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CASE REPORT
Heart failure

Multisystem inflammatory syndrome in adults with cardiac engagement: a case report and literature review

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Background Following infection with severe acute respiratory syndrome coronavirus, a post-infectious multisystem inflammatory syndrome in adults (MIS-A) has been identified. It affects multiple organ systems and can lead to multi-organic failure.

Case summary This case report describes a patient with MIS-A with significant cardiac involvement including peri-myocarditis, pulmonary hypertension, right-sided heart failure, tricuspid regurgitation, and cardiogenic shock. After being diagnosed and treated correctly for MIS-A, the patient recovered completely, without any cardiac sequelae.

Discussion The hyperinflammation in MIS-A can have cardiac engagement. Although more research is required to further clarify the underlying mechanisms, prompt diagnosis and anti-inflammatory treatment are crucial for better outcomes and cardiac recovery.

Keywords Case report • Multisystem inflammatory syndrome in adults • Right ventricular heart failure • Tricuspid regurgitation • Cardiogenic shock

ESC curriculum 2.3 Cardiac magnetic resonance • 4.5 Tricuspid regurgitation • 7.3 Critically ill cardiac patient • 9.6 Pulmonary hypertension • 6.3 Heart failure with preserved ejection fraction

Learning points

- Multisystem inflammatory syndrome in adults needs to be considered in the presence of recent coronavirus disease infection with new-onset cardiogenic shock, as prompt diagnosis and treatment are crucial for better outcomes.
- Many of the criteria for diagnosing multisystem inflammatory syndrome in adults are non-specific, with the caveat of first excluding alternative diagnoses.
- More research is required to further clarify the risk factors and the mechanisms underpinning multisystem inflammatory syndrome in adults and related cardiogenic shock.

Introduction

A post-infectious multisystem inflammatory syndrome in adults (MIS-A) was identified during the COVID-19 pandemic,[1] and a definition was suggested by Centers for Disease Control and Prevention: age of ≥21, fever of ≥38.0°C, hospitalization for ≥24 h with at least three clinical criteria, and one or more being primary. Primary clinical criteria are as follows: (i) severe cardiac illness and (ii) rash and non-purulent conjunctivitis. Secondary clinical criteria are as follows: (i) new-onset neurologic signs and symptoms; (ii) shock or hypotension;

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(iii) abdominal pain, vomiting, or diarrhoea; and (iv) thrombocytopenia. Laboratory criteria are evidence of inflammation and current or recent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.[2]

We report a case of a patient with no prior known history of cardiac disease who developed MIS-A with significant cardiac involvement including myopericarditis, pulmonary hypertension (PH), right-sided heart failure, tricuspid regurgitation (TR), and cardiogenic shock. After being treated for MIS-A, she recovered with no remaining cardiac sequelae. We review the clinical manifestations, illness progression, pathophysiology, and treatment of MIS-A available in the medical literature, focusing on the associated myocardial injuries.

Summary figure

Day 1	Sore throat, shortness of breath, lower abdominal pain and malaise. Fever 37,8°C. BP 98/60. ECG: inferolateral ST elevations. Labs: ↑ D-dimer, ↑ CRP, ↑ Trop T, ↑ NTproBNP. Covid-19 RNA in nasopharyngeal swab and serum negative. CT pulmonary angiogram: no evidence of pulmonary embolism/infiltrative lesions. CT abdomen: free abdominal fluid. TTE: LVEF 50-55%, dilated right ventricle, reduced RVEF and severe TR. Started on Ibuprofen, Colchicine and i.v. Piperacillin/Tazobactam.	Day 7	BP 103/76. Labs: ↓ CRP. Positive Covid IgG IMKR spike-antibodies. Started on i.v. Immunoglobulin.
Day 2	Raising fever 38,0°C. BP 76/60. Labs: ↑ CRP, ↑ Trop T, ↑ NTproBNP. Wide range of microbiological and immunological with negative tests results.	Day 8	BP stable at 104/74. Labs: ↓ CRP. Weaned off Norepinephrine.
Day 3	Labs: CRP peak (395 mg/L), Trop T peak (27 ng/L), NTproBNP peak (13 100 ng/L). TTE: no new findings. Started on i.v. Norepinephrine and i.v. Furosemide.	Day 9	Labs: ↓ CRP. TTE: LVEF 55%, restored RVEF and severe TR. I.v. Methyl-prednisolone and Immunoglobulin discontinued. Started on oral Betamethasone.
Day 4	BP 98/71. Labs: ↓ CRP, ↓ Trop T. Cardiac MRI: reduced RVEF of 51%, LVEF 47%, PH, signs of myopericarditis and severe TR. Started on i.v. Levosimedan.	Day 10	Labs: ↓ CRP, ↓ Trop T, ↓ NTproBNP. Piperacillin/Tazobactam discontinued.
Day 5	BP 103/75. Fever peak at 38,3°C. Labs: ↓ CRP, ↓Trop T. Right heart catheterization: no abnormal findings. Started on i.v. Anakinra.	Day 11	BP 109/78. Labs: ↓ CRP, ↓ Trop T, ↓ NTproBNP. I.v. Furosemide discontinued.
Day 6	BP 103/81. MIS-A considered. Labs: ↓ CRP. Started on i.v. Methyl-prednisolone.	Day 12	BP 107/74. Labs: ↓ CRP (13 mg/L), ↓ Trop T (11 ng/L), ↓ NTproBNP (906 ng/L). TTE: restored ejection fractions and moderate TR. I.v. Anakinra discontinued. Discharged with oral Prednisolone 30 mg/day, tapered over 5 weeks.

BP: blood pressure,CRP: C-reactive protein, CT: Computed tomography, ECG: electrocardiogram, I.v.: intravenous, LVEF: left ventricular ejection fraction, MIS-A: multisystem inflammatory syndrome in adults, MRI: magnetic resonance imaging, NTproBNP: N-terminal pro-brain natriuretic peptide, PH: pulmonary hypertension, RVEF: right ventricular ejection fraction, TR: tricuspid regurgitation, Trop T: Troponin T, TTE: Transthoracic echocardiogram.

Case presentation

A 38-year-old female with a history of smoking and a past medical history of recurrent haematuria presented to the emergency department with sore throat, shortness of breath, lower abdominal pain, and malaise. On examination, she was pyrexial at 37.8°C and hypotensive with a blood pressure of 98/60 mmHg, heart rate of 100 b.p.m., and oxygen saturation level of 100%. General abdominal tenderness and macroscopic haematuria were the clinical findings. Electrocardiogram showed sinus rhythm with inferolateral ST elevation (*Figure 1*). Laboratory blood tests revealed raised levels of C-reactive protein 243 mg/L (reference: <3 mg/L), troponin T 67 ng/L (reference: <14 ng/L), D-dimer 1.2 mg/L (reference: <0.25 mg/L), leukocytes 19.5×10^9/L (reference: $3.5–8.8 \times 10^9$/L), and N-terminal pro-brain natriuretic peptide 2790 ng/L (reference: <125 ng/L). COVID-19 RNA in nasopharyngeal swab and serum was negative. A consensus in the cardiology unit was to consider other diagnoses rather than acute myocardial infarction due to fever, elevated C-reactive protein, and mild troponin elevation. Hence, a coronary angiogram was not performed. Fulminant myopericarditis with the primary source likely arising from the abdomen was the working diagnosis. The differential diagnoses were pneumonia and pulmonary embolism due to dyspnoea and elevated D-dimer. Computed tomography (CT) pulmonary angiogram revealed no evidence of pulmonary embolism or infiltrative lesions but 2 cm bilateral pleural effusion and an overloaded right ventricle (RV). An abdominal CT scan showed free abdominal fluid.

She was treated with 400 mg ibuprofen and 1000 µg colchicine. A transthoracic echocardiogram (TTE) on Day 1 and on Day 3 (*Video 1*) showed preserved systolic left ventricular ejection fraction (LVEF) of 50–55%, dilated RV with reduced right ventricular ejection fraction (RVEF), reduced tricuspid annular plane systolic excursion, and a severe TR (*Table 1*). The patient's body temperature rose to 38.2°C, and she became more hypotensive with a blood pressure of 76/60, C-reactive protein increased up to 395 mg/L, and worsening renal function. Blood, nasopharynx, and urine cultures were taken, and the patient was administered intravenous (IV) Ringer's acetate and piperacillin–tazobactam 4 g every 8 hours, quaque octa hora (q8 h) for a total of 9 days. Inotropic support and vasopressor support with levosimendan 0.05 µg/kg and norepinephrine 0.11 µg/kg/min were administered to improve the patient's haemodynamic stability. A rheumatologic investigation was initiated to exclude Mediterranean fever, systemic lupus erythematosus, acute porphyria, myositis, and vasculitis. A wide range of microbiological and immunological tests was performed with no positive results. Endocarditis was excluded due to negative blood cultures and absence of echocardiographic findings suggesting endocarditis.

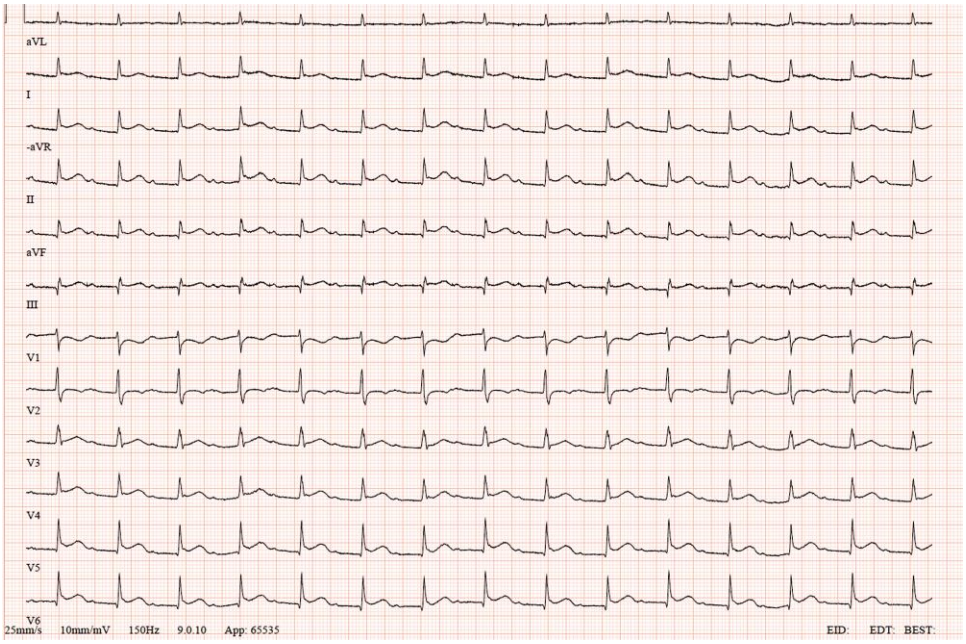
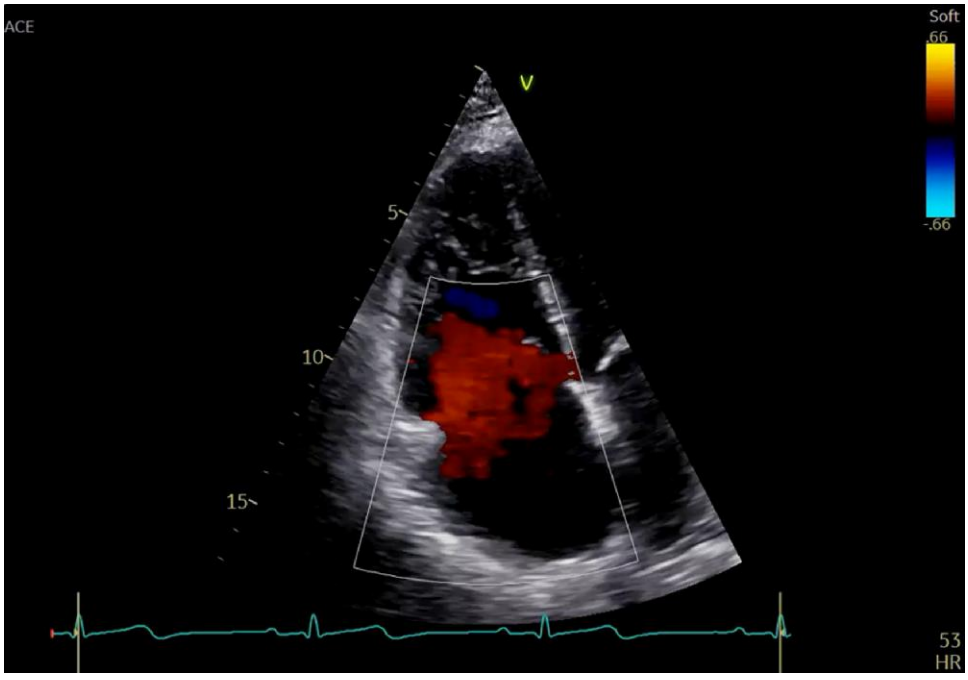


Figure 1 The patient's electrocardiogram showing sinus rhythm with general ST elevations, predominately in the inferolateral leads.



Video 1 Transthoracic echocardiogram on Day 3 of hospital stay: four-chamber view with focus on right ventricle showing severe tricuspid regurgitation with coaptation defect of 16 mm with free flow.

Cardiac magnetic resonance imaging showed dilated RV with reduced RVEF of 51%, LVEF of 47%, signs of PH including overloaded RV, severe TR, RV end-diastolic pressure higher than LV end-diastolic pressure, and signs of peri- and myocarditis with epicardial infusion and myocardial oedema (*Figure 2*; Supplementary material online, *Video S1*). The focal structural changes were inferior and not accessible for biopsy wherefore an endomyocardial biopsy could not be performed. No signs of myocardial infarction amyloidosis or cardiomyopathy were

Table 1 Echocardiographic measurements on Day 1 of hospitalization and 3 months after discharge

	TTE on Day 1 of hospitalization	TTE 3 months after discharge
RVd1	42 mm	32 mm
TAPSE	9 mm	23 mm
TR	Severe	Mild
Coaptation defect	7–8 mm	0 mm
FAC	39%	51%

FAC: right ventricular fractional area change; RVd1: basal right ventricular diameter; TAPSE: tricuspid annular plane systolic excursion; TR: tricuspid regurgitation; TTE: transthoracic echocardiogram.

seen. Due to the fact that the patient had been exposed to COVID-19 through a family member, MIS-A was considered. She was empirically treated by replacing colchicine with IV anakinra 100 mg q8 h, administration of immunoglobulin [intravenous immunoglobulin (IVIG)] infusion at 1 mg/kg/day for 2 days, and IV solumedrol 1500 mg for 3 days (*Figure 3*). Over the next 24 h, clinical improvement was observed, and she was weaned off norepinephrine. COVID IgG spike antibodies came back positive, confirming the diagnosis of MIS-A. Right heart catheterization a few days later showed no abnormal findings. A new TTE before discharge showed a moderate TR and restored ejection fractions. The patient was discharged on the 12th day with oral prednisolone 30 mg/day, tapered over a month. She was followed up at our outpatient heart failure clinic and the rheumatological outpatient clinic. All laboratory values were restored, and a TTE 3 months after discharge showed only a mild TR remaining (Supplementary material online, *Video S2*).

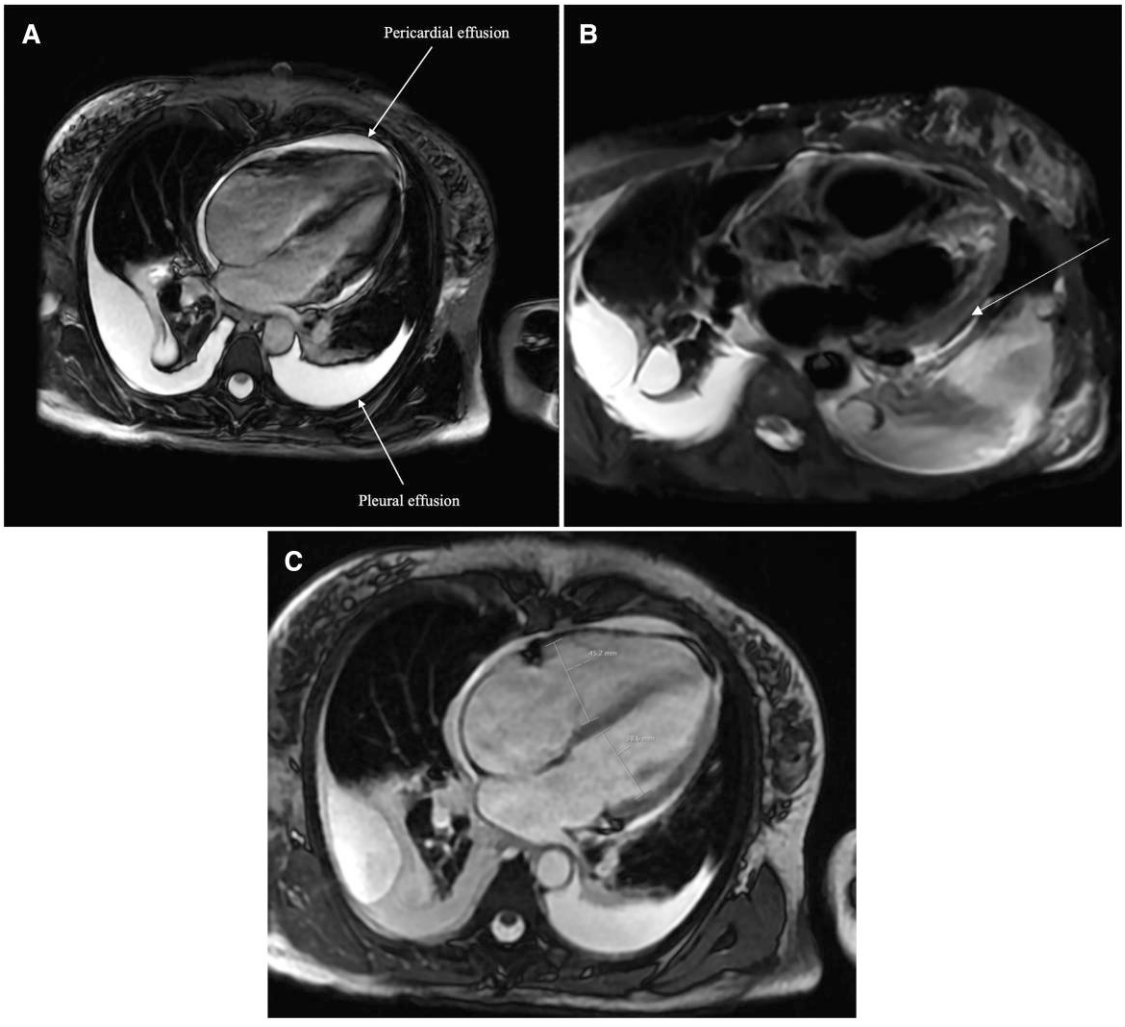


Figure 2 Cardiac magnetic resonance imaging, long-axis four-chamber views. (*A*) Black-blood contrast, T2-weighed, arrow showing oedema in the lateral wall. (*B*) Late gadolinium enhancement, showing basal right ventricle end-diastole diameter of 45.2 mm and end-diastole left ventricle diameter of 38.6 mm. (*C*) Arrows showing pericardial and pulmonary effusion.

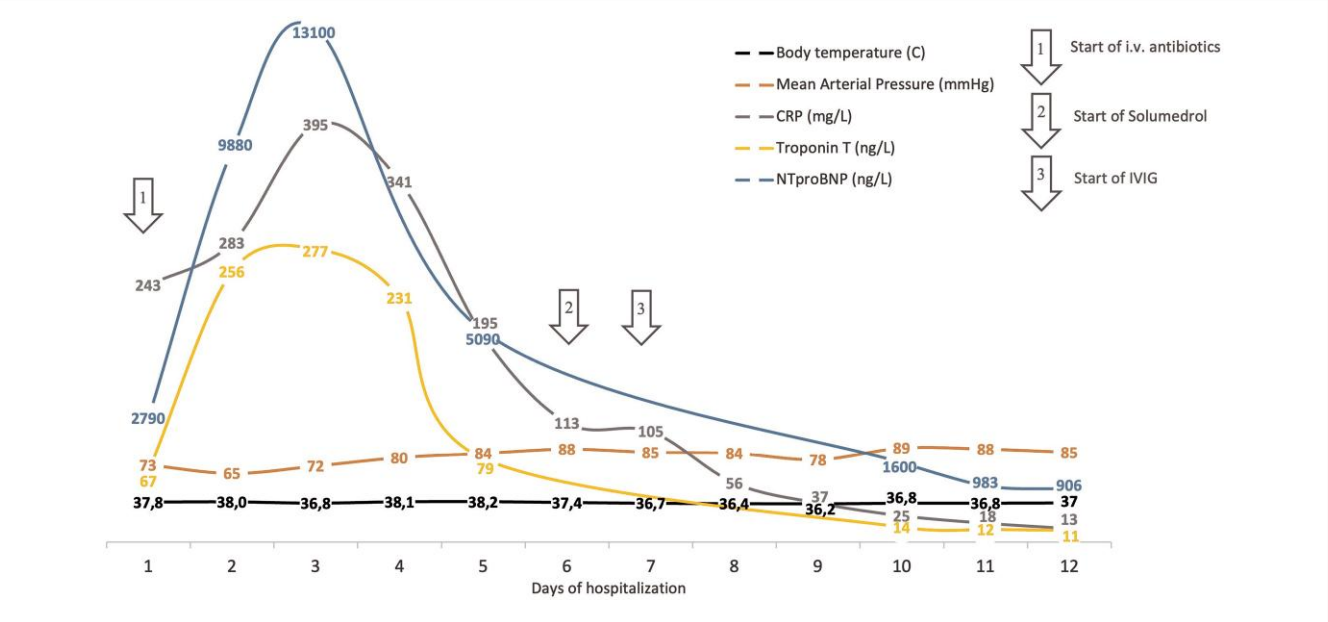


Figure 3 Linear changes of inflammatory and cardiovascular biomarkers and vital parameters during days of hospitalization. i.v.: intravenous; IVIG: intravenous immunoglobulin; NTproBNP: N-terminal pro-brain natriuretic peptide.

Discussion

Severe acute respiratory syndrome coronavirus 2 is known to be able to trigger a delayed inflammatory process weeks to months after the primary infection.[3] Such cases have been identified as MIS-A since 2020.[1] Our patient fulfilled the criteria with severe cardiac illness, elevated C-reactive protein, and positive SARS-CoV-2 antibodies.

A systematic review showed that MIS-A includes mostly extrapulmonary multi-organ dysfunction, particularly cardiovascular.[3] Both primary SARS-CoV-2 infection and MIS-A have dysregulated antibody-mediated immune response, with hyperinflammation and cytokine release in common.[3] The cardiovascular complications associated with MIS-A include myopericarditis, pericardial effusion, cardiogenic shock, coronary artery dilatation, mitral regurgitation, and arrhythmia.[1] Left ventricular dysfunction is present in 55–73.2% of adults and RV dysfunction in 20%.[1,3,4] In case reports with MIS-A-related myocarditis, TTE showed dilated ventricles with decreased ejection fractions and general/segmental hypokinesia.[4–7] Magnetic resonance imaging showed non-ischaemic myocardial injury and focal myocardial oedema.[6]

Our patient developed PH and RV failure, which has been shown on TTE exams of non-survivors of SARS-CoV-2 infection.[8] The acute myocardial tissue injury is believed to be related to elevated cytokines, hypoxaemia, RV strain, and thrombotic complications that lead to increased pulmonary vascular resistance and afterload.[9] Our patient also had a severe TR, as seen in other cases of MIS-A.[1,5,8,10] Some of the most common aetiologies of functional TR are increased RV afterload, RV dilatation, and dysfunction, present in patients with SARS-CoV-2 infection and MIS-A as we just discussed.[11]

The most common treatments of MIS-A are anti-inflammatory therapies with steroids, IVIG, and immune modulators such as tocilizumab and anakinra.[1,3,4] Patients with cardiogenic shock may require vasopressors, inotropes, and mechanical circulatory support.[1,4] Concomitant treatment for congestive heart failure, pericarditis, lung embolism, and antibiotics may be needed.[4,7]

Diuretics and IV fluids are commonly used in patients with acute right heart failure. Volume management is a critical consideration in these patients, and haemodynamic monitoring with a central venous catheter can be informative if a patient has haemodynamic instability or worsening renal function in response to therapy.[12]

Conclusion

Even in patients with negative COVID-19 RNA tests, MIS-A can have a life-threatening course with cardiogenic shock. Anti-inflammatory treatment leads to great improvement with full cardiac recovery, which suggests that hyperinflammation may have an impact on cardiac function. This case shows the importance to consider MIS-A in patients with multi-organ symptoms and giving them multi-disciplinary medical care with cooperation between cardiologists, rheumatologists, and infectiologists to start the right treatment early.

Lead author biography

Linda Massoud, MD, is a second-year resident in Cardiology at the Heart and Vascular Theme at Karolinska University Hospital, Stockholm, Sweden.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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