Systemic inflammatory response and fast recovery in a pediatric patient with COVID-19

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Running title
Severe course of pediatric COVID-19

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To the Editor:

The recently emerged SARS-CoV-2 virus causes pneumonia and, in severe cases, acute respiratory distress syndrome (ARDS) in adults, but its clinical picture can be markedly different in children, most of whom undergo only a mild or even asymptomatic course of the disease1–3. In some cases, however, profound systemic inflammatory response is triggered, sharing few similarities with the more commonly seen self-limited respiratory infection.

Here we report a case of an 8-year-old girl who manifested with fever (＞40°C), headache, abdominal pain and vomiting, but no signs of respiratory involvement with only mildly elevated C-reactive protein (CRP, 27 mg/l, Fig 1A). Over the next 2 days she developed diffuse itchy maculo-papular rash (Fig 1B) and watery diarrhea with CRP of 139 mg/l. At this point, SARS-CoV-2 nasopharyngeal swab polymerase chain reaction (PCR) was negative. The girl was started on amoxicillin/clavulanic acid. However, her condition deteriorated with ongoing high-grade fever, diarrhea and headache necessitating hospital admission on day 5 from symptom...
The adhesion molecule CD62L was low during the time of most fulminant infection, but its expression activated in mature neutrophils, reached supra-normal expression during recovery as these cells matured. Neutrophils from the bone marrow, but together with the inhibitory molecule PD-1L and CD15, a marker of function recovered to normal levels. CD10, a marker of neutrophil maturation associated with immunosuppressive expression of HLA-DR, previously described to be decreased in COVID-19.

We additionally show stark changes in neutrophil phenotype during the course of the disease (Fig 2C). The expression of HLA-DR, previously described to be decreased in COVID-19, was low on day 8 and gradually recovered to normal levels. CD10, a marker of neutrophil maturation associated with immunosuppressive function, was markedly decreased during the worst clinical symptoms, suggesting efflux of young, active neutrophils from the bone marrow, but together with the inhibitory molecule PD-1L and CD15, a marker of activation in mature neutrophils, reached supra-normal expression during recovery as these cells matured. The adhesion molecule CD62L was low during the time of most fulminant infection, but its expression.
recovered and was even elevated on day 19 at recovery. Together, these data suggest full activation and engagement of neutrophils during the disease with compensatory contraction of the response and conotr- 
gerulation of neutrophil phenotype during recovery.

In summary, our patient developed systemic inflammatory response to SARS-CoV-2 infection in absence of other infectious pathogens, which had some but not all hallmarks of secondary MAS/HLH and which quickly deteriorated and then resolved with corticosteroids, preventive anticoagulation and supportive therapy only. This case report illustrates the variability of clinical presentation of SARS-CoV-2 infection in children, which should be suspected in case of unexplained inflammatory symptoms even in the absence of signs of respiratory infection. Immunosuppressive therapy may be helpful for these patients.

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Impact statement

SARS-CoV-2 infection in children may trigger systemic inflammatory response without symptoms traditionally associated with COVID-19 in adults. Its course is characterized by the activation of the innate immune response and may resolve quickly with supportive therapy and intravenous corticosteroids.

References


**Figure legends**

**Fig 1**

Blood biochemistry and markers of inflammation over the course of the disease (A). Exanthema on day 12 (B). Chest X-ray on day 6 (C).

**Fig 2**

Leukocyte subpopulations over the course of the disease (A). Complement protein C3 and C4 levels over the course of the disease (B). Neutrophil phenotype on day 8 (fulminant disease), 12 and 19 (recovery) in comparison to a healthy control (C).