Received: 9 May 2020 | Accepted: 15 May 2020

DOI: 10.1002/pbc.28466

Pediatric Blood & Cancer

SOCIÉTÉ INTERNATIONALE D'ONCOLOGIE PÉDIATRIQUE SIOP INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY

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WILEY

LETTER TO THE EDITOR

Screening for SARS-CoV-2 infection in pediatric oncology patients during the epidemic peak in Italy

The infection by the new coronavirus-2019 (SARS-CoV-2) can be asymptomatic or mildly symptomatic in up to 80% of infected people, whereas the severe or lethal forms have been associated with several risk factors.[1-3] Children with tumors represent a special risk group because treatment is frequently based on high-dose chemotherapy and, in leukemia and lymphoma, on steroids that result in severe impairment of innate and adaptive immunity. The effect of chemotherapy on an asymptomatic patient with SARS-CoV-2 infection is unknown, although a more severe course could be expected. During the epidemic peak in Italy, to prevent the hospital admission of asymptomatic infected patients, 14 pediatric hematology-oncology centers adopted a policy to screen the patients for SARS-CoV-2 by nasopharyngeal swab (NFS) before allowing them to start chemotherapy or enter hospital for supportive measures. Geographically, 10 centers were located in northern Italy, one in central Italy, and three in southern Italy/Isles. We report the results of this screening performed from February 20 to April 19, 2020. Follow-up data are as on April 30, 2020.

At the start of screening, all centers were using the preventative measures recommended to contain the epidemic: social and physical distancing, use of hand hygiene, gloves, and surgical masks for patient, health personnel, and caregiver, screening of patients and parents for fever and signs or symptoms of respiratory tract infection, and restricted access by nonhealth personnel.

A total of 334 NFS were performed on 247 patients with a median age at diagnosis of 7 years, range 0-17.9: 167 affected by leukemia or lymphoma and 80 with solid tumors. Eighty-nine patients (77%) were undergoing first-line chemotherapy, whereas 27 patients were receiving chemotherapy after relapse. At the time of NFS, the median and range of white blood cell, polimorphonuclear, hemoglobin, and platelet count or level were 3×10^9/L, 0.1-45.5, 1.33×10^9/L, 0-26.2, 11 g/L, 4-16, 21.9×10^9/L, 12-865.

NFS was positive in 10 of 334 (3%); all positives were in northern Italian centers where the epidemic was more prevalent; so the positive rate for the centers of north Italy was 10 of 291 NFS (3.4%). Among patients with positive NFS, eight were completely asymptomatic while two presented with mild fever. All positive patients ceased chemotherapy until NFS became negative, which occurred for nine patients after a median of 14 days (range 12-26 days), while one patient, who was undergoing both chemotherapy and radiotherapy, is still positive after 38 days. Two-week quarantine was performed at home (eight patients) or in hospital (two patients).

In addition, a total of 56 NFS were performed in 35 stem cell transplant (SCT) patients (25 allogeneic and 10 autologous) affected by leukemia or lymphoma in 17 patients, solid tumors in 12 and nonmalignant hematology disease, or immunodeficiency in six. The median age at SCT was 9.6 years (range 0.3-17.6 years). The median time from SCT to NFS was 4.4 months (range 0-7.2 years). All 56 NFS were negative.

In the Chinese epidemic, only 1% of infected people were younger than 10 years or 11-18 years old.[2-4] Pediatric cases of COVID-19 overall had a good prognosis, because most of them were asymptomatic or with mild or moderate symptoms and only 2.5% were severely ill.[4,5]

The real incidence of asymptomatic infected people is unknown because it depends on how thoroughly the search is conducted but their identification and tracing are important to prevent the diffusion of infection. In this study, we found that the incidence of positive NFS in pediatric patients coming to hospital for chemotherapy was 3% for all centers, and 3.4% for the northern Italian centers. The main measure adopted for these patients was the postponing of chemotherapy until two NFS were negative at least 24 h apart. This precaution is in line with data on adult cancer patients showing that recent chemotherapy or oncology surgery was a risk factor for a more severe COVID-19 infection[6] and with a case report of a severe respiratory form of COVID-19 in a Chinese child with T-cell acute leukemia.[7] The impact of chemotherapy on the risk of progression of an asymptomatic or mildly symptomatic SARS-CoV-2 infection toward a severe or lethal form of COVID-19 is not really known. In a multicenter survey among pediatric oncology centers, only nine out of 200 symptomatic or suspected patients tested positive for SARS-CoV-2 at NFS. None of them required intensive care or ventilatory support, and only two patients were treated with hydroxychloroquine together with lopinavir/ritonavir in one patient.[8] The low morbidity documented so far in pediatric hematology-oncology patients raises the question about the risk/benefit ratio of interrupting or postponing chemotherapy in asymptomatic or mildly symptomatic SARS-CoV-2-positive patients. Interestingly, all the SCT patients tested negative. This could be due to the smaller number of patients assessed or to the fact that SCT patients are more accustomed to adopting preventative measures.

In conclusion, SARS-CoV-2 can result in asymptomatic infections in patients undergoing chemotherapy and their identification is important to preserve a hospital unit clean from COVID-19 cases. Further studies are needed to define the least-risky chemotherapy

management for asymptomatic or mildly symptomatic SARS-CoV-2-positive patients.

Simone Cesaro[1]
Francesca Compagno[2]
Daniele Zama[3]
Linda Meneghello[4]
Nagua Giurici[5]
Elena Soncini[6]
Daniela Onofrillo[7]
Federico Mercolini[8]
Rossella Mura[9]
Katia Perruccio[10]
Raffaella De Santis[11]
Antonella Colombini[12]
Angelica Barone[13]
Laura Sainati[14]
Valentina Baretta[1]
Maria Grazia Petris[14]

[1] *Pediatric Hematology Oncology, Department of Mother and Child, Azienda Ospedaliera, Universitaria Integrata, Verona, Italy*
[2] *Pediatric Hematology/Oncology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy*
[3] *Department of Pediatrics, Pediatric Oncology and Haematology Unit "Lalla Seràgnoli", Sant' Orsola Malpighi Hospital, University of Bologna, Bologna, Italy*
[4] *Department of Pediatrics, Santa Chiara Hospital, Trento, Italy*
[5] *Hemato-Oncology Unit, Department of Pediatrics, IRCCS Burlo Garofolo, Trieste, Italy*
[6] *Pediatric Hematology Oncology and BMT Unit, Ospedale dei bambini, Spedali Civili, Brescia, Italy*
[7] *Hematology-Oncology Department, Pediatric Hematology and Oncology Unit, Santo Spirito Hospital, Pescara, Italy*
[8] *Department of Pediatrics, Regional Hospital of Bolzano, Bolzano, Italy*
[9] *Pediatric Hematology Oncology, Azienda Ospedaliera Brotzu, Cagliari, Italy*
[10] *Pediatric Oncology Hematology, Santa Maria della Misericordia Hospital, Perugia, Italy*
[11] *Pediatric Hematology Oncology, Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo, Italy*
[12] *Pediatric Hemato-Oncology, Fondazione MBBM, Milano Bicocca University, San Gerardo Hospital, Monza, Italy*
[13] *Pediatric Onco-Hematology, Department of Pediatrics, Azienda Ospedaliero-Universitaria, Parma, Italy*
[14] *Clinic of Pediatric Hemato-Oncology, Department of Women's and Children's Health, University of Padua, Padua, Italy*

Correspondence
Simone Cesaro, Pediatric Hematology Oncology, Department of Mother and Child, Azienda Ospedaliera Universitaria Integrata, Piazzale Aristide Stefani 1, 37126 Verona, Italy.
Email: simone.cesaro@aovr.veneto.it

ORCID

Simone Cesaro https://orcid.org/0000-0002-8698-9547
Federico Mercolini https://orcid.org/0000-0001-9932-1944

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