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LETTER TO THE EDITOR

Benign course of SARS-CoV-2 infection in a series of pediatric oncology patients

To the Editor:

Limited studies have shown that patients with cancer infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have more severe disease than the general population, with higher rates of serious illness and death in this population[1-3] and other immunocompromised populations.[4,5] Children are susceptible to SARS-CoV-2 infection, but clinical severity of the infection is significantly less than in adults.[6,7] However, there is a paucity of data describing SARS-CoV-2 infection in pediatric patients with cancer. Here we report our experience with six pediatric oncology patients at our institution who tested positive for SARS-CoV-2 infection.

Patients were tested for SARS-CoV-2 infection either for clinical suspicion of infection or as part of a hospital surveillance program testing all admitted patients and patients undergoing procedures. Nasopharyngeal swab samples were analyzed in a CLIA-certified laboratory using an FDA emergency authorization use (EUA) PCR assay (Abbott Realtime SARS-CoV-2, m2000 instrument). Amplification cycle threshold (Ct) values were recorded from the assay results, with lower values indicating higher amounts of viral nucleic acid.

Table 1 summarizes patient characteristics, SARS-CoV-2 testing results, and clinical courses of the six pediatric oncology patients identified with SARS-CoV-2 infection at our institution. All of these patients had relatively mild SARS-CoV-2-related symptoms. None were hospitalized specifically due to SARS-CoV-2-related symptoms, and none required any respiratory support at diagnosis. Further details on the clinical courses of two high-risk leukemia patients are summarized below.

Patient 1 is a 5-year-old male 5 months post-allogeneic stem cell transplant for high-risk acute myeloid leukemia on maintenance midostaurin. His posttransplant course was complicated by graft-versus-host disease, sinusoidal obstructive syndrome, and idiopathic pneumonia syndrome. He presented to a routine clinic visit with cough. A respiratory viral panel and SARS-CoV-2 testing were both negative. The next day, he had a fever and required aggressive fluid resuscitation after becoming hypotensive with antibiotic administration, and subsequently developed respiratory distress necessitating high-flow nasal cannula oxygen. Repeat SARS-CoV-2 testing the next day was again negative, and blood cultures grew both *Acinetobacter junii* and *Pseudomonas aeruginosa*. He clinically improved over the next few days and was off supplemental oxygen within 4 days without any further respiratory symptoms. SARS-CoV-2 testing was repeated in advance of a scheduled procedure and was positive. He continued to do well and was discharged 3 days later after completing antibiotics. Repeat testing 2 weeks later was negative.

Patient 2 is a 6-year-old male with recently relapsed T-cell acute lymphoblastic leukemia undergoing reinduction chemotherapy. He presented to the oncology clinic for chemotherapy with cough and rhinorrhea, but was afebrile and otherwise well. Over the next 2 weeks, he had gradual improvement in his respiratory symptoms. It was then discovered that he had been exposed to SARS-CoV-2, 5 days prior to symptom onset. He presented 2 weeks later for another cycle of chemotherapy, at which time he tested positive. He tested positive again on day 8, and then 2 days later was admitted with fever and neutropenia without worsening cough or rhinorrhea. He had an uncomplicated hospital course, but still tested positive for SARS-CoV-2 on the day of discharge and again 5 days later. Repeat testing after another 10 days, 6 weeks after symptom onset, was negative.

Although children have milder SARS-CoV-2 infections, there is a natural concern that children with cancer are at higher risk of severe illness from SARS-CoV-2 infection and that further immunosuppressive cancer-related treatment may increase this risk, as has been reported in adults with cancer.[1-3] We found that our cancer patients with SARS-CoV-2 infections had generally mild, self-limited courses without need for any respiratory support, similar to the presentation of SARS-CoV-2 infection in the general pediatric population.[6,7] Two of the three patients requiring hospital admission were for reasons unrelated to SARS-CoV-2 infection and the respiratory symptoms of the third patient that required ICU-level care was in the setting of preexisting lung pathology from posttransplant complications, and seemed to be related to polymicrobial sepsis, given his rapid improvement with antibiotics and diuresis. Additionally, two of our patients (numbers 2 and 4 in Table 1) received further chemotherapy without clearance of SARS-CoV-2 infection. Although both experienced an increase in the level of SARS-CoV-2 RNA detected (based on decreasing Ct value), this was likely related to chemotherapy-induced lymphopenia and did not correlate with any worsening of symptoms.

Our series of pediatric oncology patients with relatively benign courses of SARS-CoV-2 infection is consistent with reports from both Italy and New York city, where five and 20 pediatric cancer patients, respectively, were identified as having mild or asymptomatic SARS-CoV-2 infection,[8,9] and mirror the experience in some patients on biologics for immune-mediated inflammatory disease.[10] Given the inherently aggressive nature of many childhood cancers, significant treatment delays can increase the risk of disease progression. While

TABLE 1 Baseline patient characteristics, SARS-CoV-2 testing results, and clinical course

Patient #	Age, years	Oncology diagnosis	Confirmed SARS-CoV-2 contact	SARS-CoV-2-related symptoms	Rationale for testing	Testing location	Current treatment regimen	SARS-CoV-2 testing history	ALC, #/μL	Patient course
1	5	AML post-HSCT	No	None	Surveillance	Oncology floor	Post-HSCT midostaurin	Initial: neg	900	Discharged after completing antibiotics
								2 days: neg	760	No further symptoms
								10 days: Ct 22.5	1650	
								23 and 26 days: neg	1750	
2	6	Relapsed T ALL	Yes	Cough rhinorrhea	Surveillance	Oncology floor	ALLR3 induction followed by NECTAR	Initial: Ct 15.9	110	Discharged after planned chemotherapy
								4 days: Ct 26.2	30	No further symptoms
								11 days: Ct 24.1	77	
								16 days: Ct 14.3	1726	
								26 days: neg	1960	
3	8	Standard risk B ALL	No	Fever Sore throat Cough	Clinical symptoms	ER	Maintenance chemotherapy per AALL0932	Initial: positive[a] 8 days: neg	230490	Discharged Asymptomatic 8 days later
4	9	Osteosarcoma	No	None	Surveillance	Oncology floor	High-dose methotrexate	Initial[b]: Ct 6.5 11 days later: Ct 19.2 20 days later: Ct 24.3	1250 N/A N/A	Discharged after planned chemotherapy Remained asymptomatic
5	16	Mixed germ cell tumor	No	Fever Sore throat Cough congestion	Clinical symptoms	ER	Cisplatin and etoposide	Initial: Ct 36 6 days: Ct 20.5 13 days: Ct 27.7 23 and 25 days: neg	750 1600 N/A 2150	Admitted to the oncology floor for F/N management Chemotherapy given after 1st neg
6	18	Hodgkin lymphoma	Yes	Fever Cough Myalgias	Clinical symptoms	ER	Mantle radiation per AHOD1331	Initial: positive[a]	917	Discharged Asymptomatic 4 days later

Abbreviations: ALC, absolute lymphocyte count; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; Ct, cycle threshold; ER, emergency room; F/N, fever and neutropenia; HSCT, hematopoietic stem cell transplant; N/A, test not performed; NECTAR, nelarabine/etoposide/cyclophosphamide; neg, negative.

[a]SARS-CoV-2 testing not performed in house; Ct not available.

[b]This patient had a prior negative test 20 days earlier after presenting with headache, cough, and fever 10 days after doxorubicin and cisplatin.

limited by small patient numbers, our experience suggests that pediatric cancer patients are not necessarily at significantly higher risk of severe disease from SARS-CoV-2 infection, and cancer therapy can be safely administered in some patients even if they continue to have detectable RNA. Any risk-benefit consideration in these patients should take into account ours and others' observations that immunosuppressed children with CoV-2 infection do not always have worse disease than their immunocompetent peers.

CONFLICT OF INTEREST

Jenna Rossoff, Ami B. Patel, and Emily Muscat declare that there is no conflict of interest or competing financial interest. Larry K. Kociolek received grant funding from Merck. William J. Muller is consulting for Seqirus, Inc. and received research funding for clinical trials from Abbott Laboratories, Ansun BioPharma, Astellas Pharma, AstraZeneca, Janssen Pharmaceutica, Karius, Melinta, Merck, Roche, and Tetraphase.

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Writing of initial manuscript, manuscript revision, and data acquisition: Jenna Rossoff, Larry K. Kociolek, and William J. Muller. Manuscript revision and data acquisition: Ami B. Patel and Emily Muscat.

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