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Severe refractory Kawasaki disease in seven infants in the COVID-19 era

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See Online for appendix

A cohort of seven infants (aged ≤ 1 year) with severe Kawasaki-like disease were diagnosed and treated at five hospitals in the UK between February and March, 2020 (appendix p 1). All of the infants received prompt intravenous immunoglobulins and steroid treatment, but none responded and all required the addition of a biological agent because of continued inflammation, recurring fever, and progressive changes on echocardiography. Six patients (86%) developed coronary artery aneurysms (Z score >2.5) and one infant died as a result of a ruptured aneurysm, despite early aggressive treatment. Five infants (71%) had negative serology for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); therefore, any correlation with the COVID-19 pandemic and paediatric inflammatory multisystemic syndrome temporally associated with SARS-CoV-2 is unclear.¹⁻³ Nonetheless, we would like to alert paediatricians to this new and very aggressive phenotype in infants.

The post-mortem examination of one infant (infant 2) showed markedly abnormal coronary arteries with multiple massive saccular aneurysms (appendix p 4). Histology of the affected vessels showed typical features of Kawasaki disease, with florid vasculitis, vessel wall destruction, and aneurysm formation in the absence of fibrinoid necrosis (appendix p 5). There was no thrombotic occlusion of the coronary arteries or any other myocardial changes (apart from the affected vessels), and no non-cardiac vasculitis. There was no inflammation in the upper or lower airways and no evidence of pneumonitis or myocarditis to suggest ongoing active viral infection. Post-mortem swabs from the nasopharynx and lung of

infant 2 were negative for SARS-CoV-2, but respiratory PCR was positive for adenovirus in vivo.

One infant (infant 1) was treated with two doses of infliximab, with the second dose given at day 42 because of new echocardiographic changes and rising C-reactive protein. This infant remains on immunosuppressant therapy 3 months after presentation. Infant 6 did not respond to anakinra and was subsequently treated with infliximab (appendix pp 1-3).

All patients had high C-reactive protein at presentation (80-276 mg/L) and high platelets in the later stages of the disease ($468-1419 \times 10^9/L$; appendix pp 1-3). The other inflammatory parameters that are typically elevated in paediatric inflammatory multisystemic syndrome temporally associated with SARS-CoV-2, such as ferritin, lactate dehydrogenase, and D-dimers, were only mildly elevated in these patients. Lymphocytopenia was present in one infant. One infant tested positive for SARS-CoV-2 on PCR and one infant tested positive on antibody testing (appendix pp 1-3).

Although it is well known that Kawasaki disease in children aged 1 year and younger has a worse prognosis than in older children (aged >1 year), particularly in boys with coronary artery disease, the severity of disease in this cohort is unusual compared with the literature, in which 10-20% of infants develop aneurysms.⁴ We cannot link these cases to the COVID-19 pandemic, as serology and PCR results for SARS-CoV-2 were mostly negative. Nevertheless, we feel that it is important that paediatricians consider early aggressive treatment and close cardiac monitoring of Kawasaki disease in infants, in whom a severe disease course might be occurring.

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An adult presentation consistent with PIMS-TS

Following reports of paediatric inflammatory multisystem syndrome temporally associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (PIMS-TS),^{1,2} a UK-born man of Somali origin, aged 21 years, was admitted to University College London Hospitals (UK) with 6 days of fever and abdominal pain associated with constipation, anorexia,



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