

## LETTER TO THE EDITOR

# SARS-CoV-2 infection in a neutropenic pediatric patient with leukemia: Addressing the need for universal guidelines for treatment of SARS-CoV-2-positive, immunocompromised patients

To the Editor:

Available literature on the clinical characteristics and natural history of pediatric patients infected with SARS-CoV-2 is limited, and very little has been established regarding guidelines for the treatment of immunocompromised pediatric patients. Our experience caring for a patient with acute lymphoblastic lymphoma infected with SARS-CoV-2 highlights the need for management guidelines in pediatric oncology patients.

The patient is a 6-year-old female with B-lymphoblastic lymphoma in the maintenance phase of treatment, who was admitted to the hospital with fever and neutropenia per hospital standard of care. Her history was significant for symptomatic family household members who had tested positive for SARS-CoV-2. The patient had a history of 1 day of cough, but was asymptomatic on admission, remained afebrile throughout her hospitalization, and denied symptoms of cough, shortness of breath, fatigue, abdominal pain, or diarrhea.

Testing was positive for SARS-CoV-2 by nasopharyngeal (NP) polymerase chain reaction (PCR). Infectious disease specialists were consulted and recommended a baseline chest X-ray (CXR) and monitoring of inflammatory markers. D-dimer, lactate dehydrogenase, and interleukin-6 were not elevated, and trended down during admission. Her ferritin was slightly elevated at 1098 ng/mL, and down-trended to 983 ng/mL on repeat testing. Her CXR was normal, and as her clinical status remained stable, imaging was not repeated prior to discharge. Her oral chemotherapy was held while neutropenic as per Children's Oncology Group AALL1131 protocol guidelines and while actively infected with the virus. The patient was discharged home after 10 days of hospitalization. She had repeat SARS-CoV-2 PCR testing of NP swab 3 weeks after her diagnosis and it was negative. Serum SARS-CoV-2 IgG testing at 6 weeks after diagnosis was positive; demonstrating that she mounted an antibody response while immunocompromised.

This case report provides an example of an immunocompromised pediatric patient who had a favorable course and outcome after infection with SARS-CoV-2. She was treated with supportive care only, and did not receive any experimental antiviral therapies or intravenous immunoglobulin. In the pediatric population overall, rate of hospitalization is lower (5.7% compared to 20% in adults), and most recover within 1-2 weeks of symptom onset.<sup>1,2</sup> It is still unclear why younger people are not as severely affected by the virus, but theories

attributing differences in immune system function prompt additional questions regarding oncology patients.<sup>3</sup> The literature available is limited, but our patient followed a similarly mild course to five case reports from a childhood cancer center in Lombardy, Italy.<sup>4</sup> We do not yet have specific guidelines for admission or discharge criteria in the United States for pediatric oncology patients who contract the virus. Our infectious diseases team recommended baseline CXR as well as trending certain inflammatory markers based on findings in the adult literature.<sup>5</sup> Other possible guidelines suggested in the World Journal of Pediatrics recommend the following criteria be met prior to discharge: afebrile for 3 days, absence of respiratory distress, and two negative SARS-CoV-2 tests.

Although a small number of case reports have demonstrated mild clinical courses for pediatric oncology patients, there is evidence that an immunocompromised state is associated with higher rates of lower respiratory tract disease.<sup>6</sup> Until we have gathered more robust data on the clinical course of immunocompromised patients, it remains prudent to observe these patients conservatively.

Current recommendations for pediatric oncology patients are being published by various specific oncology organizations.<sup>4,7,8</sup> A general theme is to reduce intense chemotherapy and prolong intervals between cycles in patients with stable disease. For asymptomatic oncology patients, particularly sarcoma patients, surgery should not be delayed despite the aerosolizing procedures required for operative management. In immunocompromised patients who are found positive for SARS-CoV-2, the French Sarcoma Group recommends delaying treatment for at least 15 days after symptom onset.<sup>8</sup>

While caring for this patient, we identified multiple areas where unified guidelines would be beneficial.

1. Admission criteria, lab monitoring and imaging recommended, treatment options/protocols, and discharge criteria.
2. Follow-up testing/monitoring in immunocompromised patients.
3. Guidelines for adjustments in chemotherapy, radiation, and surgical interventions for pediatric oncology patients.
4. Which patients may benefit from various experimental therapies.<sup>9</sup>

We have a need as providers to further investigate how immunocompromised children are responding differently to the virus, and patient families need clear recommendations. For example, additional

precautions these families should take as the country begins reopening, information on how clinical course may differ in immunocompromised children, and how treatment protocols may be adjusted during this pandemic. There has been some epidemiologic investigation into the perceived risk and anxiety regarding the pandemic in pediatric oncology patients. In a survey of young cancer patients in Milan, a large proportion of them felt "personally at risk of severe complications." SIOP, St Jude, the American Society of Hematology, and others are developing a new platform for sharing resources and experiences in the evolving time of this global pandemic.<sup>2,10</sup> It will be important to continue sharing case information and conducting additional research in the coming years.

#### ACKNOWLEDGMENTS

Consent was provided by the patient and her family to publish information regarding her medical condition and treatment.

#### CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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