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Paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS): clinical and immunological characteristics of the Berlin cohort

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Introduction

The paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) was first described in April 2020 following the first wave of the COVID-19 pandemic as a hyperinflammatory clinical syndrome in children previously infected with SARS-CoV-2. Although the clinical phenotype resembles that of Kawasaki disease, the two syndromes have been shown to be immunologically distinct and the pathogenesis of PIMS-TS is incompletely understood.

Here, we describe the Berlin cohort and provide evidence of the predominance of SARS-CoV-2-specific IgA in patients with PIMS-TS.

Methods

Patients presenting with PIMS-TS between November 2020 and May 2021 were included in the study. The clinical data were analysed retrospectively in comparison with a cohort of previously healthy children presenting with a CRP >130 mg/L due to different diagnoses. We collected serum samples from patients with PIMS-TS and patients previously infected with SARS-CoV-2 who did not develop PIMS-TS. Levels of IgG, IgM and IgA against SARS-CoV-2 spike protein and nucleocapsid protein were measured by ELISA. Additionally, the patients' sera were tested for reactivity with myocardial tissue by indirect immunofluorescence microscopy detecting human IgG.

Results

We identified 16 confirmed cases of PIMS-TS (6F; 10M) of median age 9.5 years (range: 1-19). The cohort presented with the following symptoms: fever (100%), myocardial involvement (100%), rash (76%), conjunctivitis (71%), abdominal pain (59%), mucositis (53%), diarrhoea (47%), cervical lymphadenopathy (41%), and arterial hypotension (35%). Laboratory findings included markedly elevated inflammatory and endothelial parameters as well as an increase in cardiac and liver markers. One patient showed mildly elevated monocytic CD169 expression. All patients were treated with intravenous immunoglobulins and acetylsalicylic acid ± glucocorticoids. One patient was refractory to this regimen and subsequently improved with IL-1 blockade. Another patient with a similar clinical phenotype was SARS-CoV-2-seronegative.

Simultaneously, we identified 41 children who were hospitalised with a CRP >130 mg/L over the same time period. In comparison with this cohort, patients with PIMS-TS showed higher levels of factor VIII (p=0.03), NT-pro BNP (p=0.08) and gamma-GT (p=0.005).

After a median follow-up of 47 days (range: 26-98), many patients showed persistently elevated levels of factor VIII several weeks after resolution of clinical symptoms and normalisation of inflammatory markers.

ELISA analyses revealed significantly elevated levels of SARS-CoV-2-specific IgA in the blood of patients with PIMS-TS in comparison with the SARS-CoV-2 seropositive control group. The serum of one patient showed mild reactivity to myocardial tissue.

Conclusion

In summary, we provide evidence of an immune response to SARS-CoV-2 characterised by elevated IgA levels as well as persistent endothelial activation in patients with PIMS-TS.