Kawasaki-like multisystem inflammatory syndrome associated with SARS-CoV-2 infection in an adult

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SUMMARY
Kawasaki-like hyperinflammatory syndrome has been widely described as a manifestation of SARS-CoV-2 infection in paediatric patients. We report a compatible presentation and suggest that physicians consider the potential for this multisystem inflammatory syndrome to occur in adults. A 23-year-old man presented to hospital with a 4-day history of vomiting, diarrhoea, dry cough, fever and a blanching erythematous rash on hands, feet and buttocks. He was otherwise fit and healthy. On day 3 of admission, marked bilateral conjunctivitis developed and high sensitivity troponin I increased significantly, followed by acute respiratory compromise requiring high-flow nasal oxygen therapy. Transthoracic echocardiogram on day 5 showed severe global hypokinesis of the left ventricle with an ejection fraction of 22%. SARS-CoV-2 was not detected by reverse transcription PCR on nasopharyngeal swabs, sputum or stool samples, however, SARS-CoV-2 antibody was positive. The patient’s syndrome resolved and cardiomyopathy reversed completely with supportive measures. He has since made a good recovery.

BACKGROUND
COVID-19 was declared a pandemic by the WHO in March 2020. As of 22 April 2021, there have been over 143 million cases and over 3 million deaths reported affecting every country and territory in the world.1 Much of the discourse in the media has focused on what populations are most at risk for the disease and there is a somewhat widely held perception that COVID-19 is a benign entity in young adults, children and those without underlying medical conditions. Indeed, some elements have used this as an argument against measures recommended by Public Health experts to control the spread of the virus. We report the case of an otherwise healthy young adult who developed critical illness as a result of SARS-CoV-2 infection with features compatible with the widely reported Kawasaki-like multisytem inflammatory syndrome in children (MIS-C).2,3

INVESTIGATIONS
Laboratory values on admission (summarised in table 1) were notable for a mild kidney injury and mild hyponatraemia as well as an elevated C reactive protein, D-dimers and high-sensitivity troponin I (hsTnI). SARS-CoV-2 RNA was not detected on nasopharyngeal swab reverse transcription PCR (RT-PCR). ECG revealed T-wave inversion in leads V1–V6. Chest X-ray was normal. Transthoracic echocardiogram was performed on day 1 of admission and showed a structurally normal heart and valves, with a normal left ventricular ejection fraction (LVEF) of 60%.

On day 3, laboratory tests were remarkable for a significantly raised hsTnI of 9634 ng/L. Following acute deterioration, emergent CT pulmonary angiogram was performed and was negative for pulmonary embolus but revealed dense right basal consolidation with septal thickening.

On day 5 of admission, transthoracic echocardiography was repeated and showed significant deterioration, with severe global hypokinesis of the left ventricle, and an LVEF of 20%.

Multiplex panel PCR, performed on nasopharyngeal swab, was negative for other respiratory viruses. Molecular enteric profile was negative. No other bacterial infections were identified. Serologies for common causes of viral myocarditis including parvovirus B19, coxsackievirus, enterovirus, HIV and Epstein-Barr virus (EBV) were negative.
SARS-CoV-2 was not detected by RT-PCR on nasopharyngeal swabs, sputum or stool samples. SARS-CoV-2 antibody was positive (Abbott ARCHITECT SARS-CoV-2 IgG CMIA).

**DIFFERENTIAL DIAGNOSIS**

Differential diagnosis including coxsackie virus, parvovirus B19, HIV, EBV and enterovirus were all considered, however, serological testing for these viruses was negative.

Toxic shock syndrome secondary to streptococcal or staphylococcal infection was also considered. However, there was no prior soft tissue infection and the rash resolved early in the clinical course. Blood cultures were negative and antistreptolysin O titre was normal.

Consideration was also given to a rheumatological cause of the syndrome, such as acute systemic lupus erythematosus or granulomatosis with polyangiitis. However, given the hyperacute presentation and negative autoantibody panel, these diagnoses were excluded.

Ultimately, given the clinical picture and antibody positivity for SARS-CoV-2 IgG, as well as similarities to the syndrome being reported in paediatric patients, the diagnosis of multiorgan hyperinflammatory syndrome secondary to SARS-CoV-2 infection was established.

**TREATMENT**

Treatment was largely supportive in nature.

He was admitted initially for observation and investigation. Following deterioration on day 3 of admission, he was commenced empirically on ceftriaxone and clarithromycin for suspected community-acquired pneumonia. Therapeutic low-molecular-weight heparin was commenced based on high clinical suspicion of SARS-CoV-2 infection and associated reports of hypercoagulability.

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**Figure 1** Rash on left palm.

**Figure 2** Rash on left foot.

**Figure 3** Nonsuppurative conjunctivitis right eye.

**Figure 4** Rash on buttocks.
Supportive respiratory measures were initiated when required in the form of high-flow nasal oxygen therapy with the patient requiring a maximum FiO₂ of 60% to maintain oxygen saturation of greater than 92%. Some dependent consolidation changes were noted on CT imaging and given the patient was alert and compliant, awake-proning was trialled to good effect.

Cardiovascular support was initially with intravenous fluids, but following deterioration required support with norepinephrine for fluid-refractory hypotension. Subsequent fluid overload responded well to loop diuretic therapy.

OUTCOME AND FOLLOW-UP

On day 13, cardiovascular MR scanning showed normal left ventricular size and function, an LVEF of 63% and no evidence of myocardial oedema or fibrosis. The previously noted transaminitis was resolving with an ALT of 205 U/L and AST of 62 U/L.

The patient was discharged well on day 13 of admission. He subsequently made a full recovery and is currently back at work full time with premorbid exercise tolerance. Echocardiography was repeated 2 months following admission and was again normal.

He was reviewed in clinic 4 months following his admission. He reported no subsequent issues. Full laboratory tests were repeated and were entirely within normal limits.

DISCUSSION

At the time of this patient’s presentation in May 2020, no cases of this syndrome occurring in an adult had been published in the medical literature. However, given the unusual clinical presentation, coupled with the exposure history, there was a strong suspicion from the outset that this was a manifestation of COVID-19.

Reports had begun to emerge early during the course of the pandemic about the MIS-C. Our patient met the case definition for both WHO9 and Center for Disease Control (CDC)10 definitions of the newly described MIS-C on all criteria, aside from age. Since initially being reported in paediatric patients, cases reports have since emerged of the syndrome occurring in adults.

A case series on the CDC morbidity and mortality weekly report detail 27 cases of the newly described MIS in adults (MIS-A) of whom 24 survived.10 The patients described had varying cardiovascular, gastrointestinal, dermatologic, and neurologic manifestations but generally without severe respiratory illness. Only one of the patients reported in this series was Caucasian.

Like our patient, many of the cases reported in the literature were RT-PCR not detected on nasopharyngeal swabs and required IgG testing for confirmation of diagnosis. This was the case for eight of the patients from the CDC series. A recent series of nine patients reported by Bajaj et al all were RT-PCR negative and had their diagnosis was confirmed by antibody testing.11 Four of these reported a recent history of COVID-19 symptoms followed by complete recovery. In one of the series referenced by the CDC report, four of the patients were RT-PCR not detected at the time of their cardiac presentation, two of whom had positive RT-PCR tests in the weeks prior.12 This highlights the importance of maintaining a high index of suspicion in spite of a negative RT-PCR for SARS-CoV-2. However, given the prevalence of antibodies to SARS-CoV-2 in many countries, IgG testing may now lack specificity and therefore an awareness of the clinical syndrome is important.

The available literature would suggest that this syndrome generally causes a degree of cardiac dysfunction in adults. Two separate series that included echocardiography findings found left ventricular systolic impairment in all patients. Bajaj and colleagues presenting a series of nine patients with an LVEF of between 10% and 35% (mean 24%).11 Similarly Chau et al reported seven patients with MIS-A all with reported initial LVEF of 20%–35%.12 However, in both papers, follow-up cardiac imaging indicated near complete recovery of LVEF in all but one of the patients.

The syndrome appears to be very similar to the MIS-C. A systematic review comprising a total of 662 patients found the majority to have fever, rash conjunctivitis and gastrointestinal symptoms. However, in contrast to the case series describing adults, decreased LVEF was found in only 262 of 581 (45.1%) of individuals in whom echocardiography was reported.

### Table 1: Serial blood laboratory values

| Haematology | Day 1 | Day 2 | Day 3 |
|-------------|-------|-------|-------|
| WBC (x10⁹/L) | 5.9 (3.7–9.5) | 6.8 | 5.5 |
| Neut (x10⁹/L) | 4.60 (1.7–6.1) | 5.90 | 4.45 |
| Lymph (x10⁹/L) | 0.71 (1.0–3.2) | 0.41 | 0.69 |
| Hb (g/dL) | 13.7 (13.3–16.7) | 13.5 | 12.2 |
| Platelet (x10⁹/L) | 96 (140–440) | 113 | 91 |
| D-Dimer (mg/L) | 2.30 (0–0.5) | 1.52 | 1.62 |
| ESR (mm/hr) | 17 (1–10) | 14 | 35 |
| Ferritin | 574 | 584 | 1479 |

| Biochemistry | Day 1 | Day 2 | Day 3 |
|-------------|-------|-------|-------|
| Sodium (mmol/L) | 131 (136–145) | 135 | 135 |
| Potassium (mmol/L) | 3.6 (3.5–5.1) | 3.9 | 3.6 |
| Urea (mmol/L) | 5.0 (2.76–8.07) | 4.8 | 4.5 |
| Creatinine (μmol/L) | 106 (59–104) | 96 | 106 |
| LDH (U/L) | 428 (220–450) | 416 | 521 |
| ALT (U/L) | 27 (0–45) | 121 |
| AST (U/L) | 29 (0–42) |
| Triglycerides (mmol/L) | 1.11 (0.3–1.7) | 1.79 |
| CRP (mg/L) | 104.5 (0–5) | 124.9 | 219.4 |
| hTnI (ng/mL) | 44 (<16) | 136 | 9634 |
| Procalcitonin (ng/mL) | |
| IL-6 (pg/mL) | 15.57 | 107 |
Case report

Patient’s perspective

My COVID-19 story starts in late March when I experienced a loss of taste and smell. I had no other symptoms at the time and so did not qualify for a test at the time. About a month later, the day after working a shift in my hospital’s COVID-19 intensive care unit (ICU), I began to feel unwell. It seemed at the time like a gastroenteritis with an unusual rash but eventually was so severe that I needed to be admitted to hospital.

In the evening, I deteriorated it felt very sudden. I can remember a point where it seemed that in the space of a minute I went from feeling okay to being so short of breath that I was unable to finish a sentence. The days after being admitted to ICU were extremely worrying for me. I was aware I had respiratory and heart failure and wondered would I get out alive. I was in constant contact with my girlfriend and family and got great emotional support from the staff and my friends.

Thankfully things did begin to resolve but when I got home I was by no means fixed. I was still breathless walking around and it really took 6 weeks to feel like myself again. While the elderly were most at risk, I am a fit and well 23-year old and still ended up in ICU with COVID-19.

Learning points

► The hyperinflammatory syndrome described in paediatric patients associated with SARS-CoV-2 infection may occur in young adults.
► This appears to be a rare entity with only sporadic case series and reports in the literature describing the syndrome.
► Presentation of this syndrome may be weeks after initial infection with SARS-CoV-2 and reverse transcription PCR may be negative at time of presentation necessitating antibody testing for confirmation of diagnosis.
► The syndrome can be associated with severe but reversible cardiomyopathy.
► COVID-19 is not always a benign entity in young adults and may cause critical illness.

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