeks after (3, 8, 9), with a distinct demographic reported: young, otherwise healthy men of minority background. Non-Hispanic White persons appear to be in the minority of MIS-A cases (3). Persons belonging to racial and ethnic minority groups often live in low-income neighborhoods, lack health insurance, and have greater comorbidities, which have been associated with worse outcomes with SARS-CoV-2 infections. Our patient had similar demographics and low socioeconomic background, placing him at high risk for complications from SARS-CoV-2 infection.

This hyperinflammatory syndrome leads to multiorgan compromise most commonly including the heart, liver, brain, kidney, skin, and gastrointestinal tract. Interestingly, there can be eye involvement presenting as any combination of nonexudative conjunctivitis, uveitis, episcleritis, and retinal ischemia (3, 4, 8, 9). Our patient did not have clinical evidence for pericarditis or myocarditis because he had a rapid improvement in ejection fraction with extracardiac manifestations. The pathophysiology in MIS-C and MIS-A remains unknown. There are proposed mechanisms for extrapulmonary dysfunction including direct endothelial damage, thromboinflammation, dysregulation of the immune response with reduced neutralizing antibody levels allowing for persistent low-level infection in nonpulmonary tissues, and dysregulation of the renin-angiotensin-aldosterone system (3, 9).

MIS-C has been well characterized with guidelines published by the ACR for management, whereas the parallel syndrome for adults has yet to be defined. The CDC recently published a case definition for diagnosing MIS-A, in which adult patients with fever must exhibit 3 of 8 specified criteria (cardiac illness, rash and conjunctivitis, neurologic signs and symptoms, shock, gastrointestinal symptoms, thrombocytopenia, laboratory

evidence of inflammation, and confirmed SARS-CoV-2 infection) (7). Our patient's clinical course was consistent with the working definition by the CDC because it fulfilled 6 of the 8 clinical criteria with positive COVID-19 IgM antibody.

Treatment modalities have largely been extrapolated from suggested therapies from MIS-C because there are no standard management guidelines for MIS-A. Supportive care and immunomodulator therapy including steroids, intravenous immunoglobulin (IVIg), and anti-interleukin-6 therapies have been reported (4, 8). There are observational data to support the use of steroids with IVIg in MIS-C, and the ACR guidance document for MIS-C recommends methylprednisolone and IVIg in severe cases (6, 10–13). IVIg is believed to affect the number and function of regulatory T cells that help control inflammation (10). Vaccination against COVID-19 has been shown to protect against MIS-C and is speculated to provide protection against MIS-A, though a recent report has described a fatal case of MIS-A in a vaccinated patient (5, 14).

Although most physicians have become comfortable with the recognition and management of COVID-19 infection and COVID-19 hyperinflammatory syndrome, unusual and severe phenotypic variants of the disease have yet to be recognized. Further studies on the immunopathogenesis are still needed, with consideration of vaccine implications. In addition, the chronic sequelae of this syndrome remain unclear; therefore, long-term follow-up care and monitoring should be encouraged. Unfortunately, our patient was lost to follow-up so it is unclear if he had residual symptoms or any signs of long COVID. As the COVID-19 pandemic continues to evolve, clinicians should become familiar with this new clinical entity to ensure prompt recognition and targeted management.

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