



SARS-CoV-2 infection in children with febrile neutropenia

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Dear Editor,

Acute lymphoblastic leukemia (ALL) is the most common type of cancer in children, representing approximately one-third of pediatric cancers. Febrile neutropenia (FN) is the most common and potentially lethal complication in patients undergoing chemotherapy [1]. About half of the children treated with chemotherapy for cancer develop at least one FN episode [2]. The world is currently facing a pandemic caused by a new coronavirus [3] and although SARS-CoV-2 infection appears to be less aggressive in children [4], however, the evolution of COVID-19 in children with cancer is still uncertain. Here, we describe three cases of patients with ALL who presented with FN and COVID-19.

Two patients admitted to the emergency department with a history of ALL and fever (Table 1), the initial complete blood count showed neutropenia (< 500 neutrophils per mm^3). Another hospitalized patient presented fever without initial neutropenia (patient 2), however, he developed neutropenia in subsequent days. Patients 1 and 2 were on consolidation therapy for ALL, and they had received chemotherapy drugs in the last 14 days. Patient 3 received daily immunosuppression due to hematopoietic stem cell transplantation.

Patients developed respiratory symptoms after the initial fever, one progressing to respiratory distress (patient 3), admitted to the intensive care unit. None of the patients presented gastrointestinal symptoms. The patients had a positive PCR test for SARS-CoV-2. In addition, a simple chest computed tomography was performed, with typical COVID-19 appearance in patients 1 and 3.

No other site of infection was found in our patients, the procalcitonin value did not suggest bacterial infection, and no microorganism was identified on blood cultures. Patients 1 and 2 had a hospital stay of 2 weeks; they remained hospitalized because of the uncertainty regarding their clinical evolution due to the lack of medical reports of COVID-19 in patients with ALL and FN. Patient 3 required invasive mechanical ventilation, furthermore, she deteriorated hemodynamically and presented cardiac arrest that did not respond to cardiopulmonary resuscitation.

Patients 1 and 2 were treated with enoxaparin, even though they did not meet criteria for disseminated intravascular coagulation. This treatment was given due to the multiple alterations in coagulation associated with worse prognosis that have been described in patients with COVID-19 [5, 6]. Our patients presented elevation of D-dimer, which is suggestive of thrombotic activity and severe inflammatory process. Patient 3 did not receive thromboprophylaxis due to severe thrombocytopenia.

We present this first experience in Mexican children with FN and ALL. COVID-19 should be suspected in children with FN even in the absence of other symptoms. The prognosis of these patients remains uncertain and larger series reporting the course of SARS-CoV-2 infection in children with hematological diseases are needed to develop specific clinical guidelines.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional committee and with the Helsinki declaration.

Informed consent Informed consent was obtained from all individual participants included in the study.

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Table 1 Characteristics of children with febrile neutropenia and acute lymphoblastic leukemia infected with SARS-CoV-2

	Reference range	Patient 1	Patient 2	Patient 3
Age (years)		9	4	8
Sex		Fem	Fem	Fem
Medical history				
Conditions		ALL in consolidation therapy	ALL in consolidation therapy	ALL post-hematopoietic stem cells transplantation
Medicaments		Cytarabine and cyclophosphamide	Methotrexate and mercaptopurine	Mycophenolate, prednisone
Values on admission				
White cell count (per mm ³)		1000	920	1300
Neutrophils (per mm ³)		150	350	475
Lymphocytes (per mm ³)		510	370	110
Platelets (per mm ³)		295,000	353,000	5000
Hemoglobin (gr/dL)		8.7	11.7	8.4
Prothrombin time (second)		17	11.4	11.2
Activated thromboplastin time (second)		26	26.8	27.2
Fibrinogen (mg/dL)	199–400	332	473	406
D-dimer -ng/ml	100–560	800	1700	1200
Antithrombin III (U/mL)	0.90–1.30	0.98	1.25	0.99
Lactic dehydrogenase	110–295	717	482	301
Interleukin (6 pg/mL)	0–5.9	41	-	-
Ferritin (ng/mL)	7–140	2092	2366	2190
Procalcitonin (ng/mL)	< 0.5	0.27	0.05	0.17
C-reactive protein (mg/L)		1.3	500.4	110
Antibiotics		Clarithromycin	Clarithromycin	Clarithromycin
Thromboprophylaxis		Enoxaparin	Enoxaparin	No
Survived		Yes	Yes	No
Days of hospital stay		14	13	1

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