Multisystem inflammatory syndrome in adults (MIS-A) following COVID-19 requiring venoarterial extracorporeal membrane oxygenation

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SUMMARY
The SARS-CoV-2 virus has caused a global pandemic with serious impact around the world. Patients most commonly present with severe lung involvement and acute respiratory failure; however, multisystem inflammatory syndrome in adults (MIS-A) is a known—although rare—complication. We present a case of a 49-year-old patient who presented with combined cardiogenic and vasodilatory shock and was diagnosed with MIS-A. He initially required venoarterial extracorporeal membrane oxygenation and Impella for haemodynamic support but was able to be weaned off these devices with complete recovery of left ventricular systolic function. This case demonstrates that MIS-A may present as haemodynamic collapse in adults, but complete recovery is possible with proper haemodynamic support.

BACKGROUND
The COVID-19 pandemic has caused serious illness around the world with acute respiratory failure being the most common complication. However, around April 2020, clinicians noticed a new entity called multisystem inflammatory syndrome in children (MIS-C). This presented as cardiovascular shock, fever and hyperinflammation. Since then, similar cases have been described in adults (called multisystem inflammatory syndrome in adults (MIS-A)), but the prognosis and management strategies are still unknown. We present a case of an adult with MIS-A who presented with combined cardiogenic and vasodilatory shock requiring venoarterial extracorporeal membrane oxygenation (VA-ECMO) and Impella for haemodynamic support.

CASE PRESENTATION
A man in his 40s with a medical history of hypertension presented with 2 weeks of cough, dyspnoea on exertion and intermittent fevers (Tmax: 102°F). Vital signs on presentation were blood pressure 106/70 mm Hg, heart rate 130 beats/min, respiratory rate 17 breaths/min, temperature 97.7°F (36.5°C) and oxygen saturation 95% on room air. He did not have chest pain, palpitations, dizziness or contacts with a known acute illness.

INVESTIGATIONS
Initial laboratory values were suggestive of inflammation and significant end-organ dysfunction, including creatinine 3.0 mg/dL (normal: 0.7–1.3 mg/dL), white blood cell count 19.6 x 10^9/L (normal: 5–10 x 10^9/L) and venous lactic acid 5.1 mmol/L (normal: 0.5–2.2 mmol/L). SARS-CoV-2 nasal swab was negative. His initial chest X-ray was unremarkable. ECG showed 1 mm ST-segment depressions in leads II, III and aVF.

Soon after admission, the patient became diaphoretic and dyspnoeic. Repeat vital signs showed blood pressure 90/50 mm Hg and sinus tachycardia 120 beats/min. Transthoracic echocardiogram (TTE) showed diffuse left ventricular hypokinesis with a left ventricular ejection fraction of 10%, mild LV dilation (left ventricular internal dimension in diastole 5.8 cm) and severe right ventricular hypokinesis consistent with new-onset biventricular heart failure (figure 1A,B). Inflammatory markers were significantly elevated, including C reactive protein 39.3 mg/dL, D-dimer 3.62 mg/mL, ferritin 3119.5 mg/mL and lactic dehydrogenase 483 U/L (figure 2).

Due to concern for cardiogenic shock, he was started on continuous infusions of dobutamine, epinephrine and vasopressin. However, he remained hypotensive despite escalating dosages. A pulmonary artery catheter was inserted and was consistent with combined cardiogenic and vasodilatory shock (mean arterial pressure 65 mm Hg, right atrial pressure 15 mm Hg, pulmonary artery pressure 32/20 mm Hg (mean 25 mm Hg), pulmonary capillary wedge pressure 21 mm Hg, pulmonary artery saturation 27.4%, Fick cardiac output 3.7 L/min, Fick cardiac index 1.91 L/min/m² and systemic vascular resistance 1081 dynes/sec/cm⁵). The patient underwent VA-ECMO placement.

The patient developed worsening hypoxaemic respiratory failure and pulmonary oedema on chest X-ray due to his inability to unload his left ventricle. There was minimal aortic pulsatility and pulmonary capillary wedge pressure was increased. As a result, he underwent Impella cardiac power placement. This is a percutaneous device that is placed across the aortic valve and pulls blood from the left ventricle into the aorta.

DIFFERENTIAL DIAGNOSIS
Due to concern for fulminating myocarditis, the infectious disease service was consulted. Blood cultures were negative. Infectious serologies, including hepatitis B, hepatitis C, parvovirus B19, Cytomegalovirus, Epstein-Barr virus, Lyme and Rickettsia, were negative. However, SARS-CoV-2 immunoglobulin G (IgG) nucleocapsid antibody was positive. The patient underwent endomyocardial biopsy that showed occasional neutrophils and rare eosinophils consistent with catecholamine toxicity. He was taken for emergent VA-ECMO placement and he was successfully weaned off the Impella and ECMO and discharged home on March 11, 2022.
Case report

injury (figure 3). Given his positive SARS-CoV-2 antibodies, lack of other infectious aetiologies and no evidence of myocarditis on endomyocardial biopsy, the diagnosis was MIS-A.

Figure 1  Initial TTE showing biventricular failure and follow-up TTE showing biventricular recovery. Panel (A) shows the initial TTE during systole. Panel (B) shows the initial TTE during diastole. Calculations showed an LVEF of 10%, mild LV dilatation (left ventricular internal dimension in diastole 5.8 cm) and severe right ventricular hypokinesis consistent with new-onset biventricular heart failure. Panel (C) shows the follow-up TTE at the end of systole. Panel (D) shows the follow-up TTE at the end of diastole. Calculations showed an LVEF of 60% consistent with recovery of left ventricular systolic function. LVEF, left ventricular ejection fraction; TTE, transthoracic echocardiogram.

Figure 2  Graph showing a decrease in inflammatory markers. Initial inflammatory markers were elevated at the time of VA-ECMO insertion. These markers decreased during the time of corticosteroid and intravenous Ig administration and were significantly decreased at the time of VA-ECMO decannulation compared with prior. CRP, C reactive protein; EMB, endomyocardial biopsy; Ig, immunoglobulin; LVEF, left ventricular ejection fraction; VA-ECMO, venoarterial extracorporeal membrane oxygenation; WBC, white blood cells.

Figure 3  EMB with catecholamine-induced myocardial injury. On day 3 of hospital admission, the patient underwent EMB. Blue arrows indicate neutrophils and red arrow indicates an eosinophil. The EMB was consistent with catecholamine-induced myocardial injury. EMB, endomyocardial biopsy.

TREATMENT

The patient received one dose of intravenous methylprednisolone and one dose of intravenous Ig. These were discontinued once the endomyocardial biopsy was reported. He received dobutamine and vasopressin infusions in addition to VA-ECMO and Impella for haemodynamic support.

OUTCOME AND FOLLOW-UP

By day 5 of admission, his haemodynamics had normalised, and he underwent successful VA-ECMO decannulation. On day 6, the Impella was removed. On day 10, he underwent repeat TTE that showed complete normalisation of biventricular function (figure 1C,D). He was discharged on day 11 with heart failure and infectious disease follow-up.

DISCUSSION

MIS-A is a rare manifestation of the SARS-CoV-2 infection and is often associated with serious outcomes.1 It was first observed in children and adolescents and has been reported to have a close resemblance to Kawasaki syndrome.1 Shortly after the identification of MIS-C, several similar cases in adults were reported. The Centers for Disease Control published diagnostic guidelines on reporting MIS-A.2 Our patient met Centers for Disease Control criteria for MIS-A (table 1), namely, severe illness requiring hospitalisation, over 21 years of age, negative SARS-CoV-2 PCR, severe dysfunction of one or more extrapulmonary organ system, elevated inflammatory markers and the absence of severe respiratory illness.2 4

MIS-A from SARS-CoV-2 infection often presents as multi-organ failure involving the heart, kidneys, liver and skin.5 6 Cardiac dysfunction can progress to haemodynamic collapse from cardiogenic shock.5 However, with proper circulatory support, left ventricle systolic function can improve dramatically. To date, only a few cases of VA-ECMO use in patients with MIS-A from COVID-19 infection have been reported.7–9 Our study reports one of the oldest patients with MIS-A treated with both Impella and VA-ECMO and indicates that even on the severe spectrum of the disease, prognosis can be good.

The pathogenesis of MIS-A is currently unclear. An abnormal inflammatory response is proposed as one of its aetiologies.
In previous COVID-19 outbreaks, an overactive antibody-mediated response has also been described. Patient had sustained elevated inflammatory markers several days into his clinical course (figure 2). Endomyocardial biopsy in our patient showed evidence of catecholamine-induced myocardial injury. A scant lymphocytic infiltrate has been described in COVID-19 myocarditis, while in this case the infiltrate consisted of neutrophils and eosinophils.

Currently, there are no evidence-based recommendations for the treatment of MIS-A. However, The American College of Rheumatology has published recommendations for management of MIS-C. These include the immunomodulatory agents, intravenous Ig and glucocorticoids, as the first-line treatment for patients with life-threatening manifestations of MIS-C. Given that MIS-A shares a similar pathophysiologic mechanism to MIS-C, glucocorticoids and intravenous Ig are also being recommended as a first-line treatment in case reports.

Our case further supports the use of advanced mechanical circulatory support devices such as Impella and VA-ECMO in patients with cardiogenic shock from MIS-A. Even in relatively older patients such as ours, VA-ECMO and Impella support can be used to improve haemodynamics and allow for complete recovery of left ventricle function.

Learning points

- Multisystem inflammatory syndrome in adults (MIS-A) can present with cardiogenic shock and associated haemodynamic collapse.
- Combined mechanical circulatory support with venaarterial extracorporeal membrane oxygenation and Impella may be necessary for treatment of MIS-A.
- Endomyocardial biopsy may play a useful role in differentiating cardiogenic shock from myocarditis and MIS-A.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

REFERENCES


Table 1 Definition of MIS-A as per CDC

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<th>Case definition for MIS-A</th>
<th>Clinical criteria</th>
<th>Laboratory evidence</th>
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<td>The patient must be &gt;21 years of age. Additionally, they must be hospitalised for &gt;24 hours or have an illness resulting in death that meets the following criteria</td>
<td>Subjective or objective fever (≥38.0°C) for ≥24 prior to hospitalisation or within the first 3* days of hospitalisation. Additionally, 3 of the following clinical criteria must be met prior to hospitalisation or within 3* days of hospitalisation. One must be a primary clinical criterion</td>
<td>Laboratory evidence of inflammation and SARS-CoV-2 infection</td>
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Primary clinical criteria

- Severe cardiac illness including new-onset right or left ventricular dysfunction (LVEF <50%), ventricular tachycardia, second or third degree A-V block, myocarditis, pericarditis or coronary artery aneurysm. Cardiac arrest alone does not meet this criterion
- Rash and conjunctivitis without purulence
- Secondary clinical criteria
  - New neurologic signs and symptoms, including peripheral neuropathy, seizures, meningeal signs or new-onset encephalopathy
  - New shock or hypotension
  - Diarrhoea, abdominal pain or emesis
  - Thrombocytopenia (platelet count: <150 000/μL)

*The date of hospital admission is hospital day 0.

CDC, Centers for Disease Control; CRP, C reactive protein; IL-6, interleukin 6; LVEF, left ventricular ejection fraction; MIS-A, multisystem inflammatory syndrome in adults.


