A Rare Case of Kawasaki-like Multisystem Inflammatory Syndrome following COVID-19 in an Adult

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Abstract:
In this case report, we describe a Kawasaki-like multisystem inflammatory syndrome (MIS-A) in a 33-year old man that occurred 19 days after a SARS-CoV-2 infection. The main features at presentation were profound myocarditis, bilateral non-purulent conjunctivitis, mediastinal lymphadenopathy, and acute kidney failure and laboratory evidence of hyperinflammation. He received ACE-inhibition and beta-blockers for his heart failure and made a fairly rapid spontaneous recovery over the subsequent 8 days.

Keywords: Kawasaki-like multisystem inflammatory syndrome (MIS-A), COVID-19, Kawasaki disease, Multisystem inflammatory syndrome, ACE-inhibitors, Mediastinal lymphadenopathy.

1. INTRODUCTION
Kawasaki disease is an acute and usually self-limiting vasculitis of the medium calibre vessels, which exclusively affects children [1]. Although the underlying aetiology is unknown, various lines of evidence point to viral infections playing a central role in triggering the disease [1]. The COVID-19 pandemic has been associated with outbreaks of a Kawasaki-type disease that has also predominantly affected children. This has been termed the multisystem inflammatory syndrome in children (MIS-C). More recently, it has been appreciated that SARS-CoV-2 infection may also trigger a similar multisystem inflammatory syndrome in adults (MIS-A). We report a case of MIS-A in a 33-year old man with spontaneous resolution.

2. CASE REPORT
A 33-year-old male with no past medical history was presented to the emergency department with diarrhoea and abdominal pain. His nasopharyngeal swab was positive for SARS-CoV-2 and he was diagnosed with mild COVID-19 gastroenteritis. Apart from a body mass index (BMI) of 33.9 kg/m² (<25.0 kg/m²), he had no risk factors for severe COVID-19. He was managed as an outpatient with paracetamol and within a week had complete resolution of his symptoms. Nineteen days after his initial presentation, he developed gradual onset orthopnoea, fever, myalgia and fatigue. These symptoms were progressive and necessitated ICU admission 5 days later with multiorgan failure. At this point, his predominant symptoms were severe dyspnoea and palpitations. On clinical examination, he was febrile, had bilateral non-purulent conjunctivitis (Fig. 1) and signs of heart failure. Laboratory results showed a type I respiratory failure with a pO2 of 79.2 mmHg (83.0-108.0 mmHg) on room air, and raised leucocytes 20,30 x10⁹/L (3.50-9.80 x10⁹/L), neutrophils 17,50 x10⁹/L (1.56-7.08 x10⁹/L), CRP 550 mg/L (<6 mg/L), ferritin 5344 µg/L (<275 µg/L), LDH 625 U/L (<220 U/L), CK 418 U/L (<200 U/L) and triglycerides 276 mg/dL (<150 mg/dL) (Table 1). In addition, he had a marked elevation of his highly sensitive troponin 6834.7 ng/L (<34.2 ng/L) and NT-pro BNP 10599.0 pg/mL (<125.0 pg/mL). He was not oliguric but had biochemical evidence of acute kidney failure with a creatinine of 2.20 mg/dL (<0.50-0.80 mg/dL), an estimated GFR (MDRD) of 35 mL/min/1.73m² (<90 mL/min/1.73m²) and proteinuria 872.2 mg/24hours (<140.0 mg/24hours). A nasopharyngeal swab and bronchoalveolar lavage were both negative for SARS-CoV-2 on real-time polymerase chain reaction (RT-PCR). Bacterial blood cultures were negative. Echocardiogram revealed a reduced ejection fraction (LVEF) of 30%, mild left ventricular hypertrophy and a small pericardial effusion. His D-dimers were elevated 3,28
mg/L (<0,5 mg/L), but computed tomography angiography (CT-A) was negative for pulmonary embolism. This CT-scan did, however, reveal paratracheal and subcarinal lymphadenopathy (Fig. 2).

Coronary angiography revealed normal coronary vasculature and magnetic resonance imaging of the heart showed no structural abnormalities or signs of inflammation (Fig. 3).

A diagnosis of a multisystem inflammatory syndrome (myocarditis, acute kidney failure, adenopathy and bilateral non-purulent conjunctivitis) with a Kawasaki-like disease prior to a recent SARS-CoV-2 infection was made. His heart failure was treated with beta blocker and ACE-inhibition. His fever and laboratory markers of hyperinflammation settled spontaneously over the course of a week and thus, no immune-modulatory therapy was commenced. By the time of his discharge 8 days after admission, his cardiac left ventricular ejection fraction had recovered to 62%.

Table 1. Selected laboratory findings from the day of his admission and his discharge from the hospital. (N.A. = not available)

| Laboratory Results  | Hospital Admission (Day 0) | Hospital Discharge (Day 8) | Reference Values |
|---------------------|----------------------------|---------------------------|------------------|
| Leucocytes (x10⁹/L) | 20,30                      | 13,20                     | 3,50 – 9,80      |
| Neutrophils (x10⁹/L)| 17,50                      | 18,01                     | 1,56 – 7,08      |
| CRP (mg/L)          | 550                        | 63,6                      | < 6              |
| Ferritin (µg/L)     | 5344                       | N.A.                      | < 275            |
| LDH (U/L)           | 625                        | 437                       | < 220            |
| CK (U/L)            | 418                        | 122                       | < 200            |
| Triglycerides (mg/dL)| 276                        | N.A.                      | < 150            |
| Hs-troponins (ng/L) | 4809,1                     | 136,0                     | < 34,2           |
| NT-pro BNP (pg/mL)  | 10599,0                    | N.A.                      | < 125,0          |

Fig. (1). Image of his left eye reveals non-purulent conjunctivitis that was bilateral.
3. DISCUSSION

COVID-19 is characterized by a number of inflammatory syndromes [2]. In adults, the most common of these is COVID-19-associated hyperinflammatory syndrome (cHIS), which occurs 10-12 days following symptom onset. It typically affects patients with proinflammatory conditions, for example, obesity and diabetes. This cytokine release storm is often complicated by respiratory failure, cardiac pathology and thrombotic events [2 - 5]. Therapy is mainly immunosuppressive with options including corticosteroids, immunoglobulins, selective cytokine blockade and JAK-inhibition [5]. cHIS is very rare in children, who are more likely to have pauci- or asymptomatic SARS-CoV-2 infection. One of the possible explanations is a less developed adaptive immune system and a more robust innate immune response [2].

On the other hand, a small proportion of children and an even smaller proportion of adults have been noted to develop a Kawasaki-type illness 2 to 5 weeks after onset of COVID-19.
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