Kawasaki-like disease and myocarditis in a child with recent COVID-19 infection

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Introduction

The pandemic of COVID-19 caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS CoV-2) has led to a global threat infecting individuals of all ages. It has resulted in more than 176 million confirmed cases and over three million deaths worldwide (1). In Sri Lanka, there are more than 175,000 diagnosed COVID-19 cases and still in the rise. Severe interstitial pneumonia and hyper-activation of the inflammatory cascade are commonly seen in adults, while respiratory involvement is minimal in children.

The children with COVID-19 infection show atypical presentations with inflammatory syndromes similar to Kawasaki Disease (KD), making it difficult to understand the spectrum of COVID-19 disease in children (2). Kawasaki disease is a vasculitis of medium calibre vessels that usually affects children and the aetiology is unclear but thought to be post infectious. Common presentations of KD are fever, non-exudative conjunctivitis, cervical lymphadenopathy, polymorphous rash, peripheral oedema, red lips and strawberry tongue.

Case presentation

A seven-year-old boy from Kalmunai - a COVID-19 endemic area in the Eastern province of Sri Lanka - was admitted to the local base hospital; with fever, cough, abdominal pain, vomiting and erythematous rash for three days. On admission he was febrile, tachycardic (140 /bpm), tachypnoeic (42/min) and had low volume pulse with a blood pressure of

70/40 mmHg. (Height adjusted 50th centile blood pressure 92/55 mmHg)

His father was treated for COVID-19 infection two weeks prior to the child's presentation, where the child had close contact. Child's PCR for COVID-19 was negative then.

Laboratory results revealed total white cell count of $8.82 \times 10^9/L$ with 90% neutrophils, haemoglobin of 11.8 g/dL, platelets of $87 \times 10^9/L$ with elevated C-reactive protein of 97 mg/dL and ESR of 78 mm/hr. He had hyponatraemia of 130 meq/L, renal functions were normal but had marginally elevated liver enzymes (AST 47 U/L and ALT 61 U/L). There was no growth in blood culture. His electrocardiogram (ECG) showed sinus tachycardia with nonspecific ST segment and T wave abnormalities were suggestive of myocarditis. First 2D echo-cardiogram performed at the local hospital revealed severe left ventricular dysfunction, dilated left ventricle and mild mitral regurgitation which further supported the diagnosis of myocarditis. His troponin I titre was high (207.6 ng/L).

He was transferred to the Paediatric Intensive Care Unit (PICU) at Teaching Hospital Karapitiya (THK) on the sixth day of the illness. Echo-cardiogram performed on the same day showed evidence of reduced ventricular function and dilated coronary arteries. Left main coronary artery, left anterior descending artery and right coronary artery measured 4 mm (normal 1.84 - 3.2), 3.7 mm (normal 1.29 - 2.84) and 3mm (normal 1.17 - 2.94) respectively (Figures 1, 2, 3 & 4).

Figure 1: Dilated coronaries of left main coronary artery (LMCA) 4 mm and left anterior descending artery (LAD) 3.7 mm

Figure 2: Right coronary artery (RCA) 3 mm

Figure 3: M-Mode of echocardiogram showing an ejection fraction of 40% on acute stage (Normal range 65 - 70%) LVPW - Left ventricular posterior wall, IVS - Interventricular septum

Figure 4: 2D Echocardiogram of left ventricle shows dilated left ventricle (LV), IVS - Interventricular septum, LVPW - Left ventricular posterior wall, LA - Left atrium, MV - Mitral valve

He needed dopamine-titrated $10 \mu\text{g/kg/min}$ - for pressure support and was treated with a single dose of intravenous immunoglobulin (IVIG - 2 g/kg) followed by methylprednisolone (30 mg/kg/day) and anti-inflammatory dose of aspirin (75 mg/kg/day). His improvement was remarkable; fever subsided after 24 hours of treatment. Haemodynamic parameters were stable enough to discontinue inotropes 48 hours after the treatment. Inflammatory markers reduced with clinical improvement. CRP dropped to 71 mg/dL and ESR to 80 mm/hr and platelet count increased up to $220 \times 10^9/\text{L}$ in 3 days after the treatment (day 9th of the illness). Methylprednisolone and anti-inflammatory dose of aspirin was stopped. Aspirin was continued as an anti-platelet - 5 mg/kg/day- dose. A Repeat 2D echo-cardiogram, one week after previous study showed improvement of coronary artery dilatation and significant recovery of left ventricular function. Repeat investigations, 10 days after the treatment showed CRP of 12 mg/dL, ESR of 50 mm/hr and platelet count of $550 \times 10^9/\text{L}$. Liver enzymes showed normal values. The patient was discharged home on an antiplatelet dose of aspirin (5 mg/kg/day) with a plan to follow up at paediatric cardiology clinic. Follow up 2D Echo-cardiogram at six weeks after the discharge showed normal coronaries with normal cardiac function. Therefore, aspirin was stopped and planned to review in 3 months.

Repeat COVID-19 PCR done at THK on the sixth day of the illness was negative; both IgG and IgM antibodies done on the ninth day of the illness were positive for COVID-19 infection.

Discussion

The first published case of Kawasaki disease and COVID-19 infection was reported in a 6-month-old child in Wuhan, China in early 2020 with five days of fever and typical clinical findings meeting criteria for classic Kawasaki disease (3). There were similar cases reported in Europe, Pakistan, North America that had been associated with positive PCR for COVID-19.

Children with hyper-inflammatory shock, showing features similar to atypical Kawasaki, Kawasaki disease shock syndrome, or toxic shock syndrome were reported in mid 2020. Multisystem inflammatory syndrome in children (MIS-C) is a rare condition that has been reported 2 - 4 weeks after the onset of COVID-19.

Recently, reports from Europe and North America have described clusters of children and adolescents requiring admission to intensive care units with a multi system inflammatory condition with some features similar to those of Kawasaki disease and toxic shock syndrome (4, 5). They describe a presentation of acute illness accompanied by a hyper inflammatory syndrome, leading to multi organ failure and shock. Those patients have presented with fever, variable rash, conjunctivitis, peripheral oedema, significant gastrointestinal symptoms, shock, and elevated inflammatory markers and elevated cardiac markers. All children were negative for SARS-CoV-2- RT- PCR, but had positive antibodies for COVID-19 (4, 5).

This is the first reported case of Kawasaki Shock Syndrome - Multisystem Inflammatory Syndrome in Children (MIS-C) following COVID-19 infection in a child in Sri Lanka.

World Health Organization (WHO) has developed a preliminary case definition for MIS-C (Table 1). The case definition will be revised as more data will become available (6).

Table 1: Preliminary case definition of MIS-C

Children and adolescents 0 - 19 years with fever $\geq$ 3 days
AND <u>two</u> of the following:
1. Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).
2. Hypotension or shock.
3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-pro-BNP),
4. Evidence of coagulopathy (by PT, PTT, elevated D-dimers).
5. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain)
AND
Elevated inflammatory markers (ESR/ C-reactive protein/ procalcitonin).
AND
No other diagnosis microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.
AND
Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.

According to this new case definition of MIS-C following COVID 19 infection, the child in our case report has complied with criteria to diagnose MIS-C.

Conclusions

Physicians' understanding of the myriad of COVID-19 presentations, is vital to reduce morbidity and mortality through early diagnosis and effective treatment. This case report warrants the need of further research on the diverse spectrum of clinical presentations of COVID-19 in the pediatric population.

If a child who recovered from COVID-19 infection shows fever, variable rash, conjunctivitis, peripheral oedema, significant gastrointestinal symptoms, medical advice should be sought.

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Informed consent has been obtained from parents of the child to publish this case report.

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