

Multisystem Inflammatory Syndrome in an Adult With COVID-19

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Abstract: Multisystem inflammatory syndrome (MIS) in children is a severe illness characterized by fever, laboratory evidence of inflammation, and multisystem organ dysfunction resulting from severe acute respiratory syndrome coronavirus 2 infection in a patient younger than 21 years. We present the case of a 39-year-old man with evidence of prior COVID-19 who seemed to meet all non-age-related criteria for MIS in children as well as criteria for the working definition of MIS in adults, and who improved after treatment with aspirin, corticosteroids, and intravenous immunoglobulin. Clinicians should be aware of this new inflammatory illness, not only in children but potentially also in adults with antecedent or concurrent COVID-19.

Key Words: SARS-CoV-2, COVID, coronavirus, inflammation, MIS, case report, multisystem inflammatory syndrome

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Multisystem inflammatory syndrome (MIS) has previously been described in children during or after COVID-19^{1,2} but has not been well characterized in adults, with very few cases reported globally to date.^{3–5} This report describes an adult with a severe illness characterized by fever, laboratory evidence of inflammation, and multisystem organ dysfunction without severe respiratory involvement in the context of COVID-19 who improved with aspirin, corticosteroids, and intravenous immunoglobulin.

CASE PRESENTATION

A 39-year-old African American man with diabetes mellitus type 2 presented to the emergency department in July 2020 with 3 days of fever, fatigue, myalgias, sore throat, dyspnea, vomiting, and diarrhea. He reported that 2 of his neighbors with whom he had contact were diagnosed with COVID-19 in the 10 days before presentation.

At the time of presentation to the emergency department, the patient appeared ill but was not in distress. He was febrile (temperature, 39.4°C), tachycardic (pulse, 127 beats per minute), and tachypneic (respiratory rate, 27 breaths per minute). His systolic

blood pressure was 134 mm Hg, and his diastolic blood pressure was 95 mm Hg. His peripheral capillary oxygen saturation was 98%. He exhibited dry mucus membranes with no pharyngeal erythema or exudates and mild cervical lymphadenopathy. His lungs were clear to auscultation. His abdomen was nontender and nondistended. He had a confluent, blanching rash on his chest and back. Pertinent laboratory studies on presentation are presented in Table 1. Of note, his C-reactive protein level was 366 mg/L, and his ferritin level was 1907 ng/mL. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was not detected by polymerase chain reaction (PCR) on nasopharyngeal swab using the DiaSorin LIAISON platform. A chest radiograph demonstrated no infiltrates. Computed tomography angiography of the chest showed no pulmonary embolism and mild bibasilar atelectasis. The patient's glucose was 403 (hemoglobin A1c was 9.2%), but the venous blood gas (pH 7.44 and PCO₂ 35 mm Hg) and serum beta hydroxybutyrate (0.46 mmol/L) were not consistent with diabetic ketoacidosis. Vancomycin and cefepime were administered, and he was admitted to the intensive care unit for persistent tachycardia. SARS-CoV-2 was not detected by PCR on a second nasopharyngeal swab using the platform developed by the Centers for Disease Control and Prevention.⁶

On hospital day 2, the patient developed a petechial rash on his left forearm. Doxycycline was administered for possible tickborne illness. All other antimicrobials were discontinued when blood cultures remained without growth at 48 hours. The PCR test for respiratory pathogens from a nasal swab and for *Clostridioides difficile* from a stool sample were both negative. Rocky Mountain spotted fever antibody, *Ehrlichia/Anaplasma* PCR, cytomegalovirus PCR, Epstein-Barr virus PCR, urine *Legionella* antigen, anti-nuclear antibody, and rheumatoid factor were negative.

On hospital day 4, the patient experienced new confusion. Magnetic resonance imaging (MRI) of the brain showed scattered cerebral white matter T2/flair hyperintensities potentially consistent with vasculitis or chronic microvascular changes. He experienced episodes of regular narrow complex tachycardia with heart rate of 130 to 140 beats per minute, for which he was administered metoprolol. An electrocardiogram demonstrated diffuse ST segment elevations. His troponin I increased to 1.43 ng/mL and decreased thereafter. Transthoracic echocardiogram was normal, and cardiac MRI showed increased T1 signal, suggestive of myocardial edema or inflammation. Given his elevated troponin and diffuse ST segment elevations, this study supported a clinical diagnosis of myopericarditis. SARS-CoV-2 was not detected by PCR on a third nasopharyngeal swab using the Centers for Disease Control and Prevention platform.

At this time, his immunoglobulin G (IgG) to SARS-CoV-2 was found to be positive using the Abbott Architect SARS-CoV-2 IgG assay, which has demonstrated a specificity of 99.9%.⁷ Because his systemic inflammation, myopericarditis, hepatitis/hyperbilirubinemia, erythematous rash on trunk and arms, and possible neurologic involvement with alteration in mental status resembled the manifestations of the MIS in children (MIS-C), he was administered 5 mg/kg (325 mg) of

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TABLE 1. Results of Laboratory Testing

Laboratory Assessment	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11
White blood cell count, × 10 ³ cells/μL	14.9	12.1	14	17	23.7	26	27.9	27.4	23	21.6	16.9
Hemoglobin, g/dL	14	12.9	12.7	11	11.3	10.3	9	8.8	9.2	8.6	8.6
Hematocrit, %	40	37	36	31.2	31	29	26	25	26	29	26
Platelet, × 10 ³ U/μL	163	144	134	145	166	207	223	189	213	269	272
Creatinine, mg/dL	1.58	1.2	1.1	0.96	0.89	1.11	0.93	1.1	1	0.99	0.88
C-reactive protein, mg/L	366	366		423	423	349	254	137	81	57	35
Lactate dehydrogenase, U/L		261				499 → 368	331	520	353	350	323
Fibrinogen, mg/dL						597	531	358	315	252	197
Haptoglobin, mg/dL		368									
Ferritin, ng/mL		1907				3375	2857	>2000	2658	2379	1740
Troponin I, ng/mL		0.09		1.15 → 1.43	1.28 → 1.22	0.3	0.09	0.05	0.04	0.03	0.04
B-type natriuretic peptide, pg/mL						3597	2802	1387	1949	1604	1179
Lactic acid, mEq/L	3.8 → 3.0	2.7		2.2							
Procalcitonin, ng/mL		9.7									
International normalized ratio						1.1	1.2	1.3	1.4	1.4	1.3

The reference ranges in the institution for the following values are: white blood cell count (3.9–10.7 × 10³ cells/μL), hemoglobin (11.8–16.0 g/dL), hematocrit (36%–43%), platelets (135–371 × 10³ U/μL), creatinine (0.57–1.11 mg/dL), C-reactive protein (0.0–5.0 mg/L), lactate dehydrogenase (125–220 unit/L), fibrinogen (188–450 mg/dL), haptoglobin (14–258 mg/dL), ferritin (15–204 ng/mL), troponin I (≤0.03 ng/mL), B-type natriuretic peptide (10–100 pg/mL), lactic acid (0.5–2.2 mEq/L), procalcitonin (≤0.24 ng/mL), international normalized ratio (0.8–1.1).

aspirin once, 1 mg/kg IV (70 mg) of methylprednisolone every 12 hours for 5 days, and 2 g/kg of intravenous immunoglobulin divided over 2 doses. The patients' fever, tachycardia, mental status, and laboratory markers of inflammation improved over the subsequent 48 hours, and he was discharged home after a total of 10 days.

DISCUSSION

Multisystem inflammatory syndrome in children is a recently described febrile hyperinflammatory illness associated with antecedent or concurrent COVID-19. Criteria to establish a diagnosis of MIS-C include serious illness requiring hospitalization, fever (temperature, >38.0°C) or subjective fever lasting 24 hours or more, laboratory evidence of inflammation, multisystem organ involvement, laboratory-confirmed SARS-CoV-2 infection (PCR or IgG) or a known link to a person with COVID-19 in the preceding 4 weeks, and age younger than 21 years.² Since the presentation of our patient's case, a working definition of MIS in adults (MIS-A) has been proposed.⁵ Current criteria include severe illness requiring hospitalization in a person aged 21 years or older, a positive test result for current or previous SARS-CoV-2 infection (nucleic acid, antigen, or antibody) during admission or in the previous 12 weeks, severe dysfunction of 1 or more extrapulmonary organ systems, laboratory evidence of severe inflammation, and absence of severe respiratory illness. Based on these criteria, the authors believe that this case more closely resembles MIS-A rather than severe COVID-19, primarily due to the absence of respiratory illness.

MIS-C frequently occurs 2 to 4 weeks after SARS-CoV-2 infection with widespread organ involvement. The presentation of MIS-A is less clear, although current data suggest a similar time course.⁵ In 1 review of 186 cases in children, the gastrointestinal system was involved in 92% of cases, cardiovascular in 80%, hematologic in 76%, mucocutaneous in 74%, and respiratory in 70%.² Most patients had antibodies against SARS-CoV-2, and a smaller proportion had positive SARS-CoV-2 PCR testing. Given the similarity of MIS-C to Kawasaki disease in children, many patients are treated with intravenous immunoglobulin, glucocorticoids, and aspirin.^{1,4} Our patient's evaluation for COVID-19

included 3 negative SARS-CoV-2 PCR's and a positive SARS-CoV-2 IgG. Our patient received—and appeared to clinically respond to— aspirin, glucocorticoids, and intravenous immunoglobulin.

Because the presentation of MIS-C and MIS-A is nonspecific, other causes of systemic inflammation should be considered. Infectious etiologies, such as human immunodeficiency virus, hepatitis B, and endemic fungal infections, should be excluded. Systemic inflammatory and autoimmune diseases such as adult-onset Still disease, systemic lupus erythematosus, and vasculitis syndromes should be considered. Our patient's evaluation did not demonstrate evidence of typical and atypical bacterial infections, acute fungal infection, or acute viral infection. He had neither inflammatory arthritis nor rash consistent with adult-onset Still disease. His urinalysis had no evidence of glomerular involvement to suggest systemic lupus erythematosus or primary vasculitis such as antineutrophil cytoplasmic antibody-associated vasculitis. His cardiac MRI findings were similar to those found in prior cases of COVID-19 myocarditis.⁸

CONCLUSIONS

Multisystem inflammatory syndrome after infection with SARS-CoV-2 is an established sequela of COVID-19 in children. We report one of the first cases of suspected MIS after infection with SARS-CoV-2 in an adult. Our patient improved within 48 hours after treatment with aspirin, glucocorticoids, and intravenous immunoglobulin. Clinicians and researchers should remain vigilant for the possibility that adults may also experience MIS after COVID-19.

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