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Treatment and outcomes of pediatric patients with cancer and COVID-19 at MAHAK pediatric cancer treatment and research center, Tehran, Iran

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ABSTRACT

The COVID-19 pandemic has been particularly devastating for Iran. Children with cancer are generally immunosuppressed and especially vulnerable to SARS-CoV-2 infections. We report the treatment and outcomes of pediatric oncology patients with COVID-19 at the MAHAK Pediatric Cancer Treatment and Research Center (MPCTRC) in Tehran. We enrolled pediatric oncology patients who experienced SARS-CoV-2 infections from March 18, 2020, to January 28, 2021. The COVID-19 diagnostic criteria at MPCTRC were based on imaging and clinical presentation because of specific challenges diagnosing SARS-CoV-2 infections with molecular testing, which was locally developed and conducted at centers other than MPCTRC. We enrolled nine outpatients and eight inpatients (mean age = 9 years), seven of whom had a diagnosis of leukemias, and five who had brain tumors. COVID-19 symptoms were mild in fourteen patients, and three patients were asymptomatic. Of twelve patients who received molecular testing for SARS-CoV-2 infection, eight were negative and four were positive. Of nine patients tested for IgG and IgM antibodies, one was positive. Three patients died of COVID-19, all of whom were hospitalized. Mild COVID-19 symptoms did not appear to affect the outcomes of the pediatric patients with cancer who received treatment at MPCTRC during the study period.

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Introduction

Sudden acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), introduced an important public health threat in the world beginning in 2019 [1]. Originating from Wuhan, China [2], SARS-CoV-2 can easily transmit from person to person [3]. Initial reports suggested that COVID-19 is uncommon in children [1,4–6]. In April 2020, however, She et al. reported a precipitous increase in the number of children infected with SARS-CoV-2 [7]. The virus primarily targets the respiratory system, which can lead to pneumonia [8]. The clinical features of children with COVID-19 are similar to those of adults but are generally milder [9].

From March 7 to March 30, 2020, SARS-CoV-2 infections were diagnosed in thirty-five children at Tehran University of Medical Sciences. Of these children, 22 were boys, and their median age was 7.5 years (range, 4 months to 15 years old). Of these 35 pediatric COVID-19 cases in Tehran, 29 resulted from family exposure to SARS-CoV-2. Nearly 86% of patients received oseltamivir, and 63% were administered hydroxychloroquine. In addition, many patients received azithromycin, ceftriaxone, and/or ceftiraxone [10].

Patients with cancer have a higher risk of morbidity and mortality than does the rest of the population because of their compromised immune status secondary to cancer or its treatment [11–14]. However, no reports of Iranian pediatric patients with cancer who experienced SARS-CoV-2 infections have been published. Therefore, we evaluated the characteristics and follow-up care of pediatric oncology patients with COVID-19 who received treatment at the MAHAK Pediatric Cancer Treatment and Research Center (MPCTRC). MPCTRC is a non-governmental charity-based organization that provides multidisciplinary care for pediatric patients with cancer. Despite administrative safety and protective controls at the time of the COVID-19 pandemic, some patients receiving care at MPCTRC experienced symptoms that met our diagnostic criteria for COVID-19. We describe the COVID-19 clinical presentation, treatment, and outcomes of these children.
Table 1
Clinical presentation of COVID-19.

| Infection Severity | Carlotti et al. [15]                                                                                   | Dong et al. [16]                                                                                      |
|--------------------|---------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
| Asymptomatic       | Absence of clinical signs and symptoms of the disease and normal chest X-ray scan associated with a positive test for SARS-CoV-2 | Without any clinical symptoms and signs, and the chest imaging results normal, whereas the 2019-nCoV nucleic acid test result is positive |
| Mild               | Upper airway symptoms such as fever, fatigue, myalgia, cough, sore throat, runny nose and sneezing. Pulmonary clinical exam is normal. Some cases may not have fever and others may experience gastrointestinal symptoms such as nausea, vomiting, abdominal pain and diarrhea | Symptoms of acute upper respiratory tract infection, including fever, fatigue, myalgia, cough, sore throat, runny nose, and sneezing. Physical examination shows congestion of the pharynx and no auscultatory abnormalities. Some cases may have no fever or have only digestive symptoms, such as nausea, vomiting, abdominal pain, and diarrhea. With pneumonia, frequent fever, and cough (mostly dry cough, followed by productive cough); some may have wheezing, but no obvious hypoxemia such as shortness of breath, and lungs can hear sputum or dry and/or wet snoring. Some cases may have no clinical signs and symptoms, but chest computed tomography shows lung lesions, which are subclinical. Early respiratory symptoms, such as fever and cough, may be accompanied by gastrointestinal symptoms, such as diarrhea. The disease usually progresses at ~1 week, and dyspnea occurs with central cyanosis. Oxygen saturation is <92% with other hypoxia manifestations. |
| Moderate           | Clinical signs of pneumonia. Persistent fever, initially dry cough, which becomes productive, may have wheezing or crackles on pulmonary auscultation but show no respiratory distress. Some individuals may not have symptoms or clinical signs, but chest scan reveals typical pulmonary lesions | Children can quickly progress to acute respiratory distress syndrome or respiratory failure and may also have shock, encephalopathy, myocardial injury or heart failure, coagulopathy, acute kidney injury, and multiple organ dysfunction. Organ dysfunction can be life-threatening. |
| Severe             | Initial respiratory symptoms may be associated with gastrointestinal symptoms such as diarrhea. The clinical deterioration usually occurs in a week with the development of dyspnea and hypoxemia (blood oxygen saturation [SaO₂] <94%) | Children can quickly progress to acute respiratory distress syndrome or respiratory failure and may also have shock, encephalopathy, myocardial injury or heart failure, coagulopathy, acute kidney injury, and multiple organ dysfunction. Organ dysfunction can be life-threatening. |
| Critical           | Patients can quickly deteriorate to acute respiratory distress syndrome or respiratory failure and may present shock, encephalopathy, myocardial injury or heart failure, coagulopathy, acute kidney injury, and multiple organ dysfunction | Children can quickly progress to acute respiratory distress syndrome or respiratory failure and may also have shock, encephalopathy, myocardial injury or heart failure, coagulopathy, acute kidney injury, and multiple organ dysfunction. Organ dysfunction can be life-threatening. |

Patients and methods

Study design and patients

We performed a cross-sectional, retrospective study of children with cancer who received treatment at MPCTRC from March 18, 2020, to January 28, 2021, and met our diagnostic criteria for SARS-CoV-2 infection. Two children with COVID-19 who were referred to other Iranian centers for treatment were excluded from the study. These two patients had newly diagnosed cancer, and their parents elected for treatment at pediatric cancer units closer to their homes. The data collected included patient sex, age at the time COVID-19 diagnosis, and cancer type. We also evaluated laboratory test findings, imaging studies, types of cancer-directed therapy, and patient status at their last follow-up visits. The study was approved by the MAHAK ethical committee (IR. MAHAK.RESEARCH.1399.230).

Clinical presentations

We used the COVID-19 clinical presentations described by Carlotti et al. and Dong et al.[15,16] to divide the clinical symptoms of our patients into five categories: asymptomatic, mild, moderate, severe, and critical (Table 1). All patients with cough, fever, and/or respiratory symptoms (with or without digestive symptoms) were screened for SARS-CoV-2 infection.

Laboratory tests

At the time of admission, patients had laboratory testing performed for white blood cell count, absolute neutrophil count, absolute lymphocyte count, and C-reactive protein level [17].

Imaging evaluation

Chest computed tomography (CT) scans were performed for all patients with suspected COVID-19 at the time of their first reported symptoms to evaluate the severity of SARS-CoV-2 infections because children with severe infections exhibit bilateral multiple lobar lesions [17].

Detection of SARS-CoV-2 infections

Real-time reverse transcriptase polymerase chain reaction (RT-PCR) can detect the presence of SARS-CoV-2 nucleic acids in infected tissues [18]. Therefore, nasopharynx or nasal swabs were
Fig. 2. Computed tomography images without contrast of lungs from three patients. Panels A and B, from cases 2, and 3, respectively, from the inpatient cohort. Panel C from case 10 of the outpatient cohort.
collected from the patients at the time of reporting their first symptoms. Because of global shortages of RT-PCR test reagents at the beginning of the COVID-19 pandemic, RT-PCR was performed only in patients with severe or critical COVID-19 symptoms [15,19].

**Diagnosis of COVID-19 at MPCTRC**

The COVID-19 diagnostic criteria at MPCTRC were based on clinical symptoms, known exposure to SARS-CoV-2, and CT imaging findings. RT-PCR was not performed for all suspected cases because it was developed locally at other hospitals and its quality assurance could not be confirmed or validated at the time of diagnosis. CT imaging was performed at the time of diagnosis and at 14 days after treatment or supportive care. Fig. 1 depicts a schematic diagram of the diagnostic and treatment workflow for the patients who were referred to MPCTRC during the study period.

**Treatment of COVID-19 at MPCTRC**

Treatment of SARS-CoV-2 infections at MPCTRC was based on CT findings and clinical symptoms rather than nasal swab/RT-PCR results. The inpatient cohort (n = 8, all symptomatic) consisted of patients who were hospitalized and received oseltamivir, an antiviral medication used to treat influenza, and hydroxychloroquine, in consultation with a pediatric infectious diseases specialist [20], in addition to azithromycin [15]. The outpatient cohort (n = 9, three asymptomatic and six symptomatic) consisted of patients who were observed at home and received supportive care (ie, intravenous fluids) with azithromycin (10 mg/kg on the first day, then 5 mg/kg per day for 4 days) [15].

Oseltamivir was administered for 5 days according to body weight for patients older than 12 months: 15–23 kg received 45 mg twice per day; 24–40 kg received 60 mg twice per day; and ≥40 kg received 75 mg twice per day [20]. Hydroxychloroquine (5 mg/kg per day) was administered for 10 days, and 10 mg/kg azithromycin was administered on the first day of treatment followed by 5 mg/kg per day for 4 days [15]. Hospitalization and treatment were offered for the six symptomatic patients in the outpatient cohort, but the parents refused. Therefore, these six patients were treated at home with intravenous fluids and oral azithromycin. Cancer-directed therapies (radiation and chemotherapy) were suspended for all patients until recovery from COVID-19 symptoms, except for two patients who had finalized their treatment and were receiving follow-up examinations.

**Statistical analysis**

Statistical analyses were performed with SPSS software, version 23. Parametric and nonparametric analyses were performed, as appropriate.

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**Table 2**

Clinical characteristics of pediatric patients with cancer and COVID-19 treated at MPCTRC in Tehran, Iran.

| Characteristics                | Inpatient cohort (n = 8) | Outpatient cohort (n = 9) | Total patients (n = 17) |
|--------------------------------|--------------------------|---------------------------|-------------------------|
| **Sex**                        |                          |                           |                         |
| Male                           | 5                        | 5                         | 10                      |
| Female                         | 3                        | 4                         | 7                       |
| **Age at the time of symptoms**|                          |                           |                         |
| Mean ± SE (years)              | 12.6 ± 2.5               | 6.1 ± 1.1                 | 9.17 ± 1.5              |
| Range (years)                  | 3–25                     | 3–13                      | 3–25                    |
| No. patients <5 years          | 2                        | 3                         | 5                       |
| Cancer                         |                          |                           |                         |
| Leukemia                       | 4                        | 3                         | 7                       |
| Brain tumor                    | 0                        | 5                         | 5                       |
| Lymphoma                       | 3                        | 0                         | 3                       |
| Sarcoma                        | 1                        | 1                         | 2                       |
| **Number treated for recurrence**|                         |                           |                         |
|                                | 5                        | 4                         | 9                       |

SE = standard error.

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**Results**

**Patients**

From March 18, 2020, to January 28, 2021, 637 pediatric patients were admitted to or visited MPCTRC for cancer diagnoses and treatment. Of these, 356 had newly diagnosed neoplasms. COVID-19 was suspected in two of these new cases at the time of admission. However, the parents of these children preferred treatment at other centers closer to their homes and were therefore excluded from our analysis.

A total of 17 patients who received treatment at MPCTRC were eligible for our study. All 17 patients had previous exposure to a person with COVID-19. Fourteen patients exhibited clinical symptoms consistent with COVID-19, and three were asymptomatic. All 17 cases had CT findings consistent with COVID-19. The most common cancer diagnoses in our cohort included leukemia (n = 7), brain tumors (n = 5) and lymphoma (n = 3). The patients with leukemias had acute lymphoblastic leukemia (ALL, n = 4) and acute myeloid leukemia (AML, n = 3). The patients with brain tumors had pilocytic astrocytoma (n = 2), ependymoma (n = 1), optic pathway glioma (n = 1), and medulloblastoma (n = 1). The patients with lymphoma diagnoses comprised Burkitt lymphoma (n = 1), Hodgkin lymphoma (n = 1), and non-Hodgkin lymphoma (n = 1). Finally, the two remaining cases had rhabdomyosarcoma (n = 1) and osteosarcoma (n = 1). The clinical characteristics of the two patient cohorts (ie, inpatient and outpatient) are summarized in Table 2.

**Clinical presentations**

All COVID-19 symptoms were mild in the 14 patients who exhibited symptoms. Of these patients, 71.4%, 42.9%, and 28.6% had fever, upper airway symptoms, and cough, respectively. All eight patients in the inpatient cohort had mild symptoms (fever, 62.5%; upper airway symptoms, 50%; and cough, 37.5%). Of the six symptomatic patients in the outpatient group, all had mild clinical symptoms and were referred with fever (83.3%), and only two cases exhibited upper airway symptoms, with one experiencing cough.

**Laboratory tests**

Laboratory test findings in the all patients and the inpatient and outpatient cohorts are provided in Table 3. The laboratory test findings were unremarkable for the total patient population and each cohort.

**Imaging evaluations**

Chest CT imaging findings are summarized in Table 4. These findings were based on chest axial spiral CT scans without con-
### Table 3

Laboratory test findings of pediatric patients with cancer and COVID-19 treated at MPCTRC in Tehran, Iran.

| Laboratory test | Inpatient cohort | Outpatient cohort | All patients |
|-----------------|------------------|-------------------|-------------|
|                 | Mean ± SE | Range | Mean ± SE | Range | Mean ± SE | Range |
| WBC (cells/L)   | 6,217 ± 3,501 | 320–15,970 | 6,481 ± 2,976 | 200–19,300 | 6,375 ± 2,142 | 200–19,300 |
| ANC (cells/L)   | 10,331 ± 5,313 | 263–18,307 | 5,565 ± 2,430 | 1,777–12,552 | 7,607 ± 2,578 | 263–18,307 |
| ALC (cells/L)   | 968 ± 493 | 34–1,709 | 2,232 ± 720 | 567–4080 | 1,690 ± 498 | 34–4,080 |
| Platelets (cells/L) | 46,500 ± 19,538 | 6,000–99,000 | 188,333 ± 86,963 | 12,000–392,000 | 131,600 ± 55,751 | 6,000–392,000 |
| Hgb (g/dL)      | 8.1 ± 1.2 | 6.6–12.1 | 9.7 ± 1.2 | 7–14 | 9.8 ± 0.8 | 6–14 |
| CRP (mg/L)      | 67.4 ± 42.4 | 6–192 | 31.5 ± 10.2 | 6–48 | 49.5 ± 21.3 | 6–192 |
| LDH (IU/L)      | 474 ± 161 | 241–784 | 542 ± 163 | 241–784 | 508 ± 103 | 241–868 |

**Notes:**
- ALC = absolute lymphocyte count; ANC = absolute neutrophil count; CRP = C-reactive protein; Hgb = hemoglobin; LDH = lactate dehydrogenase; SE = standard error; WBC = white blood cell count.

### Table 4

Chest computed tomography imaging findings in pediatric patients with cancer and COVID-19 treated at MPCTRC in Tehran, Iran.

| Case Number | Cohort | Age (years) | Computed tomography (CT) imaging findings |
|-------------|--------|-------------|------------------------------------------|
| 1           | Inpatient | 13        | Significant ground-glass opacity with peripheral location, pleural effusion |
| 2           | Inpatient | 16        | Moderate ground-glass opacity with peripheral location |
| 3           | Inpatient | 13        | Significant ground-glass opacity with peripheral location, pericardial effusion, mild pleural effusion |
| 4           | Inpatient | 25        | Peripheral ground-glass opacities |
| 5           | Outpatient | 3         | Poor quality |
| 6           | Outpatient | 7         | Ground-glass opacity |
| 7           | Outpatient | 5         | Moderate ground-glass opacity with peripheral location |
| 8           | Outpatient | 3         | Poor quality |
| 9           | Outpatient | 3         | Bilateral peripheral opacities |
| 10          | Outpatient | 9         | Nodular opacities in the parenchyma of both lungs |
| 11          | Outpatient | 5         | Low-grade COVID-19 pneumonia |
| 12          | Inpatient | 10        | Massive extensive bilateral multi-lobar ground glass opacity and consolidations with air bronchograms |
| 13          | Outpatient | 13        | Not applicable |
| 14          | Inpatient | 3         | Both lung, but predominantly right lung with multi-lobar ground glass opacity and consolidation |
| 15          | Inpatient | 7         | In both lung lower lobes consolidation and air bronchograms seen |
| 16          | Inpatient | 4         | Bilateral multi-lobar consolidation with ground glass opacities with air bronchograms and small right side pleural effusion |
| 17          | Inpatient | 17        | Bilateral pulmonary subpleural patchy infiltration |

### Table 5

Summary of cancer diagnoses, treatment, and outcomes of pediatric patients with cancer and COVID-19 treated at MPCTRC in Tehran, Iran.

| Case no. | Sex | Cancer type | Cancer therapy phase at the time of COVID-19 | RT | BMT | Tumor recurrence | COVID-19 symptoms | RT-PCR results | IgC/IgM levels | COVID-19 outcomes |
|----------|-----|-------------|---------------------------------------------|----|-----|-----------------|------------------|-----------------|----------------|----------------|
| 1        | F   | NHL         | Course AA with BFM-NHL-90 protocol          | No | No  | 0               | Fever, UAS       | Neg            | ND             | Recovered       |
| 2        | M   | BL          | Chemotherapy with RICE for relapse          | No | No  | 1               | Fever, cough     | Neg            | ND             | Death           |
| 3        | M   | OS          | Chemotherapy after surgery                 | No | No  | 0               | UAS             | ND             | ND             | Death           |
| 4        | M   | AML         | Relapse after BMT                          | No | Yes | 1               | Cough           | Neg            | Neg            | Recovered       |
| 5        | F   | OPG         | Maintenance with vincristine and carboplatin| No | No  | 0               | Fever           | ND             | ND             | Recovered       |
| 6        | F   | PA          | Metronomic therapy with vinblastine         | No | No  | 1               | Asymptomatic     | ND             | ND             | Recovered       |
| 7        | M   | ALL         | Intensification 2 with isolated CNS relapse | No | No  | 2               | Fever, UAS      | Neg            | ND             | Recovered       |
| 8        | F   | ALL         | Phase II induction ALL-BFM 2009            | No | No  | 0               | Fever, cough    | Neg            | Neg            | Recovered       |
| 9        | M   | EP          | Course A in postoperative chemotherapy      | Yes| No  | 1               | Asymptomatic     | ND             | Neg            | Recovered       |
| 10       | F   | MB          | Cycle 5 high-risk medulloblastoma           | Yes| No  | 1               | Fever           | ND             | Neg            | Recovered       |
| 11       | M   | RMS         | Week 24, regimen 47 RMS                    | Yes| No  | 0               | Asymptomatic     | Neg            | Neg            | Recovered       |
| 12       | M   | ALL         | Subsequent maintenance for ALL relapse     | Yes| No  | 1               | UAS             | Pos            | ND             | Death           |
| 13       | M   | ALL         | Maintenance ALL-BFM 2009                   | No | No  | 0               | Fever           | Neg            | Pos            | Recovered       |
| 14       | M   | AML         | Maintenance IBFM-2012                      | No | No  | 0               | Fever, UAS      | Neg            | Neg            | Recovered       |
| 15       | M   | PA          | Follow-up after finalizing treatment       | No | No  | 0               | UAS             | Pos            | Neg            | Recovered       |
| 16       | F   | AML         | Reduction with HAM                        | No | No  | 1               | Fever           | Pos            | Neg            | Recovered       |
| 17       | F   | HL          | Follow-up after finalizing treatment       | No | Yes | 1               | Fever, cough    | Pos            | ND             | Recovered       |

**Notes:**
- ALL = acute lymphoblastic leukemia; AML = acute myeloid leukemia; BL = Burkitt lymphoma; BMT = bone marrow transplant; CNS = central nervous system; EP = ependymoma; F = female; M = male; MB = medulloblastoma; ND = not determined; Neg = negative; NHL = non-Hodgkin lymphoma; OPG = optic pathway glioma; OS = osteosarcoma; PA = pilocytic astrocytoma; RB = retinoblastoma; RMS = rhabdomyosarcoma; RT = radiation therapy; UAS = upper airway symptoms.
Table 6

Studies reporting COVID-19 in pediatric patients with a diagnosis of cancer.

| Study                          | Incidence and severity among children on anticancer treatment | Author conclusions: | Limitations: |
|-------------------------------|-------------------------------------------------------------|---------------------|--------------|
| Hrusak et al [26]             | Reports from 25 countries where up to 10,000 patients at risk are followed | Should not delay oncologic treatment | Many centers tested only symptomatic patients hence true rate of infection not known |
| Boulad et al [27]             | COVID-19 in children with cancer in New York City | | 4/9 cases same as reported by Balduzzi et al |
| Balduzzi et al [28]           | Bergamo area and Emilia Romagna in Lombardy region of Italy | | |
| Mehrvar et al [this study]    | MAHAK Pediatric Cancer Treatment and Research Center (MPTCRC) in Tehran, Iran | | |

Molecular detection and treatment of COVID-19

SARS-CoV-2—specific IgG and IgM antibody levels were evaluated in nine patients, and were negative in all patients except for case 13 (IgG: 6.78; IgM: 3.78). Twelve patients had RT-PCR screening for SARS-CoV-2 performed, and four were positive (cases 12, 16, 17, and 18). Five patients did not undergo RT-PCR screening for SARS-CoV-2 infection.

Before the COVID-19 pandemic, all patients were receiving active cancer therapy, with the exception of cases 16 and 18 who were receiving follow-up examinations. Nine patients were receiving treatment for relapsed neoplasms. Case 7 was receiving treatment for a second ALL relapse, and case 4 was receiving chemotherapy for relapsed AML after having undergone a bone marrow transplant. The remaining thirteen patients were receiving various phases of chemotherapy treatment at the time of COVID-19 diagnosis (Table 5).

At the time of this writing, three patients in our study had died of COVID-19, and all other patients had recovered. The deceased patients were a 16-year-old male with Burkitt lymphoma who was...
receiving chemotherapy for recurrence, a 13-year-old male with osteosarcoma who was receiving chemotherapy after surgery, and a 10-year-old male with ALL who was in a subsequent maintenance phase of chemotherapy after relapse. All three patients died because of respiratory failure, despite hospitalization and treatment with hydroxychloroquine, oseltamivir, and azithromycin.

Discussion

Despite the devastation of the COVID-19 pandemic, we still know very little about its biology in children with cancer. Some studies have reported that patients with cancer have an increased risk of contracting COVID-19 [21–23]. Our study is the first report of COVID-19 in children with cancer referred to a cancer center in Iran. During the period of our study, 17 of 637 patients contracted COVID-19, according to our institutional criteria. Unfortunately, three of these patients who were hospitalized and received oseltamivir, hydroxychloroquine, and azithromycin therapy died of COVID-19. Because nine children in our study refused hospitalization but recovered at home with only supportive care, we cannot draw meaningful conclusions as to the benefit of hospitalization coupled with antiviral/hydroxychloroquine therapy on the outcomes of our patients.

In April 2020, Ruggiero et al. systematically reviewed published reports of pediatric patients with cancer who contracted COVID-19 [24]. At that time, information on only one pediatric oncology patient with COVID-19 had been published [25]. Chen et al. reported the experience of an 8-year-old male patient with ALL in Wuhan, China, who contracted COVID-19 6 days after completing his maintenance chemotherapy regimen. The authors suggested that SARS-CoV-2 was transmitted to the patient from his attending physician at the hospital [25].

To date the literature describing COVID-129 in pediatric patients with a diagnosis of cancer remains very sparse (Table 6). Hrusak et al. conducted a web-based survey characterizing COVID-19 cases in pediatric hematology-oncology centers. Thirty-two countries participated in the survey, and of 200 cases who received SARS-CoV-2 testing, only eight were positive. Moreover, the severity of COVID-19 symptoms was mild in these cases [26]. The Memorial Sloan Kettering Cancer Center established a program for screening COVID-19 in pediatric oncology patients (Table 6). Over a brief one-month period from March 10 to April 12, 2020, 20 of 178 patients who were screened for SARS-CoV-2 infections were positive. The mean age of these patients was 15.9 years, and only three were female. One of the patients was hospitalized for a noncritical condition, three asymptomatic patients were hospitalized because of their cancer comorbidity, and the remaining 16 experienced mild COVID-19 symptoms and recovered at home [27]. Finally through March 18, 2020, only five pediatric oncology cases exhibiting mild COVID-19 symptoms were reported in the Lombardy region of Italy. These cases included patients with ALL in second remission, osteosarcoma, hepatoblastoma, and rhabdoid tumors. Three patients recovered at home, and two were hospitalized without any antiviral medications [28].

Our findings and those of others suggest that treatment in the outpatient setting without antivirals or antibiotics is a viable option for pediatric oncology patients with COVID-19. Indeed, all of the patients in our study with mild COVID-19 symptoms who refused hospitalization recovered at home. However, our experience also demonstrates that COVID-19 can be fatal in a meaningful fraction of infected pediatric patients, and it is hoped that going forward when these cases are recognized, the availability of novel therapeutics and our greater understanding of the management of this disease may help in their management.

Conclusion

We suggest that a majority of pediatric patients with cancer who experience mild COVID-19 symptoms can most likely receive supportive care at home without hospitalization helping to prevent further SARS-CoV-2 transmission. Finally, the quality of molecular diagnostic testing for SARS-CoV-2 infections in Iran should be improved.

Conflict of interest

The authors declare that there is not any conflict of interest.

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References

[1] Lee PI, Hu YL, Chen PY, Huang YC, HsuEH. Are children less susceptible to COVID-19? J Microbiol Immunol Infect 2020;53(3):371–2.
[2] Bai Y, Yao L, Wei T, et al. Presumed asymptomatic carrier transmission of COVID-19. JAMA 2020;323(14):1466–7.
[3] Qiu H, Wu J, Hong L, Luo Y, Song Q, Chen D. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. Lancet Infect Dis 2020;20(6):689–96.
[4] Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA 2020;323(11):1061–9.
[5] Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. N Engl J Med 2020;382(13):1199–1207.
[6] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395(10223):497–506.
[7] She J, Liu L, Liu W. COVID-19 epidemic: disease characteristics in children. J Med Virol 2020;92(7):274–57.
[8] Lee PI, HsuEH. Emerging threats from zoonotic coronaviruses-from SARS and MERS to 2019-nCoV. J Microbiol Immunol Infect 2020;53(3):365–7.
[9] Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults. Pediatr Pulmonol 2020;55(5):1169–74.
[10] Mahmoudi S, MehdiZadeh M, Badrv RS, et al. The coronavirus disease 2019 (COVID-19) in children: a study in an Iranian Children's Referral Hospital. Infect Drug Resist 2020;13:2649–55.
[11] Hanna TP, Evans GA, Booth CM, Cancer, COVID-19 and the precautionary principle: prioritizing treatment during a global pandemic. Nat Rev Clin Oncol 2020;17(5):268–70.
[12] Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395(10229):1054–62.
[13] Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol 2020;21(3):335–7.
[14] Burki TK. Cancer guidelines during the COVID-19 pandemic. Lancet Oncol 2020;21(5):629–30.
[15] Carlotti A, PCCP, Carvalho WB, Johnston C, Rodrigo IS, Delgado AF. COVID-19 diagnostic and management protocol for pediatric patients. Clinics 2020;75:e1894.
[16] Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. Pediatrics 2020;145(6):e20200702.
[17] Chen ZM, Fu JF, Shu Q, et al. Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus. World J Pediatr 2020;16(3):240–6.
[18] Brown JR, Atkinson L, Shah D, Harris K. Validation of an extraction-free RT-PCR protocol for detection of SARS-CoV2 RNA. MedRxiv 2020.
[19] Resolucjo 55-28, 17-03-2020. Diario Oficial do Estado de São Paulo. 130(54):24–25.
[20] Karimi A, Tabatabaie SR, Rajabnejad M, et al. An algorithmic approach to diagnosis and treatment of coronavirus disease 2019 (COVID-19) in children: Iranian expert’s consensus statement. Arch Pediatr Infect Dis 2020;8(2):e102400.
[21] Yu J, OuYang W, Chua ML, Xie C. SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China. JAMA Oncol 2020;6(7):1108–10.
[22] Dai MY, Liu D, Liu M, et al. Abstract CT406: Patients with cancer appear more vulnerable to SARS-CoV-2: A multi-center study during the COVID-19 outbreak. AACR 2020.
[23] Robiotti E, Babady NE, Mead PA, et al. Determinants of COVID-19 disease severity in patients with cancer. Nat Med 2020;26(6):1218–23.
[24] Ruggiero A, Romano A, Atiná G. COVID-19 and children with cancer: are they at increased risk of infection? Pediatr Res 2020. doi:10.1038/ s41390-020-0919-1.
[25] Chen Z, Xiong H, Li J, et al. COVID-19 with post-chemotherapy agranulocytosis in childhood acute leukemia: a case report. Zhonghua Xue Ye Xue Za Xhi 2020;41(4):341–1.

[26] Hrusak O, Kalina T, Wolf J, et al. Flash survey on severe acute respiratory syndrome coronavirus-2 infections in pediatric patients on anti-cancer treatment. Eur J Cancer 2020;132:11–16.

[27] Boulad F, Kamboj M, Bouvier N, Mauguen A, Kung AL. COVID-19 in children with cancer in New York City. JAMA Oncol 2020;6(9):1459–60.

[28] Balduzzi A, Brivio E, Rovelli A, et al. Lessons after the early management of the COVID-19 outbreak in a pediatric transplant and hemat-oncology center embedded within a COVID-19 dedicated hospital in Lombardia, Italy. Estote parati. Bone Marrow Transplant 2020;55(1):1900–5.