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Could the COVID-19 infection have a better prognosis than expected in pediatric hematology oncology and bone marrow transplant patients?

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Coronavirus disease 2019 (COVID-19) is a pandemic that spread rapidly worldwide (1). So far, very few reports concerning the impact of COVID-19 among patients with pediatric hematologic-oncologic diseases are available (2). We aimed to describe the clinical features, prevalence, treatments, and outcomes in the COVID-19 patient population.

A total of 219 patients were admitted for treatment of hematology-oncology disease between March 1, 2020 and May 31, 2020. Five patients were treated for COVID-19, and the mean age was 12.6 years (Table 1). Three out of these five patients had a confirmed diagnosis, and the other two were treated as suspected cases. The prevalence of COVID-19 in our clinic was 2.3% for the specified date range. COVID-19 cases are identified according to national clinical guidelines (3).

Patient A received chemotherapy with the diagnosis of pediatric resistant blastic plasmacytoid dendritic cell neoplasm. The patient was admitted to the intensive care unit with fever, cough, dyspnea, and hypotension. He received treatment for COVID-19 and pseudomonas aeruginosa sepsis and improved after a couple of days with treatment.

Patient B's diagnosis was Burkitt lymphoma. He was admitted to hospital with fever, myalgia, and fatigue 10 days after receiving chemotherapy treatment.

Patient C was a patient with hematopoietic stem cell transplant (HSCT) for thalassemia major. Four days after transplantation, Escherichia coli sepsis was diagnosed. A swab test for COVİD-19 was taken for recurring fever despite the proper treatment and revealed a positive diagnosis.

Patient D had previously undergone HSCT for acute myeloblastic leukemia and had been hospitalized for gastrointestinal

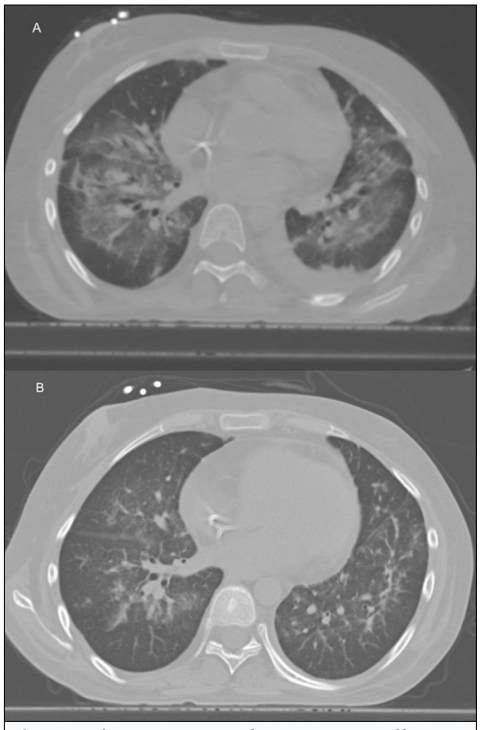

Figure 1. Chest CT images of patient D. (a) Diffuse bilateral ground-glass opacity and unilateral pleural effusion (b) lesions regressed significantly; pleural effusion absorbed.

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Table 1. Clinical characteristics, laboratory results, and treatments of five pediatric hematology-oncology patients treated for COVID-19

Characteristics	Patient A	Patient B	Patient C	Patient D	Patient E
Age	17 y	16 y	4 y	18 y	8 y
Gender	Male	Male	Female	Female	Male
Hematologic-oncologic disease	Resistant blastic plasmacytoid dendritic cell neoplasm	Chemotherapy-resistant Burkitt lymphoma	Thalassemia major	AML	High-risk neuroblastoma
HSCT history (days after TX)	-	-	20	120	30
Last chemotherapy ending time	2 days (Hyper-CVAD)	7 days (Hyper-CVAD)	21 days after TX	4 months after TX	1 month after TX
Immunosuppressive therapy at the time of diagnosis	-	-	CSA	CSA - MP	-
Signs and symptoms					
Fever	+	+	+	+	+
Cough	+	-	+	+	+
Fatigue/myalgia	+	+	+	+	-
Nausea/vomiting	+	+	-	-	-
Dyspnea	+	-	-	+	-
Diarrhea	-	-	+	-	-
Thorax CT changes	Lobar pneumonia, bilateral GGO	Patch-like shadow, unilateral GGO	Multiple patch-like shadows, GGO	Multiple patch-like shadows, GGO, pleural effusion	GGO
Laboratory result					
WBC (×109 cells/L) normal range = 3.98-10.2	0.02	3.14	1.24	2.39	3.93
Neutrophil count (×109 cells/L) normal range = 1.78-5.38	0	1.20	0.82	1.61	2.31
Lymphocyte count (×109 cells/L) normal range = 1.32-3.57	0	0.52	0.19	0.55	0.81
C-reactive protein (mg/dL) normal range = 0-5	69	169	17.9	117	54
Ferritin (ng/dL) normal range = 22-274	5.750	20.086	37.951	2.000	1.022
Prothrombin time (s) normal range = 12-16.5	17.6	14.4	12.8	12.9	16.1
Activated partial thromboplastin time (s) normal range = 25-40	28.6	36	36.8	41.5	55
RT-PCR on symptom onset	-		+		
RT-PCR control 1	+	+	+	-	
RT-PCR control 2	-	-	+	-	-
RT-PCR control 3	-	-	+	-	-
Rapid antibody test	IgM - IgG -	IgM + IgG -	IgM - IgG -	IgM - IgG -	IgM + IgG -
Clinical treatment					
Nasal oxygen	+	+	+	+	
NIMV	+	-	-	+	-
İnotropic therapy	NRA, MI	-	-	-	-
Oseltamivir	+	+	+	+	+
Hydroxychloroquine	+	+	-	+	+
Azithromycin	-	+	+	-	+

CSA: cyclosporine; CT: computed tomography; CVAD: cyclophosphamide, vincristine, doxorubicin, dexamethasone; GGO: ground-glass opacity; HSCT: hematopoietic stem cell transplant; IgM: immunoglobulin M; IgG: immunoglobulin G; MP: metilprednisolone; MI: milrinone; NIMV: non-invasive mechanical ventilation; NRA: noradrenaline; RT-PCR: reverse transcriptase–polymerase chain reaction; TX: transplantation; WBC: white blood cell; y: year.

graft-versus-host disease. The patient presented with a sudden onset of fever, cough, and dyspnea. The patient's accompanying mother tested positive for COVID-19 immunoglobulin M (IgM). The patient's swab test was negative; however, computerized chest tomography (CT) changes were consistent with a COVID-19 diagnosis (Figure 1). After 4 weeks of treatment, lesions clearly improved and pleural effusion was absorbed.

Patient E had an autologous HSCT for neuroblastoma and presented with a sudden onset of fever and cough. The patient's COVID-19 IgM was positive.

All patients were neutropenic and lymphopenic during hospitalization.

None of the patients needed invasive mechanical ventilation. Two patients received non-invasive mechanical ventila-

tion. Four patients are now in a stable condition; one patient died because of complications of his primary malignancy 40 days after his COVID-19 polymerase chain reaction (PCR) test showed negative results.

All patients were screened for other respiratory pathogens using multiplex reverse transcriptase-PCR (RT-PCR). Swabs and rapid antibody tests were performed for medical staff and accompanying parents. Results revealed an asymptomatic RT-PCR–positive nurse, who was then isolated. Since isolating the asymptomatic nurse, no new COVID-19 cases have been detected.

COVID-19 is already mostly asymptomatic in children (4,5). Pediatric hematologic-oncologic disease–induced immunosuppression and malnutrition are potential comorbidities that might be associated with a worsened prognosis. Fortunately, the course of COVID-19 is mild in this patient population (6,7). Possible explanations for relatively favorable outcomes in our patient population could be as follows: (i) Severe acute respiratory syndrome coronavirus 2 infection increases proinflammatory cytokines and causes a cytokine storm (1). Immunosuppression may limit pulmonary inflammation and extensive lung damage; (ii) A higher virus load is associated with a severe disease (8). Social isolation and usage of personal protective equipment is already in use for these patients and a continuous exposure to the virus is less likely; (iii) Because these patients are already under close monitoring, disease symptoms can be noticed earlier and treatment can start in the early phases.

We predict that pediatric hematology-oncology patients have relatively favorable outcomes for COVID-19. Because of a high rate of asymptomatic COVID-19, screening medical staff and accompanying parents only in terms of symptoms and exposure may not be sufficient. It may be appropriate to periodically screen medical staff with swab tests for COVID-19.

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