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LETTER TO THE EDITOR

COVID-19 infection in children and adolescents with cancer in Madrid

To the Editor:

The incidence of COVID-19 is remarkably less in the pediatric population than in the adult population, with children accounting for 1-5% of diagnosed cases,[1-3] 0.8% in Madrid.[4] Although children with cancer are considered a high-risk population, data specifically addressing the pediatric oncology population are still limited.[3,5] We present a case series of all pediatric oncology patients infected with COVID-19 in Madrid to date to provide updated epidemiological data and to describe the most relevant clinical features and outcomes.

All pediatric oncology patients (0-18 years) with proven infection of COVID-19 in Madrid up to April 15, 2020 were identified and included. Approval was obtained by the local Ethics Committee. The total number of current pediatric oncology patients in the Madrid region was estimated through 2015-2019 data from the Madrid Tumor Registry "RTMAD."[6]

The main patient (n = 15) characteristics are shown in Table 1. Median age was 10.6 years (range 0.6-18.6). The cancer types included hematological malignancies (73%, 11) and solid tumors (27%, four). Four patients (27%) had received hematopoietic stem cell transplantation (median interval to COVID-19 infection: 209 days, range 113-749). Most patients (60%, nine) had received chemotherapy in the 15 days prior to the COVID-19 infection. Chemotherapy had to be interrupted or delayed in six (40%).

Seven (47%) patients were hospitalized due to the COVID-19 infection, four (27%) were already hospitalized (nosocomial infection), and four (27%) were managed in the outpatient clinic. The most frequent symptoms were fever (67%, 10) and cough (40%, six). Two patients were asymptomatic.

Chest radiographs were performed in most patients (93%, 14), with pathological findings in 57% (8/14). Noteworthy laboratory findings included median white blood cell count at diagnosis of 3195 (range 90-10 690), median lymphocyte count of 580 (range 0-6310), and median D-dimer 291 ng/mL (range 0.7-2620).

Most patients received hydroxychloroquine (73%, 11), three of them in different combinations (including azithromycin, tocilizumab, lopinavir-ritonavir, corticoids, remdesivir; Table 1). Four (29%) patients did not receive any treatment. No COVID-19 treatment-related severe adverse events were identified. Two patients required oxygen therapy (nasal cannula, <2 LPM), one of them still requiring support. All patients presented favorable clinical outcomes so far, although four of them remained hospitalized. The median hospital stay due to the infection was 8 days (range 3-26).

Given that the estimated total number of pediatric oncology patients in the Madrid region is 1140, we observed a COVID-19 infection rate of 1.3% among this patient population over the first 2 months of the pandemic.

This study is particularly relevant for several reasons. First, it presents all pediatric oncology patients infected with COVID-19 in Madrid, one of the epicenters of the pandemic. Second, it provides an accurate estimation of the real incidence for this patient population, as both the total number of susceptible patients and the total number of infected patients are well known. For the former, the robustness of the local tumor registry (RTMAD) was the key; for the latter, the well-established collaboration network among pediatric oncologists in Madrid enabled the identification of all infected patients. Furthermore, the fact that children with cancer are considered high-risk patients for the COVID-19 infection leads to thorough and repeated testing in this population, even in asymptomatic patients. This is not the case for the general pediatric population, as most healthy children are not being tested for COVID-19 unless they require hospitalization. Hence, we believe the accuracy of the calculated infection prevalence among pediatric oncology patients to be notably reliable, as opposed to estimations in the general pediatric population or in other subpopulations. Additionally, all patients were tested by polymerase chain reaction, which continues to be the gold standard and, in our opinion, should not be substituted by rapid serology-based testing in the pediatric oncology population.[7]

The COVID-19 infection prevalence among adult cancer patients has been reported to be higher than in the general population (1% vs 0.29%).[8] No robust data exist to date regarding the infection prevalence in pediatric cancer patients. In our series, the estimated 1.3% is difficult to compare with the general pediatric population, estimated 0.8% in Madrid,[4] since the latter is likely to be underestimated. In spite of these limitations, the incidence seems higher in children and adolescents with cancer.

A worrisome finding is the high proportion of patients (27%) that presented with nosocomial infection. The infection rates of health care professionals in Spain have been among the highest in the world,[9,10] which may explain the proportion of nosocomial infection.

The clinical, radiological, and laboratory findings are similar to previously published data for the general pediatric population.[1,3] Although there is no solid evidence for the treatment of the COVID-19 infection beyond support therapy in children with cancer, hydroxychloroquine was the most frequently used drug in our series, with a good safety profile. Remarkably, all patients had favorable outcomes so

TABLE 1 Main characteristics of the patients

Age (years)	Gender	Baseline disease	Disease status	CT interruption	COVID-19 symptoms	Chest X-ray	COVID-19 treatment
16.5	M	NHL	Active	No	Fever hypoxemia	Pneumonia	HCQ, Tocilizumab, Lopinavir, Ritonavir, Azithromycin, Oxygen support
8	M	B-ALL	CR	No	Fever coughing	Pneumonia	HCQ
10.6	M	B-ALL	CR	No	Fever	Normal	HCQ
0.6	M	HR-NBL	R/R	Yes	Asymptomatic	–	–
12.9	M	Myelo-dysplastic syndrome	CR	Yes	Throat pain	Peribronchial cuffing	–
12.7	M	B-ALL	CR	No	Fever	Peribronchial cuffing	HCQ
9	M	T-ALL	CR	Yes	Fever	Peribronchial cuffing	HCQ, remdesivir
6.8	M	Melanoma	R/R	Yes	Coughing	Peribronchial cuffing	–
11.2	M	AML	CR	No	Fever	Normal	HCQ
6.8	F	B-ALL	CR	No	Coughing, chest pain	Pneumonia	HCQ
5.2	M	B-ALL	CR	No	Fever	Normal	HCQ
14.6	M	T-ALL	Active	No	Asymptomatic	Normal	HCQ
18.6	M	Ewing sarcoma	R/R	Yes	Fever, cough, hypoxemia	Pneumonia	HCQ, azithromycin, corticoids, oxygen support
11	M	Wilms tumor	R/R	No	Fever, cough	Normal	HCQ
3	M	B-ALL	CR	Yes	Fever, cough	Normal	–

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloblastic leukemia; CR, complete remission; CT, chemotherapy; HCQ, hydroxychloroquine; HR-NBL, high-risk neuroblastoma; NHL, non-Hodgkin lymphoma; R/R, refractory/relapse.

far, with mild-moderate disease, and only two of them required oxygen therapy, in line with general pediatric population data.[3]

In conclusion, the prevalence of COVID-19 infection among children with cancer in Madrid is 1.3%. Although this patient population is managed as high risk, the clinical features are milder and the prognosis better than in the adult population.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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ETHICAL STATEMENT

Approval for this study was obtained by the local Ethics Committee (at Children's University Hospital Niño Jesús, Madrid, Spain).

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