Case Report of Multisystem Inflammatory Syndrome in Adults (MIS-A): A 31-Year-Old Man with Fever, Rash, and Cardiac Symptoms 6 Weeks Following SARS-CoV-2 Infection, Successfully Resuscitated Following Cardiac Arrest

ABDEF 1
Grant Gerstner
ABDE 2
Thomas A. Rafalski
ABDEFG 3
Debra Pankiewicz

Corresponding Author: Debra Pankiewicz, e-mail: dpankiew@lhs.org
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Patient: Male, 31-year-old
Final Diagnosis: Multisystem inflammatory syndrome in adults (MIS-A)
Symptoms: Abdominal pain • diarrhea • fever • neck stiffness • rash • tachycardia
Medication: —
Clinical Procedure: —
Specialty: Critical Care Medicine

Objective: Rare disease
Background: Multisystem inflammatory syndrome in adults (MIS-A) is an uncommon condition after a confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, manifesting as multiorgan failure despite apparent resolution of initial symptoms. While this syndrome shares similar characteristics with a syndrome found in children, fewer cases are reported in adults. This report details a 31-year-old man fulfilling the diagnostic criteria of MIS-A, who was successfully resuscitated following cardiac arrest.

Case Report: A 31-year-old man was admitted to the intensive care unit for 3 days of progressively worsening fever, chills, diaphoresis, exanthematous rash, headache, and neck stiffness. The patient had a history of mild, resolved SARS-CoV-2 infection 6 weeks prior to his presentation, diagnosed by rapid antigen and reverse transcription polymerase chain reaction (RT-PCR) testing. Meningitis and autoimmune pathologies were initially suspected but were ruled out. Given the patient’s symptoms, prior SARS-CoV-2 infection, and positive inflammatory markers, findings correlated with the Centers for Disease Control and Prevention’s diagnostic criteria for multisystem inflammatory syndrome in adults. On hospital day 1, the patient decompensated into severe respiratory distress requiring intubation. Shortly after, the patient developed cardiac arrest and was successfully resuscitated. He was transferred from our rural hospital to an intensive care unit at a facility with additional resources. He remained critically ill for several weeks while receiving high-dose steroids, intravenous immunoglobulin (IVIG), and hemodialysis until his recovery.

Conclusions: Early diagnosis and treatment of MIS-A would significantly improve outcomes in this subset of patients, especially in clinical settings with limited resources.

Keywords: SARS-CoV-2 • Exanthema • Adult Multisystem Inflammatory Disease, COVID-19 Related

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/938127
Background

SARS-CoV-2 is a positive-sense, single-stranded RNA virus responsible for the coronavirus disease 2019 (COVID-19) pandemic. This novel virus is known for its classic respiratory symptoms with additional atypical presentations. Symptoms include fever, myalgias, ageusia, anosmia, dyspnea, and gastroenteritis. Acute respiratory failure, disseminated intravascular coagulation, and distributive shock may appear as sequelae of cytokine storm in severe cases [1,2]. Many survivors suffer from post-COVID-19 syndrome with effects such as dyspnea, sleep disorders, cough, anxiety, and depression [3]. Post-COVID-19 syndrome is classified by initial symptom severity, duration, period of quiescence, and return of symptoms [4]. Two post-COVID-19 phenomena have been described in the medical literature as multisystem inflammatory syndrome in children and adults (MIS-C and MIS-A, respectively) [5,6].

In April 2020, an inflammatory, post-COVID-19, Kawasaki-like response was first described in children. With more cases reported in the literature, this disease process was coined MIS-C [7]. As such, the Centers for Disease Control and Prevention (CDC) outlined inclusion criteria for diagnosing this novel syndrome [8]. The prognosis of MIS-C is encouraging, with nearly 2% mortality [9,10]. Comparably, MIS-A occurs in patients older than 21 years following similar CDC diagnostic criteria but has a much higher mortality rate of 7% [11]. This syndrome typically follows a SARS-CoV-2 diagnosis by 2-12 weeks with associated complications such as encephalopathy, conjunctivitis, cardiomyopathy, respiratory distress, hepatitis, colitis, and dermatitis [11-15]. Severe cases have advanced to end-organ failure, including cardiogenic shock [16-19].

In summary, the CDC diagnostic criteria for MIS-A include a fever plus 3 subsequent new-onset clinical manifestations unrelated to medical therapy, prior to or within 72 hours of hospitalization, with at least 1 being a primary clinical criterion. Primary clinical criteria include: (1) cardiac disease and (2) rash with non-purulent conjunctivitis. Secondary clinical criteria include: (1) neurologic signs and symptoms, (2) hypotension or shock, (3) gastrointestinal symptoms, and (4) thrombocytopenia. Laboratory evidence must show: (1) elevated inflammatory markers and (2) a positive SARS-CoV-2 test result for current or recent infection [11,20].

The literature regarding the pathophysiology of both multisystem inflammatory syndrome diseases is still emerging, although molecular mimicry and cytokine storm have been hypothesized [11,18,21,22]. Further, cases can occur without known comorbidities or preceding symptoms [11,21]. Early diagnosis and treatment of MIS-A can improve a patient’s prognosis. Here, we report the case of an otherwise healthy 31-year-old man who presented with fever, rash, and neck stiffness, resulting in cardiac arrest with successful resuscitation and subsequent life support until recovery.

Case Report

A 31-year-old man status-post 6 weeks SARS-CoV-2 infection with otherwise no past medical history presented to the Emergency Department with 3 days of progressively worsening tactile fever, chills, diaphoresis, headache, conjunctivitis, neck stiffness, diffuse abdominal pain, diarrhea, rash on his trunk and extremities, and shortness of breath. He denied weight loss, visual disturbances, congestion, sore throat, chest pain, palpitations, leg swelling, cough, vomiting, hematochezia, dysuria, hematuria, weakness, dizziness, or altered mentation. The patient reported testing positive for SARS-CoV-2 6 weeks prior via nasopharyngeal BinaxNOW Rapid Antigen test (Abbott Laboratories, Chicago, USA), followed by confirmation with Cue RT-PCR (Cue Health, San Diego, USA). At that time, he underwent testing at his employee health office for symptoms of mild cough, myalgias, ageusia, and anosmia — all resolving within 3 days of diagnosis. He was nonimmunized against SARS-CoV-2. He had no significant past medical, surgical, or familial history. He admitted to smoking 2 cigarettes daily and drinking alcohol occasionally but denied illicit drug use. He was in a monogamous relationship and worked in a paper mill.

At the time of admission, the patient’s vital signs were temperature of 38.2°C, heart rate of 136 beats/minute, respiratory rate of 24 breaths/minute, blood pressure of 129/78 mmHg, O₂ saturation of 95% on room air, and body mass index of 38.4 kg/m².

Physical examination upon admission revealed an anxious-appearing, obese man with labored breathing. His head was normocephalic and atraumatic. His pupils were equal, round, and reactive to light, with extraocular movements intact. He had some conjunctival injection, which he states had significantly improved from 3 days prior. The mucous membranes were moist, without lesions or exudate. His neck had moderate stiffness with flexion. On his cardiopulmonary exam, he had tachycardia with a regular rhythm. No murmurs, rubs, or gallops were appreciated. He was in mild respiratory distress with accessory muscle use and diffuse wheezes throughout all lung fields. His abdomen was soft and non-tender, with no rebound. The musculoskeletal system had a full range of motion and no tenderness or edema. Neurologically, he was alert and oriented to self, time, place, and situation. Cranial nerves II-XII were intact bilaterally. He had 5/5 strength and intact sensation to light touch in all extremities bilaterally, as well as normal finger-nose-finger and heel-to-shin tests. The patient’s dermatological exam revealed a blanching, maculopapular rash.
spanning his bilateral upper and lower extremities, upper chest, and most of his back. The patient’s skin folds, palms, soles, and mucosa were spared (Figure 1A). The presumptive diagnosis of meningitis was made at admission, and the patient was administered broad-spectrum antibiotics and antivirals.

Remarkable initial serology showed: leukocytosis (12×10³/µL), transaminitis with aspartate aminotransferase (AST) 138 U/L and alanine aminotransferase (ALT) 80 U/L, lactate within normal limits, erythrocyte sedimentation rate (ESR) elevated at 48 mm/hour, c-reactive protein (CRP) elevated to 21.80 mg/L, ferritin elevated to 1140 µg/L, negative hepatitis B surface antibody, negative hepatitis C antibody, negative human immunodeficiency virus RNA, and negative treponemal antibody. Urine analysis was unremarkable. Nasopharyngeal PCR swabs were negative for SARS-CoV-2 and influenza A/B. Cerebrospinal fluid (CSF) analysis indicated: a clear appearance, glucose 72 mg/100 mL, protein 32 mg/100 mL, 6 nucleated cells/100 mL with lymphocyte predominance (98%), red blood cell count 403/uL, negative gram stain, negative extractable nuclear antigen tests, negative VDRL, and negative PCR for cryptococcus, enteroviruses, and human immunodeficiency virus. His initial chest X-ray showed mild central airway thickening without consolidation (Figure 2A).

Based on the evidence of widespread inflammation, Rheumatology was consulted. Autoimmune screenings (anti-Jo1, anti-RNP, anti-Ro52, anti-Ro60, anti-Scl70, anti-Sm, and anti-SSB) were obtained, all of which were negative. Additionally, a skin punch biopsy was harvested from the patient’s back, with the pathology interpreted as nonspecific with diagnostic considerations including a viral exanthem, cutaneous drug reaction, or another nonspecific dermal hypersensitivity (Figure 1B).

Infectious Disease was consulted on hospital day 1 when the patient’s autoimmune labs returned inconclusively, and he did not improve clinically. The Infectious Disease specialist reviewed the patient’s symptoms, clinical findings, and laboratory studies, suggesting a diagnosis of MIS-A aligning with CDC criteria [20]. The patient’s antibiotics and antivirals were discontinued, and treatment was initiated for presumed MIS-A, consisting of an intravenous steroid burst.

Upon receiving his first dose of steroids, the patient developed dyspnea, tachycardia, hypertension, and severe anxiety. A computed tomography scan of the chest was attempted for concern of an acute cardiopulmonary process. However, due to his dyspnea and anxiety, the patient could not lie prone. A repeat portable chest X-ray showed increased central bronchial wall thickening correlating with reactive airway disease (Figure 2B).

An echocardiogram, laboratory studies, and an electrocardiogram (ECG) were ordered. The ECG showed sinus tachycardia with anterior ST changes (Figure 3). Troponin I (0.23 ng/mL) and white blood cell count (19×10³/µL) were elevated. Cardiology’s ECG interpretation was congruent with possible pericarditis or myocarditis secondary to suspected MIS-A rather than an acute coronary syndrome.
While awaiting an echocardiogram, the patient’s dyspnea worsened. He attempted NPPV without relief. Intravenous epinephrine was administered with a trial of an ipratropium bromide/albuterol nebulizer for bronchodilation. The patient became severely anxious, so lorazepam was administered. Despite receiving anxiolytics, the patient’s anxiety worsened, with associated tachycardia, tachypnea, and dyspnea. Given the patient’s rapidly deteriorating vital signs, intubation was necessary.

Figure 2. Chest X-rays in anteroposterior view showing rapid pulmonary decompensation. (A) The initial chest X-ray taken at the time of admission, showing hypoventilatory changes with mild central airway thickening, likely accentuated by poor breath-hold. No lobar consolidation. (B) Chest X-ray on hospital day 1 due to respiratory distress, showing central bronchial wall thickening, which would correlate with airway diseases such as asthma or bronchitis. There is no confluent consolidation and persistently low lung volumes.

Figure 3. An electrocardiogram (ECG) that was obtained due to prolonged tachycardia. The cardiologist’s interpretation of this ECG revealed sinus tachycardia with anterior lead ST-elevation (arrows) in lead V2. ST-elevation myocardial infarction (STEMI) was doubtful but could not be ruled out with consideration for pericarditis.
discussed and agreed upon with the patient. Ketamine was used as a sedative, and succinylcholine as a paralytic. The patient was rapidly intubated.

Immediately after intubation, the patient’s cardiac monitor showed ventricular fibrillation. Chest compressions were initiated, and the first defibrillating shock was delivered. Intraosseous access was established with respective doses of calcium chloride, epinephrine, amiodarone, and magnesium given per advanced cardiac life support guidelines. At the second pulse check, the patient’s heart rhythm declined into pulseless electrical activity. After another dose of epinephrine, a return of spontaneous circulation (ROSC) with sinus tachycardia was achieved.

Post-ROSC, the patient developed acidosis, with an arterial pH of 6.9. One amp (100 mEq/50 mL) of sodium bicarbonate was administered, with a repeat arterial pH of 7.2. He was maintained with a sodium bicarbonate drip. The patient became hypotensive due to decreased cardiac output. Norepinephrine and vasopressin drips were maintained to address this hypotension. A limited bedside echocardiogram was obtained, showing heart failure with a reduced ejection fraction of 20.2%, consistent with acute left ventricular systolic failure. Secondly, the patient developed hyperthermia, reaching a temperature of 41.6°C. The patient was administered 1 g acetaminophen and treated with ice packing, cooling blankets, and foley catheter cold saline irrigation. A representative from the Malignant Hyperthermia Association of the United States was consulted and endorsed that this was not malignant hyperthermia but rather a neurological recovery response after cardiopulmonary resuscitation. The recommendation was to administer 1 mg/kg of Dantrolene. The patient responded well to these interventions and defervesced.

Given the patient’s acuity level, he was transferred from our rural, critical-access hospital to an urban intensive care unit with access to further resources. There, he remained intubated for several weeks, receiving high-dose steroids, IVIG, and pressors. Extracorporeal membrane oxygenation (ECMO) was considered; however, the patient maintained adequate gas exchange with mechanical ventilation. The patient’s course was complicated by an upper gastrointestinal bleed and acute kidney injury, requiring parenteral nutrition and hemodialysis. Eventually, the patient was extubated once hemodynamically stable. He was discharged home with outpatient hemodialysis.

Similar symptomology has been reported in the literature. Several case reports describe comparable maculopapular rashes. As with our patient, these reports described similar lymphocytic infiltration [13-15]. Further, myocarditis and cardiacogenic shock have also been reported [16-19]. Myocarditis was diagnosed in these reports with the aid of endomyocardial biopsy and cardiac magnetic resonance imaging, both of which our small facility did not have access to [16,17]. Additionally, these reports identify similar inflammatory markers, and the patients responded well to high-dose corticosteroids plus IVIG. While it is unknown if the mechanisms mentioned above were responsible for our patient’s presentation, his skin biopsy’s lymphocytic infiltrate, cardiac findings, and eventual therapeutic response may suggest similar processes.

Two factors may have improved this patient’s prognosis: early identification and immunization. Early diagnosis proved especially difficult in a rural hospital. By the time the patient’s working diagnosis shifted to MIS-A, his status had already declined. He continued to decompensate to cardiac arrest despite initiating corticosteroids and NPPV. Fortunately, this patient was resuscitated and fully recovered. In addition, the BNT162b2 and mRNA-1273 vaccines have greater than 90% effectiveness in preventing symptomatic diseases from the SARS-CoV-2 Delta variant, which was widespread during this patient’s hospital course [23,24]. There are limited data regarding the prevention of MIS-A after immunization. However, given the manifestations of MIS-A requiring a SARS-CoV-2 infection, vaccination likely prevented or dampened the patient’s inflammatory response. With both factors considered, early diagnosis and immunization would likely improve outcomes in patients with MIS-A.

Discussion

Above, we reported a case of MIS-A in a 31-year-old man, 6-weeks post-SARS-CoV-2 infection, resulting in cardiac arrest and successful resuscitation. In the setting of a rural, critical-access hospital, limited resources hindered the early diagnosis and treatment of MIS-A. Initially, the patient had a working diagnosis of meningitis, given his neck stiffness, fever, and exanthematous rash. A negative lumbar puncture ruled out meningitis and neurodegenerative disorders. Other sources of infection and autoimmune diseases were negative despite the patient’s sustained fevers and elevated inflammatory markers. The CDC case definition of MIS-A aligned with our patient’s findings, with alternative diagnoses excluded. A fever ≥38.0°C for at least 24 hours is required, where the patient presented with a temperature of 38.2°C, remaining elevated throughout his stay. He met the primary criteria: severe cardiac illness (ventricular fibrillation leading to left ventricular systolic failure and cardiogenic shock) and maculopapular rash with conjunctivitis. Secondary criteria were established with new-onset neurological symptoms (neck stiffness) and abdominal pain with diarrhea. Lastly, laboratory evidence included elevated inflammatory markers (CRP, ESR, ferritin, procalcitonin) and 2 positive SARS-CoV-2 tests 6 weeks prior to admission [20].

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Conclusions

MIS-A manifests in a wide range of organ involvement, easily mistaken for infectious or autoimmune etiology. The CDC’s inclusion criteria are readily available for MIS-A diagnosis, but many of the criteria are nonspecific, with the caveat of first excluding alternative diagnoses. This diagnostic approach requires timely yet extensive ruling out of disease processes, which may be difficult in clinical settings with limited resources. With MIS-A being a relatively novel syndrome, further investigation is necessary to guide prompt diagnosis and intervention.

References:


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