CASE REPORT

SARS-CoV-2 infection in a child with primary immunodeficiency: a case report

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Abstract

Most cases of coronavirus-19 (COVID-19) disease in pediatrics have been described as mild or asymptomatic when compared to adult’s patients. However, in the last few months, the number of reports about children who developed more severe conditions, with dysfunction of multiple systems and high inflammatory tests has grown, currently called multisystem inflammatory syndrome in children (MIS-C). We describe the case of an infant who had a history of primary immunodeficiency, who developed a severe form of SARS-CoV-2 infection, associated with multiple organ dysfunction and increased inflammatory tests. Despite the clinical presentation compatible with MIS-C, his previous disease may have contributed to its unfavorable outcome. As it is a newly documented condition in the literature, the reports of the experienced cases of SARS-CoV-2 are imperative to better understand its evolution and improve its clinical management.

Keywords: Pediatric, Coronavirus Infections, Inflammation, Immunodeficiency Syndromes, Agamaglobulinemia, Intensive Care Units.
INTRODUCTION

In December 2019, China witnessed the outbreak of a new Coronavirus, currently called SARS-CoV-2, which soon spread around the world causing a major pandemic. In general, the pediatric population has been shown to be more resistant to the severe evolution of COVID-19 than adults. However, there are increasing reports of an exacerbated inflammatory response, with multiple organ and system failure, currently described as Multisystemic Inflammatory Syndrome in Children (MIS-C). When it comes to immunosuppressed patients, the evolution of the disease and the immunological mechanisms associated with the worst outcome are even more controversial, both in children and adults.

We describe a case of a 10-month-old infant who had a primary immunodeficiency (hypogammaglobulinemia) and developed a severe form of the disease, with multiple organ dysfunction and high inflammatory tests, compatible with MIS-C.

CASE REPORT

A brown boy, 10 months old, who had a morbid history of primary immunodeficiency (hypogammaglobulinemia) and cholestatic liver disease, was routinely followed up in a specialized pediatric immunology service, with monthly gamma globulin replacement.

He was admitted to the emergency department complaining of lack of appetite, irritability and increased abdominal volume for about a week and fever for one day. He had no respiratory symptoms. Laboratory tests showed no changes: blood count, coagulation, renal function or electrolytes. Only direct hyperbilirubinemia and liver enzymes slightly increased by the underlying disease. Based on the hypothesis of cholangitis, empirical antibiotic therapy with ampicillin and cefotaxime was started.

On the second day of admission, he started a severe respiratory condition (dyspnea and bronchospasm) and was referred to the Pediatric Intensive Care Unit. In the context of a COVID-19 pandemic, RT-PCR was collected from the oropharynx for SARS-CoV-2, which was positive. On the third day of hospitalization, still with fever and progressive dyspnea, he presented a generalized tonic-clonic seizure, followed by a lower level of consciousness, and then we chose orotracheal intubation.

In the following days, due to hypoxemia refractory to conventional mechanical ventilation, it was coupled with high-frequency oscillatory ventilation (VAFO), which temporarily guaranteed better pulmonary gas exchange. In addition to respiratory and neurological dysfunction, he also presented renal dysfunction (refractory hypervolemia and the need for continuous hemodiafiltration), hematological dysfunction (leukopenia, thrombocytopenia and hypocoagulability) and cardiovascular dysfunction (hypotension and shock). Not all of these outcomes were related to an evident infectious worsening, since the serial cultures of blood, urine, ascitic fluid and secretions were negative for relevant pathogenic microorganisms.

His laboratory tests yielded high inflammatory results: CRP 70mg/L (<5), ESR 140mm/h (<10), Ferritin 1301ng/mL (<100), D-dimer 3221ng/mL (<500), DHL 1069U/L (120-300), in addition to severe lymphocytopenia (158 cells/mm³) and hypoalbuminemia (2.7g/dL). The patient even received a dose of intravenous immunoglobulin (500mg/kg), but not because of Kawasaki syndrome (he did not show clinical signs or typical echocardiographic changes), but because he was already using monthly replacement.

On the 14th day of hospitalization, the patient developed subcutaneous emphysema, pneumomediastinum and hypertensive pneumothorax secondary to barotrauma due to mechanical ventilation (Fig 1), and was promptly drained. Despite adequate hemodynamic and volume optimization, he died on the 15th day.

DISCUSSION

According to the recent definitions of the United States Centers for Disease Control (CDC) and the World Health Organization, the reported patient had diagnostic criteria for MIS-C. In addition to prolonged fever and a critical condition with dysfunction of several systems, he had high inflammatory tests (CRP, ESR, D-dimer, DHL, Ferritin), lymphocytopenia and hypoalbuminemia. The CRP value was probably not so increased due to liver disease. Fibrinogen was low, probably

Figura 1. Simple chest X-Ray. There are large subcutaneous emphysematous areas, mild pneumomediastinum and small pneumothorax on the left.
due to coagulopathy. It was not possible to evaluate IL-6 and procalcitonin values.

This hyperinflammatory state associated with COVID-19, also called cytokine storm, has been broadly discussed recently\(^6\), although it is commonly described in a later stage of the disease, even when RT-PCR is already negative, unlike what happened with the patient in question. In addition, he did not show signs and symptoms of Kawasaki Syndrome, as described in other series of pediatric cases (without skin rash, bilateral non-purulent conjunctivitis, mucocutaneous inflammation, coronary dilation)\(^7\)\(^8\). Therefore, another factor may also have contributed to the clinical worsening of the case described.

Although still unclear, the clinical evolution of COVID-19 depends primarily on the interaction of the virus with its host, which can produce effective mechanisms for viral bleaching, as well as induce a harmful hyperinflammatory response to the host. Cells infected by the virus activate innate immunity, mainly by macrophages, which recruit cytotoxic neutrophils and T lymphocytes\(^9\). In the next phase, humoral adaptive immunity has a fundamental action to fight the virus, activating specific B-lymphocytes that produce immunoglobulins\(^10\).

The patient’s low levels of immunoglobulins may have contributed to his unfavorable outcome, although this association is still unclear in the literature. A recent meta-analysis shows a tendency for worse outcomes in immunocompromised patients, but without statistical difference\(^4\).

Viral tropism for cells of the nervous system has been reported in some studies, but the majority based on the physiological basis of SARS-CoV and MERS-CoV. The neurological manifestations of COVID-19 reach 36.4%, but the presence of seizures is rare (0.5%)\(^11\). This patient, with no neurological history, presented a seizure at the beginning of hospitalization, but his diagnostic clarification was not possible due to his clinical instability, which limited the performance of tests such as cerebrospinal fluid or cranial tomography.

**CONCLUSION**

This is a new disease, and there are still many questions about the immunological mechanisms that cause different clinical manifestations of COVID-19, especially in pediatric patients. Although there are already many reports in the literature on the Multisystemic Inflammatory Syndrome in Children (MIS-C), its pathophysiological mechanisms are still poorly understood. When it comes to immunosuppressed children, these mechanisms are even more difficult to elucidate.

It is possible that primary immunodeficiency causes more severe conditions of the disease, both by direct action of the virus and by an inadequate inflammatory response. This patient had a deficiency in the production of immunoglobulins, but he also developed hyperinflammation typical of MIS-C.

New studies are important to elucidate such question, mainly to guide pediatricians and intensivists in the diagnosis and proper handling of these patients.

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