Multisystem inflammatory syndrome in adults: a case report and review of the literature

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Abstract

Background: The current coronavirus disease pandemic has brought recognition of multisystem inflammatory syndrome in adults as a de novo entity, temporally associated with severe acute respiratory syndrome coronavirus 2 viral infection in adults. Hypothesis about its true pathophysiology remains controversial.

Case report: The patient was a 22-year-old African American female presenting to the emergency department with fever, sore throat, and neck swelling for the past 3 days. During her initial emergency department visit, her blood pressure was stable at 110/57 mmHg, temperature of 39.4 °C, and heart rate of 150 beats per minute. While in the emergency department, she received broad-spectrum antibiotics (vancomycin and ceftriaxone) and 30 cc/kg bolus of normal saline. Originally, she was admitted to a telemetry floor. The following night, a rapid response code was called due to hypotension. At that time, her blood pressure was 80/57 mmHg. She appeared comfortable without signs of respiratory distress. She received intravenous fluids and vasopressors, and was transferred to the intensive care unit. The patient had reported a previous coronavirus disease infection a few weeks prior. She was diagnosed and treated for multisystem inflammatory syndrome in adults. Intravenous immunoglobulin infusion was initiated and completed on hospital day 5. She was weaned off vasopressors by day 6, and discharged home on day 11.

Conclusion: Our case report is an example of the presentation, diagnosis, and management of multisystem inflammatory syndrome. Our research into previous case reports illustrates the wide range of presentations, degree of end organ damage, and treatment modalities. This diagnosis needs to be considered in the presence of recent coronavirus disease infection with new-onset end organ failure, as prompt diagnosis and treatment is crucial for better outcomes.

Keywords: COVID, MIS-A, Organ failure, Pandemic, Case report

Background

The current coronavirus disease (COVID-19) pandemic has brought the recognition of multisystem inflammatory syndrome in adults (MIS-A) as a de novo entity temporally associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral infection in adults. Hypothesis about its true pathophysiology remains controversial. Its initial presentation, response to empiric therapy, and clinical outcomes are widely variable. We report the case of a 22-year-old female who presented with distributive shock after 3 days of fever, sore throat, and right-sided neck pain. She was diagnosed with MIS-A and successfully treated. We further provided the reader with an in-depth review of the current published case report of MIS-A available in the medical literature, and review the pathophysiology and clinical resemblance and difference to Kawasaki disease.
Case description

A 22-year-old overweight African American female, with a body mass index (BMI) of 29.1 kg/m², presented to the emergency department (ED) with 3 days of fever, sore throat, right-sided neck pain, and swelling. She denied any respiratory symptoms. She had tested positive for SARS-CoV-2 by polymerase chain reaction (PCR) 4 weeks prior, complaining of fever, chills, cough, headache, and diarrhea for 1 week. At that time, she had visited the ED and had been discharged with acetaminophen. Per the patient, she was not discharged with steroids or antibiotics.

During her initial ED visit, her blood pressure was stable at 110/57 mmHg, temperature of 39.4 °C, and heart rate of 150 beats per minute (BPM). While in the ED, she received broad spectrum antibiotics (vancomycin and ceftriaxone), 30 cc/kg bolus of normal saline, and blood cultures were obtained. Computed tomography (CT) of the neck with intravenous contrast revealed bilateral reactive lymphadenopathy with enlarged adenoids and mildly enlarged tonsillar pillars without abscesses. Initial chest X-ray was negative, without signs of pleural effusions or consolidations. Her electrocardiogram showed sinus tachycardia. She was admitted for persistent tachycardia and otolaryngology evaluation. Originally, the patient was admitted to a telemetry floor. The following night, a rapid response code was called due to hypotension. At that time, her blood pressure was 80/57 mmHg, heart rate was 125 BPM, respiratory rate of 25, and temperature of 103 F. She appeared comfortable, without signs of respiratory distress. She exhibited mild bilateral periorbital and lower extremities edema. Neck examination was notable for bilateral posterior lymphadenopathy with mild decreased range of motion. Her pulmonary and cardiac examinations were unremarkable other than tachycardia. Additionally, the rapid response team noted bilateral conjunctivitis as well as small strawberry rash diffusely. Another electrocardiogram was performed, which showed low voltage and sinus tachycardia. A point of care ultrasound (POCUS) was performed that was negative for pericardial effusion, right ventricular dilation, or signs of obstructive shock. She was fluid resuscitated with an additional 2 L of normal saline, with transient/negligible improvement of blood pressure. She was bolused another liter of lactated Ringer’s, initiated norepinephrine infusion, and admitted to the intensive care unit (ICU) for the management of distributive shock.

Her follow-up studies showed a peak d-dimer of 3557 ng/mL, C-reactive protein (CRP) of 47 mg/dL, and ferritin of 344 ng/mL. Fibrinogen was 460 mg/dL and remained within normal limits. She has a nadir hemoglobin of 10.6 g/dL, 24-hour urinary protein of 560 mg with preserved glomerular filtration rate through her entire hospital admission. Initial white blood cell count was 7000 cells/mm³ and only increased slightly after corticosteroid use. She exhibited a mild elevation of aspartate transaminase (AST) to 46 U/L, alanine transaminase (ALT) of 49 U/L, and alkaline phosphate (ALP) of 51 U/L. Her pro-B-type natriuretic peptide (BNP) was 3590 pg/mL on hospital day 2 and her troponin I peaked at 0.257 ng/m on day 3.

Official transthoracic echocardiography revealed a mild systolic dysfunction, grade 2 diastolic dysfunction and an ejection fraction of 40–45%, and a concentric small pericardial effusion. Coronary angiography revealed normal coronaries without evidence of obstruction or aneurysms. CT angiogram of the chest was negative for pulmonary embolism but notable for moderate-sized pleural effusions bilaterally. Cardiac magnetic resonance imaging (MRI) was not performed.

The patient received supportive treatment with dynamic hemodynamic-driven preload resuscitation and vasopressor support with norepinephrine. Her maximum dose of norepinephrine was 5 mcg/minute. Infectious disease was consulted on hospital day 3, who broadened antibiotic coverage with 3.375 mg piperacillin/tazobactam every 8 hours (q8) for 1 week. Broad infectious and immunologic workup was ordered and is summarized in Table 1. She tested negative for immunoglobulin (Ig) M and positive for IgG SARS-CoV-2 antibody. Dexamethasone 4 mg was initiated in the ED and continued q12 hours until hospital day 5 when it was changed by infectious disease team to hydrocortisone 50 mg q6 hours. Full-dose aspirin was initiated on hospital day 4 and continued until discharge. Intravenous immunoglobulin (IVIG) infusion was initiated and completed on hospital day 5, when she received 80 g over 16 hours. She was weaned off vasopressors by hospital day 6. An MRI of the neck without contrast on day 6 revealed resolution of her prevertebral soft tissue swelling and persistent nonspecific cervical lymphadenopathy bilaterally without any fluid collection. She received intravenous furosemide and albumin 25% intermittently with improvement in her interstitial edema. Blood and urine cultures remained negative during her hospitalization. She was discharged home on day 11.
Discussion
Multisystem inflammatory syndrome in adults (MIS-A) was first mentioned in 2020 following the initial description of this syndrome in the pediatric population (multi-inflammatory syndrome in children) during the COVID-19 pandemic. Since its first recognition, several case reports have been published in the literature, with a wide range of clinical manifestations and therapeutic interventions. MIS-A is suspected to be caused by an abnormal immune response to SARS-CoV-2 infection and is commonly associated with clinical features such as fever, systemic inflammation, and shock with end-organ damage [1, 2]. Many of these features have been proposed to resemble Kawasaki-like manifestations [1, 2]. According to the Centers of Disease Control (CDC), five criteria should be fulfilled to diagnosed MIS-A: (1) concurrent or previous (within the past 12 weeks) COVID-19 diagnosed by either PCR or antigen/antibody testing, (2) severe sickness necessitating hospitalization in those aged 21 years or more, (3) marked involvement or dysfunction of single or multiple extrapulmonary organs (acute kidney injury, acute liver injury, neurological involvement, cardiac insult, shock, hypotension, and so on), (4) absence of severe respiratory affection (respiratory signs and symptoms), and (5) exhibiting severe inflammation as per laboratory findings: elevated CRP, d-dimer, serum ferritin, erythrocyte sedimentation rate (ESR), fibrinogen, interleukin-6 (IL-6) [3]. In our case, the patient fulfilled all five criteria to make the diagnosis.

Thirty-six documented cases of MIS-A were reviewed and are summarized in Table 2. The mean age of patients was 33 years, with male predominance (23/36; 63%). Most of the patients had no past medical history of significance (23/36; 63%), while 17/36 (47%) contracted SARS-CoV-2 infection, suggested by PCR, antibody testing, or clinically. Fever was recorded in 31/36 cases (86%). Gastrointestinal symptoms were less frequently reported: nausea (7/36, 19%), abdominal pain (11/36; 30%), vomiting (5/36; 13%), and diarrhea (7/36; 19%). Like our case report, sore throat was present in five patients (5/36; 14%) [4–8] and unilateral cervical pain/swelling in four other cases (6/36; 16%) [8–12]. Some patients had predominant visual symptoms [5, 13–17].
| Authors       | Age, sex, ethnicity | Past medical history | Signs and symptoms at presentation | Previous COVID-19 infection | Initial COVID-19 testing | ICU stay | Laboratory findings | Imaging studies                                                                 | Treatments      | Outcome  |
|--------------|---------------------|----------------------|------------------------------------|-----------------------------|--------------------------|---------|---------------------|--------------------------------------------------------------------------------|----------------|----------|
| Kofman, 2020 | 25, female          | None                 | Fever, dyspnea, sore throat, diarrhea, vomiting, cough, and adenopathy | No                          | PCR (+) IgG (+)          | Yes      | Increased neutrophils, ESR, CRP, d-dimer, ferritin, Tn, and creatinine; lymphopenia | Chest X-ray and CT: No detected abnormalities | Aspirin, IVIG | Recovery |
|              |                     |                      |                                    |                             |                          |         |                     | CT angiography: dilated main pulmonary artery CT abdomen/pelvis: acute uncomplicated pancreatitis Echo: dilated IVC then right ventricular dysfunction |                |          |
|              |                     |                      |                                    |                             |                          |         |                     | CT abdomen/pelvis: acute uncomplicated pancreatitis Echo: dilated IVC then right ventricular dysfunction |                |          |
| Fox, 2020    | 31, female, African-American | HTN, DM, and obesity (BMI 36.1 kg/m²) | Fever, tachycardia, left-sided neck pain, nausea, vomiting, and parotitis by examination | Yes, 12 days prior | PCR (−) | NR                   | Elevated d-dimer, lactic acid, CRP, and creatinine | CT neck: bilateral parotid enlargement and swelling of the posterior nasopharynx to the oropharynx CT chest: bilateral basal GGO plus anterior mediastinal lymphadenopathy | NR             | Deceased |
Table 2 (continued)

| Authors         | Age, sex, ethnicity | Past medical history | Signs and symptoms at presentation | Previous COVID-19 infection | Initial COVID-19 testing | ICU stay | Laboratory findings | Imaging studies | Treatments | Outcome |
|-----------------|---------------------|----------------------|-------------------------------------|----------------------------|--------------------------|----------|---------------------|----------------|------------|---------|
| Shaigany, 2020  | 45, male, Hispanic  | No PMH BMI of 26.6 kg/m² | Fever, diarrhea, sore throat, painful lower extremities, diffuse exanthema, conjunctivitis, periorbital edema, left neck swelling with lymphadenopathy, plaques and papules diffuse, hypotension, tachycardia, and atrial fibrillation | No                         | PCR (+)                  | No       | Increased neutrophils, low lymphopenia, ESR, CRP, d-dimer, ferritin, Tn, AST, ALT, PCT (3179 ng/mL), IL-6 (117 pg/mL) | Chest X-ray: diffuse interstitial haziness, CT neck with contrast: inflamed edematous lower eyelids and preseptal spaces, reactive lymphadenopathy, ECG anterolateral ST segment elevation, PCI: normal coronary, TTE: global hypokinesia of the left ventricle with reduced EF of 40, Slit-lamp examination: conjunctivitis and uveitis | Full dose enoxaparin, IVIG (2 g/kg over 2 days), and single dose of IL-6 inhibitor (tocilizumab) | Recovery |
| Ahsan, 2020     | 28, male            | Thalassemia minor, BMI of 28.48 kg/m² | High-grade fever (40.6 °C), anorexia, vomiting, nausea, lower limb pain, generalized weakness, red eye, difficult urination, and constipation, Bilateral facial nerve palsy, optic neuritis | Yes, 2 weeks before Ab (+), PCR (−) | Not done | NR       | Anemia hypalbuminemia leukocytosis with neutrophilia, Elevated ESR, ferritin, and CRP | ECG normal, Chest X-ray: normal, MRI brain and orbit: normal | Ceftriaxone 2 g daily and prednisolone 1 mg/kg/day orally for 6 weeks | Recovery |
| Authors          | Age, sex, ethnicity | Past medical history | Signs and symptoms at presentation | Previous COVID-19 infection | Initial COVID-19 testing | ICU stay | Laboratory findings | Imaging studies | Treatments                                                                 | Outcome       |
|------------------|---------------------|----------------------|-----------------------------------|---------------------------|--------------------------|---------|---------------------|----------------|---------------------------------------------------------------------------|---------------|
| Bettach, 2021 [14] | 54, female          | None                 | Fever, septic shock, GI symptoms, skin rash, heart failure, bilateral acute anterior uveitis | No                        | PCR (−) IgG (+)                        | Yes     | NR                  | Slit-lamp examination: bilateral corneal edema with Descemet's membrane and keratin precipitates, Fundus examination: small localized intracranial bleed Fluorescein angiography: no vascular abnormalities | Recovery      |
| Razavi, 2020 [15] | 23, male, African-American | BMI of 35.4 kg/m²    | Fever, fatigue, myalgia, dyspnea, orthopnea, watery diarrhea, and temporal headache. Hypotension, bilateral scleral, and conjunctival injection | Yes, 1 month prior        | PCR (−) IgG (+)                        | NR      | Leukocytosis, lymphocytopenia, high Tn I and BNP (NSTEMI) High CRP, D-dimer, ferritin, and fibrinogen | Echo: global hypokinesia with reduced EF (40–45%) Chest X-ray: no focal consolidations CT chest with contrast: no abnormalities Cardiac MRI: pericardial effusion and borderline EF (54%) | Recovery      |
| Authors          | Age, sex, ethnicity | Past medical history | Signs and symptoms at presentation | Previous COVID-19 infection | Initial COVID-19 testing | ICU stay | Laboratory findings | Imaging studies | Treatments | Outcome                        |
|------------------|---------------------|----------------------|------------------------------------|----------------------------|--------------------------|---------|---------------------|-----------------|------------|--------------------------------|
| Gulersen, 2021   | 31, female          | Obesity, asthma, pregnant (28 weeks) | Fever, left-sided pleuritic chest pain, shortness of breath. Late-onset hypotension and tachypnea | Yes, 4 weeks prior PCR (+) | PCR (−) IgG (+) | Yes    | Leukocytosis. Elevated CRP, normal lactate, ferritin, PCT, late-onset increased in cardiac enzymes and inflammatory markers | CT angiography of the chest: normal with no pulmonary embolism or lung pathology detected TTE: On admission, EF 65–70% with a hypodynamic left side, rim pericardial effusion, and well-functioning right ventricle. On day 4: global dysfunction of the right and left ventricles with rim pericardial effusion Non-stress test: reactive fetus | Intravenous heparin, IVIG, dexamethasone (10 mg every 6 hours), mechanical ventilation, inotrope and vasopressor | Extubated on day 8, elective delivery, and discharged home on day 15 |
| Authors                  | Age, sex, ethnicity | Past medical history | Signs and symptoms at presentation | Previous COVID-19 infection | Initial COVID-19 testing | ICU stay | Laboratory findings | Imaging studies | Treatments | Outcome |
|--------------------------|---------------------|----------------------|------------------------------------|-----------------------------|--------------------------|----------|---------------------|----------------|------------|---------|
| Malangu, 2020 [19]       | 46, male            | History of pneumonia | Fever (39.1 °C), atrial fibrillation, mild hypoxia (SatO₂ 91% on room air), bilateral exudative conjunctival injection, oral mucositis, bilateral cervical lymphadenopathy, and macular skin rash | No                          | PCR (−) IgG (+)         | NR       | Leukocytosis and thrombocytopenia Elevated d-dimer, CRP, ferritin, LDH fibrinogen. Mildly elevated ALT, AST, kidney injury with hematuria and proteinuria | CT angiography of the chest: bilateral apical patchy consolidations Chest X-ray: basal and middle lobe opacities TTE: left ventricular dysfunction with EF 31% and eccentric hypertrophy Cardiac MRI: perihilar lymph nodes with no infiltrative lesions Bronchoscopy: no malignant cells | Antibiotics and apixaban | Recovery |
| Othenin-Girard, 2020 [20]| 22, male, East African | None                | Five days of chills, myalgia, asthenia, diarrhea, and abdominal pain. Three weeks of loss of taste and smell sensations, and 1 day of dry cough, odynophagia, and rash (over trunk, extremities, palms) | Yes, 3 weeks prior IgG (+) | PCR (+) IgG (+)          | Yes      | Leukocytosis, elevated CRP (275 mg/L), fibrinogen (85 g/L), d-dimer (3322 ng/mL), and creatinine (1.5 mg/dL). Autoimmune workup: negative ANA, ANCA, and rheumatoid factor | CT abdomen and chest: normal lung parenchyma with pulmonary embolism and inflamed mesenteric lymph nodes TTE: biventricular dysfunction/ endomyocardial biopsy: myocarditis with necrotic foci Nerve conduction study: mononeuritis multiplex | IVIG, tocilizumab, rituximab, corticosteroids, and cyclophosphamide. Mechanical ventilation and extracorporeal membrane oxygenation (ECMO) | Recovery |
| Authors | Age, sex, ethnicity | Past medical history | Signs and symptoms at presentation | Previous COVID-19 infection | Initial COVID-19 testing | ICU stay | Laboratory findings | Imaging studies | Treatments | Outcome |
|---------|---------------------|----------------------|-------------------------------------|---------------------------|-------------------------|---------|---------------------|-----------------|------------|---------|
| Moghadam, 2020 [16] | 21, male, Caucasian | None | Seven days of fever (40 °C), watery non-bloody diarrhea, chest tightness, vasoplegic shock, rash, tachypnea, bilateral conjunctivitis, and truncal and palmar rash | No | PCR (−) IgG (+) | Yes | Leukocytosis, CRP (365 mg/L), PCT (3.4 ng/mL), ferritin (1.282 mg/L), high lactate, Tn (55 n/L) | Skin biopsy: inflammatory infiltrates TTE: hyperkinetic left ventricle with preserved EF CT scan chest and abdomen: compatible with congestive heart failure | Fluid resuscitation, noradrenaline, antibiotics (amikacin and ceftriaxone) | Recovery |
| Lidder, 2020 [5] | 45, male | None | Five days of fever, red eyes, diarrhea, sore throat, eyelids edematous rash, nonexudative conjunctivitis, and abnormal perioral mucosa | No | PCR (+) NR | Lymphopenia, elevated CRP, ESR, ferritin, d-dimer, and elevated Tn | TTE: global hypokinesia with reduced EF (40%) CT neck: unilateral lymphadenopathy | Eye-lubricating medications, topical prednisolone acetate 1%, IVIG, tocilizumab, and triamcinolone ointment for the rash | Recovery |
| Tung-Chen, 2021, Spain [6] | 25, male | None | One-day history of nausea and abdominal pain. One week of fever (38 °C), sore throat, fatigue, anosmia, and orthopnea. Shock at presentation | No | PCR (−) IgM (+) IgG (+) | Yes | Lymphopenia (043 x 109/L), elevated fibrinogen (> 1200 mg/dL), CRP (337.1 mg/L), TnT I, and BNP | TTE: global hypokinesia with severely impaired left ventricular function (EF 29.7%) and rim pericardial effusion. EF improved after 8 days CT chest: no abnormalities Chest X-ray: no abnormalities ECG: sinus tachycardia with no other abnormalities | Antibiotics, ganciclovir, norepinephrine, milrinone, and diuretics | Recovery |
| Authors               | Age, sex, ethnicity | Past medical history | Signs and symptoms at presentation | Previous COVID-19 infection | Initial COVID-19 testing | ICU stay | Laboratory findings | Imaging studies | Treatments | Outcome          |
|-----------------------|---------------------|----------------------|------------------------------------|---------------------------|-------------------------|---------|---------------------|-----------------|------------|-------------------|
| Uwaydah, 2021 [7]     | 22, male            | None                 | Four days of fever (39 °C), sore throat, diarrhea, nausea, vomiting, myalgia, headache, fatigue, erythematous rash involving the torso, tachycardia, hypotension, edema, and proteinuria | Yes, 40 days prior PCR (+) | PCR (−) IgG (+) | Yes | Leukocytosis, elevated creatinine, AST (53 U/L), ALT (81 U/L), direct bilirubin, CRP (249 mg/L), ferritin (4357 ng/mL), d-dimer (14 mg/mL), PCT (9 ng/mL), IL-6 (90 pg/mL), low platelets (122) and albumin (16 g/L) | TTE: severe tricuspid regurgitation, pulmonary HTN (46 mmHg), left ventricle dysfunction (EF 45%), and rim pericardial effusion. Normal echo after recovery CT chest: bilateral moderate pleural effusion and basilar atelectasis | Antibiotics, intravenous hydrocortisone | Recovery |
| Ahmad, 2021 [21]     | 26, male, Caucasian | None                 | Fever, abdominal pain, loose stool, nausea, reduced urine output, hypotension tachypnea (38 breath/minute) and hand/foot rash | PCR (+) | PCR (+) Abs (+) | Yes | Leukocytosis. Elevated lactic acid (9.7 mg/dL), CRP (246 mg/L), PCT (105.12 ng/mL), d-dimer (203), LDH (236 U/L), creatinine (4.66 mg/dL), and urea (38 mg/dL) | Lower limb doppler: left peroneal DVT Chest X-ray: penbrochial thickening Noncontrast CT abdomen: perinephric edema and mesenteric lymphadenopathy TTE: severely impaired left ventricular function (EF 15–20%) as well as right ventricular dysfunction. EF increased to 60% after 10 days | Vasopressors, IVIG, methylprednisolone (250 mg/6 hours), aspirin, anakinra (IL-1 receptor antagonist), mechanical ventilation, and CRRT | Recovery |
| Authors            | Age, sex, ethnicity | Past medical history | Signs and symptoms at presentation | Previous COVID-19 infection | Initial COVID-19 testing | ICU stay | Laboratory findings | Imaging studies | Treatments                                      | Outcome           |
|--------------------|---------------------|----------------------|------------------------------------|----------------------------|--------------------------|----------|---------------------|----------------|------------------------------------------------|-------------------|
| Li, 2021 [10]      | 28, male            | None                 | Five days of right-sided neck pain and swelling, enlarged tonsils, tenderness of the right submandibular, fever, malaise, tachycardia, pruritic rash | 4 weeks prior, PCR (+) IgG (+) NR | Leukocytosis (13,800/mm³), anemia (10.7 g/dL), Elevated hs-Tn I (11,926 ng/L), BNP (1661 pg/mL), CRP (304.2 mg/L), and ferritin (1588 mg/L) | CT neck: cervical lymphadenopathy, more on the right side | TTE: mildly impaired left ventricular function (EF 45–55%) Cardiac MRI: rim pericardial effusion and slightly impaired right ventricular function | CT neck: cervical lymphadenopathy, more on the right side | Leukocytosis (13,800/mm³), anemia (10.7 g/dL), Elevated hs-Tn I (11,926 ng/L), BNP (1661 pg/mL), CRP (304.2 mg/L), and ferritin (1588 mg/L) | Recovery | Broad-spectrum antibiotics, fluid resuscitation, beta-blocker, ACE inhibitor |
| Veyseh, 2021 [23]  | 43, female          | None                 | Fever, hypotension, tachycardia, erythematous rash, diarrhea, and cramping abdominal pain | No | PCR (–) Yes | High WBCs, CRP, ferritin, D-dimer, fibrinogen, LDH, AST, and ALT | TTE: reduced EF (toxic cardiomyopathy), EF improved after IVIG and steroids | Antibiotics, vasopressors, IVMG, and intravenous solumedrol | Recovery | Recovery |
| Diakite, 2021, [17]| 33, male HTN        | Fever, diarrhea, chest pain, dyspnea, conjunctivitis, and cheilitis. Hypotension, tachycardia, and elevated hepatojugular reflux | Possible 6 weeks prior | PCR (–) IgG (+) NR | Leukocytosis (21,000/mm³), anemia (107 g/dL), high AST, ALT, creatinine, CRP, D-dimer, BNP, and Tn | TTE: global hypokinesia, reduced EF (20%), and dilated IVC. Cardiac MRI revealed improved cardiac function after a week of treatment | Coronary CT: aneurysms involving the right coronary, interventricular artery, and the left circumflex | Dobutamine, norepinephrine, IVIG, aspirin, prednisolone | Recovery | Recovery |
### Table 2 (continued)

| Authors                  | Age, sex, ethnicity | Past medical history | Signs and symptoms at presentation | Previous COVID-19 testing | Initial COVID-19 testing | ICU stay | Laboratory findings | Imaging studies | Treatments | Outcome       |
|--------------------------|---------------------|----------------------|------------------------------------|--------------------------|--------------------------|----------|---------------------|-----------------|------------|---------------|
| Bastug, 2021, Turkey [24] | 40, male, Caucasian | None                 | Fever (39 °C), tachycardia, tachypnea, abdominal pain, diarrhea, and skin rash | PCR (−) IgM (+) IgG (+) | NR | Lymphopenia, leukocytosis as well as high liver function tests, ferritin, D-dimer, troponin, BNP, CRP, fibrinogen, PCL, and IL-6 | CT abdomen: inflamed intestine and mesentery, mesenteric lymphadenopathy, and effusion | TTE: global hypokinesia, reduced left ventricle function (EF 45%), and mild pericardial effusion. EF increased to 60% and the effusion resolved after treatment | Antibiotics, methylprednisolone, IVIG, full-dose enoxaparin | Recovery |
| Sokolovsky, 2021, [31]   | 36, female, Hispanic| None                 | Fever, vomiting, abdominal pain, diarrhea, arthralgia, rash, hypotension, and tachycardia | No | PCR (+) Abs (+) | NR | Elevated liver enzymes, direct bilirubin, albumin, CRP, ferritin, D-dimer, ESR, and hyponatremia (115 mmol/L) | TTE: normal EF (65%) and moderate tricuspid regurgitation. CTA coronaries: normal with rim pericardial effusion. CT chest: trace pleural effusion | Steroids, acetylcysteine, IVIG, aspirin | Recovery |
| Julius, 2021, [11]       | 59, female, Caucasian | HTN and dyslipidemia | Fever, right cervical lymph node swelling, odynophagia, hypotension, and rash (neck and chest) | 20 days prior, PCR (+) | Yes | Slightly elevated AST, ALT, high Tn, CRP, and ferritin | CT neck: enlarged right nodes with one exhibiting liquefaction. EKG: ST elevation in V1 and V2 | Antibiotics, steroid, norepinephrine, epinephrine, terlipressin mechanical ventilation | Deceased |
### Table 2 (continued)

| Authors          | Age, sex, ethnicity | Past medical history | Signs and symptoms at presentation | Previous COVID-19 infection | Initial COVID-19 testing | ICU stay | Laboratory findings | Imaging studies | Treatments                                      | Outcome |
|------------------|---------------------|----------------------|-------------------------------------|----------------------------|--------------------------|----------|---------------------|-----------------|------------------------------------------------|---------|
| Parpas, 2021     | 67, male            | HTN, cirrhosis       | Dyspnea weakness, weight loss, anorexia, nausea, extremities edema, tachycardia, and cognitive impairment | 68 days prior PCR (−) Abs (+) | NR | Low sodium (109 mEq/L) and albumin (3 g/dL), leukocytosis (35,000/mm³). High d-dimer, LDH, and PCL | Chest X-ray: bilateral basal infiltrative lesions CT chest: lung atelectasis/collapse TTE: Pulmonary HTN and grade I diastolic dysfunction Duplex of lower limbs: no DVT Renal biopsy: moderate to severe acute tubular necrosis | Antibiotics, unfractionated heparin, dexamethasone, and hemodialysis | Recovery |
| Pérez, 2021      | 88, male            | HTN, dyslipidemia, essential tremors | Hypoxia (saturation 87%), dyspnea, and peripheral edema | 54 days prior PCR (+) Abs (+) | NR | Creatinine (2.14 mg/dL), proteinuria (> 600 mg/dL), and low albumin 3 g/dL. High LDL, CRP, and d-dimer | Chest X-ray: typical COVID-19 picture and pleural effusion Renal biopsy: findings suggesting acute IgA-dominant infection-associated glomerulonephritis | Intravenous furosemide, intravenous methylprednisolone | Recovery |
| Balan, 2021      | 46, male            | Obesity (BMI 42 kg/m²) | Hypotension, hypoxia, tachypnea, right hemiparesis, ataxia, and left hemianesthesia | 60 days prior PCR (−) Abs (+) | Yes | Elevated ferritin, CRP, LDH, PCT, high creatinine (41.6 mg/dL) and Tn | TTE: normal EF and elevated right ventricular pressures CT chest: bilateral apical and basal as well as right middle ground-glass opacities | Norepinephrine, antibiotics unfractionated heparin, dexamethasone, tocilizumab, and hemodialysis | Deceased |
| Authors              | Age, sex, ethnicity | Past medical history | Signs and symptoms at presentation | Previous COVID-19 infection | Initial COVID-19 testing | ICU stay | Laboratory findings | Imaging studies | Treatments                                      | Outcome        |
|---------------------|---------------------|----------------------|-------------------------------------|-----------------------------|----------------------------|----------|---------------------|----------------|------------------------------------------------|----------------|
| Mieczkowska, 2021, [22] | 32, male            | None                 | Fever, tachycardia, right-sided swollen groin lymph nodes, diarrhea, and palms and soles rash | Two months prior            | PCR (−) IgG (+)              | No       | Elevated AST, ALT, and direct bilirubin. Elevated inflammatory markers (CRP, ferritin, PCL, IL-6, ESR, and d-dimer). | TTE: EF 55% and pericardial effusion. CT: lymphadenopathy of the right groin. | Enoxaparin and intravenous methylprednisolone. | Recovery         |
| Mieczkowska, 2021, [22] | 43, female          | None                 | Fever, myalgia, headache, cough, and skin rash. Hypotension, cardiomyopathy, and acute kidney injury | No                          | PCR (−) Serology (+)         | NR       | Leukocytosis (21,500/mm³). Elevated ESR, CRP, ferritin, and d-dimer. Elevated AST, ALT, and ALP. | Chest X-ray: right basal pneumonia. Abdominal ultrasound: pericholecystic fluid, hepatomegaly, and steatosis. | TTE: EF 40%. | Recovery                                     |
| Hékimian, 2021 [12]  | 40, male            | DM (BMI 26 kg/m²)    | Apyretic, dyspnea, severe asthenia   | No                          | PCR (+) IgG (−)              | Yes      | Elevated PCT, CRP, ferritin. Elevated AST, ALT, and ALP. Elevated LDH, CPK. Peak troponin 439 ng/L. Peak BNP 6025 pg/mL. | Chest CT: severe multifocal PNA. TTE: EF 45%. | Mechanical ventilation, dobutamine, norepinephrine, ECMO. | Recovery         |
| Hékimian, 2021 [12]  | 19, female          | None (BMI 24 kg/m²)  | Fever, dyspnea, cough                | No                          | PCR (−) IgG (+)              | Yes      | Elevated CRP, ferritin, LDH. Peak troponin 10,652 ng/L. Peak BNP 2585 pg/mL. | Chest CT: mild infiltrates. TTE: EF 30%. | Mechanical ventilation, dobutamine, norepinephrine, ECMO. | Recovery         |
| Hékimian, 2021 [12]  | 22, male            | DM, asthma (BMI 38 kg/m²) | Fever, dyspnea, cough, severe asthenia | No                          | PCR (−) IgG (−)              | Yes      | Elevated CRP, ferritin, LDH. Peak troponin 166 ng/L. | Chest CT: severe infiltrates. TTE: EF 30%. | Mechanical ventilation, ECMO. | Recovery         |
| Authors       | Age, sex, ethnicity | Past medical history | Signs and symptoms at presentation | Previous COVID-19 testing | ICU stay | Laboratory findings | Imaging studies | Treatments                      | Outcome         |
|---------------|---------------------|----------------------|------------------------------------|--------------------------|---------|---------------------|----------------|---------------------------------|-----------------|
| Hékimian, 2021 | 19, male            | None (BMI 22 kg/m²)  | Fever, headache, diarrhea, dyspnea, severe asthenia | No                        | PCR (−) | IgG (+)             | Yes            | Elevated CRP, ferritin, LDH     | Recovery        |
|               |                     |                      |                                    |                           | Peak troponin 806 ng/L | BNP 26,956 pg/mL |                 | Chest CT: negative TTE: EF 15% | Dobutamine, norepinephrine | Recovery        |
|               |                     |                      |                                    |                           | Yes                |                     |                 |                                 |                 |
| Hékimian, 2021 | 16, male            | None (BMI 18 kg/m²)  | Fever, anosmia, abdominal pain, rash to hands and feet, conjunctivitis, strawberry tongue, adenopathy, severe asthenia, chest pain | No                        | PCR (+) | IgG (+)             | Yes            | Elevated CRP, ferritin, LDH     | Recovery        |
|               |                     |                      |                                    |                           | Peak troponin 2545 ng/L | BNP 26,956 pg/mL |                 | Chest CT: mild infiltrates TTE: EF 20% | Mechanical ventilation, norepinephrine, IVIG | Recovery        |
|               |                     |                      |                                    |                           | Yes                |                     |                 |                                 |                 |
| Hékimian, 2021 | 16, female          | None (BMI 24 kg/m²)  | Fever, headache, abdominal pain, rash to hands and feet, dyspnea, severe asthenia | Yes, anosmia and cough 1 month prior | PCR (−) | IgG (+)             | Yes            | Elevated CRP, ferritin, and LDH | Recovery        |
|               |                     |                      |                                    |                           | Peak troponin 64 ng/L | BNP 1689 pg/mL |                 | Chest CT: negative TTE: EF 45% | None | Recovery                        |
|               |                     |                      |                                    |                           | Yes                |                     |                 |                                 |                 |
| Hékimian, 2021 | 17, male            | Moderate aortic regurgitation (BMI 32 kg/m²) | Fever, headache, abdominal pain, diarrhea, dyspnea, severe asthenia, conjunctivitis | No                        | PCR (+) | IgG (+)             | Yes            | Elevated ferritin and LDH       | Recovery        |
|               |                     |                      |                                    |                           | Peak troponin 138 ng/L | BNP 35,000 pg/mL |                 | Chest CT: mild pulmonary edema TTE: EF 20% | Mechanical ventilation, norepinephrine, IMG, corticosteroids 2 mg/kg/day | Recovery        |
| Hékimian, 2021 | 25, female          | None (BMI 23 kg/m²)  | Fever, headache, abdominal pain, dyspnea, severe asthenia, myalgias, arthralgias, adenopathy | No                        | PCR (−) | IgG (+)             | Yes            | Elevated CRP, ferritin, LDH     | Recovery        |
|               |                     |                      |                                    |                           | Peak troponin 2542 ng/L | BNP 24,540 pg/mL |                 | Chest CT: negative TTE: EF 50% | Nasal cannula | Recovery                        |
|               |                     |                      |                                    |                           | Yes                |                     |                 |                                 |                 |
| Hékimian, 2021 | 17, female          | None (BMI 18 kg/m²)  | Chest pain, dyspnea | No                       | PCR (+) | IgG (+)             | Yes            | Elevated CRP, ferritin, LDH     | Deceased        |
|               |                     |                      |                                    |                           | Peak troponin 4905 ng/L | BNP 3362 pg/mL |                 | Chest CT: pulmonary edema TTE: 20% | Mechanical ventilation, norepinephrine, ECMO, IMG, corticosteroids 2 mg/kg/day | Deceased        |
|               |                     |                      |                                    |                           | Yes                |                     |                 |                                 |                 |
| Authors                  | Age, sex, ethnicity | Past medical history | Signs and symptoms at presentation | Previous COVID-19 testing | ICU stay | Laboratory findings | Imaging studies | Treatments                      | Outcome     |
|-------------------------|--------------------|----------------------|-------------------------------------|--------------------------|----------|---------------------|----------------|-----------------------------|-------------|
| Hékimian, 2021 [12]     | 37, male           | HTN (BMI 35 kg/m²)   | Fever, headache, diarrhea, severe asthenia | PCR (−) IgG (+)                 | Yes      | Elevated ferritin, LDH Peak troponin 1164 ng/L Peak BNP 35,000 pg/mL | Chest CT: Negative TTE: EF 45% | Intravenous immunoglobulins, corticosteroids 2 mg/kg/day | Recovery    |
| Hékimian, 2021 [12]     | 29, female         | None (BMI 22 kg/m²)  | Fever, abdominal pain, diarrhea, rash, conjunctivitis, severe asthenia | PCR (−) IgG (+)                 | Yes      | Elevated CRP, ferritin, LDH Peak troponin 200 ng/L Peak BNP 21,298 pg/mL | Chest CT: Negative TTE: EF 50% | Intravenous immunoglobulins | Recovery    |

PMH past medical history, HTN hypertension, BMI body mass index, BPM beats per minute, MIS-A multisystem inflammatory syndrome in adults, PCT procalcitonin, AST aspartate transaminase, ALT alanine transaminase, ALP alkaline phosphatase, CPR C-reactive protein, ESR erythrocyte sedimentation rate, LDH lactate dehydrogenase, EKG electrocardiogram, CAP community-acquired pneumonia, PNA pneumonia, HD hospital day, ANA antinuclear antibodies, ANCA antineutrophil cytoplasmic antibodies, OD once daily, Tn troponin, BNP brain natriuretic peptide, DVT deep vein thrombosis, TTE transthoracic echocardiogram, EF ejection fraction, MRI magnetic resonance imaging, MV mechanical ventilation, CRRT continuous renal replacement therapy, IVIG intravenous immunoglobulins, LMWH low molecular weight heparin, Abs antibodies, SatO₂ saturation of O₂
Cardiovascular impairment was also noted in the literature. Specifically, tachycardia (22/36; 61%) and hypotension/cardiogenic shock with documented impaired ejection fraction (23/36; 64%) [5–8, 10, 12, 15, 17–24]. The left ventricular function/ejection fraction normalized with treatment in 15 patients [6, 7, 12, 17, 21, 23, 24], of whom 7 patients received IVIG with or without aspirin [10, 12, 17, 23, 24]. Overall, 28/36 (78%) patients recovered and were safely discharged. Cardiac MRI has been discussed in the literature in terms of assessing for myocarditis. It can confirm signs of diffuse myocardial inflammation while ruling out ischemic or stress-induced cardiomyopathy [12].
There is no consensus on the mechanism causing MIS-A during or post-CoVID-19 infection. MIS-A is viewed as an atypical immune response causing systemic vasculitis and multiple acute organ injury. The dramatic response to IVIG and high-dose aspirin supports the occurrence of vasculitis, which was demonstrated in our patient. She was successfully weaned off vasopressors following the IVIG treatment, and discharged without any complications in her hospital course. Target management of MIS-A with immunomodulatory therapy has reversed acute kidney injury [25] and heart failure, with normalization of cardiac function in many patients [6, 7, 12, 17, 21, 23, 24]. Many theories were proposed to uncover the linkage between vasculitis and SARS-CoV-2 infection. For example, IL-6 increases markedly during CoVID-19 infection, and it is the same cytokine that mediates vasculitis in Kawasaki syndrome. IL-6 enhances the adhesion of lymphocytes to endothelial cells causing their damage [26]. Another theory points toward complement activation and capillary deposition of immune complexes as initial insult, which could be suggested in our case based on her low complement C3 and C4 levels [27].

MIS-A of CoVID-19 shares many similarities with Kawasaki-like multisystem inflammatory syndrome, a syndrome which has been linked to other viral infections. Diagnosis of Kawasaki disease requires (1) fever for \( > 5 \) days and (2) at least four signs of conjunctivitis, involvement of the oropharyngeal mucosa or IgA infiltration of the upper respiratory tract, cervical lymphadenopathy, rash, and extremity changes (edema or erythema) [28]. Furthermore, Kawasaki may present with acute kidney injury or aneurysms, especially in coronaries and abdominal aorta.

COVID-19 Kawasaki-like syndrome is diagnosed by (1) fever for \( > 3 \) days, (2) at least two signs of rash, hypotension/shock, or acute cardiac injury (infarction, pericarditis, left ventricle dysfunction, right ventricular dysfunction, or coronary syndrome), (3) coagulopathy, or (4) acute gastrointestinal (GI) symptoms in the setting of elevated inflammatory markers (CRP, d-dimer, and/or ferritin) during or after COVID-19 infection, after excluding other infections [29]. This description was consistently seen with our patient. She exhibited fever, strawberry-like rash, hypotension requiring vasopressors, decreased ejection fraction, nephropathy, and significant elevations in her CRP and d-dimer.

Figure 1 illustrates the clinical features and possible pathophysiology basis of MIS-A and classic Kawasaki syndromes. Our patient did not fulfill the criteria of classic Kawasaki. Furthermore, the acute cardiac injury and hypotension, acute renal injury, fever, sore throat, unilateral lymphadenopathy, and elevated inflammatory markers in the setting of positive SARS-CoV-2 IgG antibody support a diagnosis of MIS-A.

In terms of management, there was considerable variation in treatment modalities when reviewing the literature. In our case, the patient was aggressively fluid resuscitated and started on broad spectrum antibiotics, steroids, and ultimately vasopressors. In conjunction with the infectious disease team, full-dose aspirin and IVIG was initiated, with resolution of her symptoms and ultimate discharge. To demonstrate the variability in treatments, we reviewed previously documented cases of MIS-A. Summarizing Table 2, 44% of patients were given IVIG, 56% given steroids, 39% antibiotics, 13% given immunomodulators (tocilizumab, anakinra, cyclophosphamide, rituximab), 11% given aspirin, 22% anticoagulation, and 36% requiring vasopressors. Despite the differences in management, recent literature studying the treatment modalities of MIS-C concluded that were was no evidence that IVIG alone or IVIG with steroids or immunomodulators leads to higher rates of recovery [30]. These findings may not be generalizable to the adult population who experience MIS-A, but it gives insight into the challenges of choosing a treatment modality.

**Conclusion**

Our case report is an example of the presentation, diagnosis, and management of MIS-A. As we dove into the literature and discovered other documented cases of MIS-A, we created Fig. 1 to illustrate the similarities and differences when compared with Kawasaki-like multisystem inflammatory syndrome. Our research into previous case reports illustrates the wide range of presentations, degree of end-organ damage, and treatment modalities. This diagnosis needs to be considered in the presence of recent COVID infection with new onset end organ failure, as prompt diagnosis and treatment is crucial for better outcomes.
Abbreviations
MIS-A: Multisystem inflammatory syndrome in adults; ED: Emergency department; ICU: Intensive care unit; NIG: Intravenous immunoglobulin; BMI: Body mass index; PCR: Polymerase chain reaction; CT: Computed tomography; POCUS: Point of care ultrasound; CRP: C-reactive protein; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; BNP: Brain natriuretic peptide; CDC: Centers for Disease Control; ESR: Erythrocyte sedimentation rate; IL-6: Interleukin-6.

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Declarations
Ethics approval and consent to participate
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
All the authors declare that they have no conflicts of interest

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