Correspondence

Hyperinflammatory shock in children during COVID-19 pandemic

South Thames Retrieval Service in London, UK, provides paediatric intensive care support and retrieval to 2 million children in South East England. During a period of 10 days in mid-April, 2020, we noted an unprecedented cluster of eight children with hyperinflammatory shock, showing features similar to atypical Kawasaki disease, Kawasaki disease shock syndrome,1 or toxic shock syndrome (typical number is one or two children per week). This case cluster formed the basis of a national alert. All children were previously fit and well. Six of the children were of Afro-Caribbean descent, and five of the children were boys. All children except one were well above the 75th centile for body-mass index (BMI).

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| Patient | Age (years); gender; ethnicity | BMI (kg/m²); comorbidities | Clinical presentation | Organ support | Pharmacological treatment | Imaging results | Laboratory results | Microbiology results | PICU length of stay; outcome |
|---------|-------------------------------|---------------------------|-----------------------|---------------|------------------------|----------------|-------------------|---------------------|--------------------------|
| Patient 1 | Male, Afro-Caribbean | 14; 95 kg; 33 kg/m²; no comorbidities | 4 days ≥40°C; non-bluody diarrhea; abdominal pain; headache | BP 80/40 mm Hg; HR 120 beats per min; RR 40 breaths per min; work of breathing; SatO₂ 99% NCO₂ | Dopamine, noradrenaline, argirepsin, adrenaline, cafrine, clindamycin | RV dysfunction; elevated RVSP; acute GI oedema and dilated biliary tree, ascites, bilateral basal lung consolidations and diffuse nodules | Ferritin 4220 μg/L; D-dimers 124 mg/L; troponin 6.5 mg/L; NT-proBNP 3.5 pg/mL; CRP 1556 μg/mL; procalcitonin 100 μg/mL; albumin 20 g/L; platelets 123×10⁹ | SARS-CoV-2 positive (post mortem) | 6 days; demise (right MCA and ACA ischaemic infarction) |
| Patient 2 | Male, Afro-Caribbean | 8; 30 kg; 18 kg/m²; no comorbidities | 5 days ≥29°C; non-bluody diarrhea; abdominal pain; conjunctivitis; rash | BP 81/37 mm Hg; HR 165 beats per min; RR 40 breaths per min; SatO₂ 91% NCO₂ | Noradrenaline, adrenaline, IVIG, infliximab, methylprednisolone, clindamycin | Mild biventricular dysfunction, severely dilated coronaries, ascites, pleural effusions | Ferritin 277 μg/L; D-dimers 8.4 mg/L; troponin 25 mg/L; CRP 295 μg/mL; procalcitonin 8.4 μg/mL; albumin 18 g/L; platelets 61×10⁹ | SARS-CoV-2 negative; likely COVID-19 exposure from mother | 4 days; alive |
| Patient 3 | Male, Middle Eastern | 4; 18 kg; 17 kg/m²; no comorbidities | 4 days ≥39°C; non-bluody diarrhea and vomiting; abdominal pain; rash; conjunctivitis | BP 90/30 mm Hg; HR 170 beats per min; RR 35 breaths per min; SatO₂ 96% NCO₂ | Noradrenaline, adrenaline, IVG, clindamycin | Acutes; pleural effusions | Ferritin 574 μg/L; D-dimers 11.7 mg/L; troponin 65 mg/L; CRP 322 μg/mL; procalcitonin 10.3 μg/mL; albumin 22 g/L; platelets 103×10⁹ | Adenovirus positive; HVR positive | 4 days; alive |
| Patient 4 | Female, Afro-Caribbean | 13; 64 kg; 33 kg/m²; no comorbidities | 5 days ≥39°C; non-bluody diarrhea; abdominal pain; conjunctivitis | BP 77/41 mm Hg; HR 127 beats per min; RR 24 breaths per min; SatO₂ 92% NCO₂ | Noradrenaline, clindamycin, methylprednisolone, IVIG | Moderate to severe LV dysfunction; ascites | Ferritin 631 μg/L; D-dimers 3.4 mg/L; troponin 250 mg/L; NT-proBNP 5427 μg/mL; CRP 307 mg/mL; procalcitonin 12.1 μg/mL; albumin 21 g/L; platelets 146×10⁹ | SARS-CoV-2 negative | 5 days; alive |
| Patient 5 | Male, Asian | 6; 22 kg; 14 kg/m²; no comorbidities | 4 days ≥39°C; odynophagia; myalga, myalgia; rash; 3 days diarrhea and vomiting; conjunctivitis | BP 85/43 mm Hg; HR 150 beats per min; RR 50 breaths per min; SatO₂ 98% NCO₂ | Methylprednisolone, aspirin, ceftriaxone | Dilated LV, AVR, pericoronary hyperechogenicity | Ferritin 550 μg/L; D-dimers 11.1 mg/L; troponin 47 mg/L; NT-proBNP 7004 pg/mL; CRP 183 mg/L; albumin 24 g/L; platelets 165×10⁹ | SARS-CoV-2 positive; likely COVID-19 exposure from father | 4 days; alive |
| Patient 6 | Female, Afro-Caribbean | 6; 26 kg; 15 kg/m²; no comorbidities | 5 days ≥39°C; non-bluody diarrhea; abdominal pain; conjunctivitis | BP 77/46 mm Hg; HR 120 beats per min; RR 40 breaths per min; SatO₂ 98% NCO₂ | Noradrenaline, adrenaline, myalgia, IVIG, methylprednisolone, clindamycin | Mild LV systolic impairment | Ferritin 1023 μg/L; D-dimers 9.9 mg/L; troponin 45 mg/L; NT-proBNP 9375 pg/mL; CRP 169 mg/L; procalcitonin 11.6 μg/mL; albumin 25 g/L; platelets 158 | SARS-CoV-2 negative; confirmed COVID-19 exposure from grandfather | 3 days; alive |
| Patient 7 | Male, Afro-Caribbean | 12; 50 kg; 20 kg/m²; no comorbidities | 4 days ≥39°C; diarrhea and vomiting; abdominal pain; rash; odynophagia; headache | BP 80/48 mm Hg; HR 125 beats per min; RR 47 breaths per min; SatO₂ 98% NCO₂ | Noradrenaline, adrenaline, clindamycin, methylprednisolone, heparin, ceftriaxone | Bestretch venous impairment; ileitis, ascites, pleural effusions | Ferritin 558 μg/L; D-dimer 24.5 mg/L; troponin 813 μg/mL; NT-proBNP 3530 pg/mL; CRP 251 mg/L; procalcitonin 71.5 μg/mL; albumin 24 g/L; platelets 273×10⁹ | SARS-CoV-2 negative | 4 days; alive |
| Patient 8 | Female, Afro-Caribbean | 8; 50 kg; 25 kg/m²; no comorbidities | 4 days ≥39°C; odynophagia; diarrhea and vomiting; abdominal pain | BP 82/41 mm Hg; HR 120 beats per min; RR 35 breaths per min; SatO₂ 97% NCO₂ | Noradrenaline, methylprednisolone, clindamycin, IVIG | Moderate LV dysfunction | Ferritin 460 μg/L; D-dimers 4.3 mg/L; troponin 120 mg/L; CRP 3.47 μg/mL; procalcitonin 7.42 μg/mL; albumin 22 g/L; platelets 296×10⁹ | SARS-CoV-2 negative; likely COVID-19 exposure from parent | 7 days; alive |

ACAs= anterior cerebral artery; ADHD= attention deficit hyperactivity disorder; AVR= atriocventricular valve regurgitation; BMI= body-mass index; BP= blood pressure; COVID-19= coronavirus disease 2019; CRP=C-reactive protein; FiO₂= fraction of inspired oxygen; HERR = human endogenous retrovirus; HFlNC= high-flow nasal cannula; HR=heart rate; IVIG= intravenous immunoglobulin; LV=left ventricle; MCA= middle cerebral artery; MV= mechanical ventilation via endotracheal tube; NIV= non-invasive ventilation; NT-proBNP= N-terminal pro-B-type natriuretic peptide; PI= paediatric intensive care unit; RR= respiratory rate; RRT= renal replacement therapy; RV= right ventricle; RVSP= right ventricular systolic pressure; SARS-CoV-2= severe acute respiratory syndrome coronavirus 2; SatO₂= oxygen saturation; SVIA= sodium bicarbonate; TIVA= total intravenous anaesthesia; VAP= ventilator-associated pneumonia.

Table: Demographics, clinical findings, imaging findings, treatment, and outcome from PICU.
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COVID-19: PCR screening of asymptomatic healthcare workers at London hospital

The exponential growth in coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) across the UK has been successfully reversed by social distancing and lockdown.1 RNA testing for prevalent infection is a key part of the exit strategy, but the role of testing for asymptomatic infection remains unclear.2 Understanding the determinants of asymptomatic or pauci-symptomatic infection will provide new opportunities for personalised risk stratification and reveal much-needed correlates of protective immunity, whether induced by vaccination or natural exposure. To address this, we set up COVIDsortium (NCT04318314), a bioresource focusing on asymptomatic healthcare workers (HCWs—doctors, nurses, allied health professionals, administrators, and others) at Barts Health NHS Trust, London, UK, to collect data through 16 weekly assessments (unless ill, self-isolating, on holiday, or redeployed) with a health questionnaire, nasal swab, and blood samples and two concluding assessments at 6 months and 12 months. HCWs were self-declared as healthy and fit to work for study visits. Participants were not given swab results, and those with symptoms or in self-isolation resumed study visits on return to work.

Across London, case-doubling time in March, 2020, was approximately 3–4 days. The number of nasal swabs testing positive for SARS-CoV-2

for weight. Four children had known family exposure to coronavirus disease 2019 (COVID-19). Demographics, clinical findings, imaging findings, treatment, and outcome for this cluster of eight children are shown in the table.

Clinical presentations were similar, with unrelenting fever (38–40°C), variable rash, conjunctivitis, peripheral oedema, and generalised extremity pain with significant gastrointestinal symptoms. All progressed to warm, vasoplegic shock, refractory to volume resuscitation and eventually requiring noradrenaline and milrinone for haemodynamic support. Most of the children had no significant respiratory involvement, although seven of the children required mechanical ventilation for cardiovascular stabilisation. Other notable features (besides persistent fever and rash) included development of small pleural, pericardial, and ascitic effusions, suggestive of a diffuse inflammatory process.

All children tested negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on bronchoalveolar lavage or nasopharyngeal aspirates. Despite being critically unwell, with laboratory evidence of infection or inflammation including elevated concentrations of C-reactive protein, procalcitonin, ferritin, triglycerides, and D-dimers, no pathological organism was identified in seven of the children. Adenovirus and enterovirus were isolated in one child.

Baseline electrocardiograms were non-specific; however, a common echocardiographic finding was echobright coronary vessels (appendix), which progressed to giant coronary aneurysm in one patient within a week of discharge from paediatric intensive care (appendix). One child developed arrhythmia with refractory shock, requiring extracorporeal life support, and died from a large cerebrovascular infarct. The myocardial involvement in this syndrome is evidenced by very elevated cardiac enzymes during the course of illness.

All children were given intravenous immunoglobulin (2 g/kg) in the first 24 h, and antibiotic cover including ceftriaxone and clindamycin. Subsequently, six children have been given 50 mg/kg aspirin. All of the children were discharged from the PICU after 4–6 days. Since discharge, two of the children have tested positive for SARS-CoV-2 (including the child who died, in whom SARS-CoV-2 was detected post mortem). All children are receiving ongoing surveillance for coronary abnormalities.

We suggest that this clinical picture represents a new phenomenon affecting previously asymptomatic children with SARS-CoV-2 infection manifesting as a hyperinflammatory syndrome with multiorgan involvement similar to Kawasaki disease shock syndrome. The multifaceted nature of the disease course underlines the need for multispecialty input (intensive care, cardiology, infectious diseases, immunology, and rheumatology).

The intention of this Correspondence is to bring this subset of children to the attention of the wider paediatric community and to optimise early recognition and management. As this Correspondence goes to press, 1 week after the initial submission, the Evelina London Children’s Hospital paediatric intensive care unit has managed more than 20 children with similar clinical presentation, the first ten of whom tested positive for antibody (including the original eight children in the cohort described above).

We declare no competing interests.

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