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Original paper

The impact of SARS-CoV-2 infection on the course and prognosis of hematologic malignancies – a single-center experience

Jakub Kołodziej[1], Aleksandra Skowronek[1], Marta Mielczarek[1], Kinga Cogiel[1], Monika Prokurat[1], Gabriela Bronikowska[1], Tomasz Szczepański[2], Aneta Pobudejska-Pieniążek[2]

[1]Students' Scientific Club, Department of Pediatric Hematology and Oncology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice, Poland
[2]Department of Pediatric Hematology and Oncology, Faculty of Medical Sciences in Zabrze Medical University of Silesia, Katowice, Poland

Address for correspondence:
Jakub Kołodziej
Students' Scientific Club
Department of Pediatric Hematology and Oncology
ul. 3 Maja 13/15, 41-800 Zabrze
SPSK Nr 1 im. prof. S. Szyszko ŚUM
e-mail: s84032@365.sum.edu.pl

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ABSTRACT

Introduction: Patients with hematologic malignancies are at increased risk of severe COVID-19 due to disease-related and treatment-induced immunosuppression. The aim of this study was to analyze the clinical course and outcomes of pediatric patients with hematologic cancers who developed SARS-CoV-2 infection.

Material and methods: Three pediatric patients with hematologic malignancies hospitalized at the Department of Pediatric Hematology and Oncology in Zabrze between 2021 and 2023 were included. SARS-CoV-2 infection was confirmed by antigen or RT-PCR testing. Clinical course, laboratory findings, treatment, and outcomes were analyzed retrospectively.

Results: All patients required temporary discontinuation of antineoplastic therapy due to COVID-19. Respiratory symptoms and hematologic abnormalities (lymphopenia, agranulocytosis) were common. Two patients developed cytokine release syndrome treated with tocilizumab. One child survived, while two died due to progression of the underlying malignancy after infection.

Conclusions: SARS-CoV-2 infection in pediatric patients with hematologic malignancies can cause significant hematologic disturbances and treatment interruptions, potentially affecting prognosis. Individualized management and close cooperation between hematology and infectious disease teams are essential for optimal care.

KEYWORDS

hematological malignancies, pediatric patients, SARS-CoV-2, COVID-19

INTRODUCTION

The emergence of the first documented cases of SARS-CoV-2 infection in December 2019 profoundly altered the functioning of oncology departments. Infection with a previously unknown pathogen significantly increased the risk of severe COVID-19 symptoms and reduced the effectiveness of treatment of the primary malignancy, which in some cases led to further disease progression.

Coronaviruses constitute a zoonotic group of pathogens. Until 2019, two highly pathogenic strains were of the greatest clinical relevance, capable of causing fatal respiratory illness in humans: the Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome coronavirus (MERS-CoV). The newly identified SARS-CoV-2 strain rapidly surpassed both SARS and MERS in terms of the number of infected individuals and global spread [1]. Similar to SARS-CoV, the virus responsible for COVID-19 exerts its effects through the angiotensin-converting enzyme 2 (ACE2) receptor. Viral entry and replication within host cells lead to reduced ACE2 receptor availability and a subsequent increase in angiotensin II production. Elevated levels of this renin–angiotensin–aldosterone system hormone enhance pulmonary vascular permeability,

contributing to lung injury. Approximately 80% of ACE2 receptors are located on type II pneumocytes, making the lungs the primary reservoir for SARS-CoV-2. Multiorgan dysfunction observed in infected patients may result from widespread ACE2 expression in extrapulmonary tissues, including the heart, kidneys, and intestinal endothelium [2].

Profound immunosuppression due to the myelotoxicity of antineoplastic agents, combined with the necessity for frequent medical contact, renders oncology patients particularly susceptible to infection. Among them, individuals with hematologic malignancies and lung cancer are at the highest risk.

Data published in *JAMA Oncology*, based on the IBM Watson Health Explorys database, demonstrated a strong association between COVID-19 and increased hospitalization and mortality rates among cancer patients compared with individuals without cancer. According to these data, cancer patients with SARS-CoV-2 infection required hospitalization more frequently than non-cancer patients (47.5% vs. 24.6%) and had a higher mortality rate (14.9% vs. 5.3%). By contrast, among patients with cancer but without COVID-19, hospitalization and mortality rates were 12.39% and 4.03%, respectively [3]. The aim of the study was to analyze the clinical course, laboratory changes, treatment strategies, and outcomes of COVID-19 infection in this group.

MATERIAL AND METHODS

The case series study included three pediatric patients with diagnosed hematologic malignancies hospitalized at the Department of Pediatric Hematology and Oncology, University Clinical Hospital No. 1 in Zabrze, between 2021 and 2023. In all patients, SARS-CoV-2 infection was confirmed during active treatment or follow-up for the primary disease.

Infection was confirmed using antigen testing or reverse transcription polymerase chain reaction (RT-PCR) from nasopharyngeal swabs. Clinical, laboratory, and imaging data were retrospectively collected from medical records. The course of the hematologic malignancy, clinical manifestations, laboratory findings, treatment administered during infection, and patient outcomes were analyzed. Parameters assessed included complete blood count, C-reactive protein (CRP), lactate dehydrogenase (LDH), and interleukin-6 (IL-6) levels, as well as chest imaging results. The data were presented descriptively and compared with relevant reports from the literature.

The study was conducted in accordance with the principles of the Declaration of Helsinki, ensuring full anonymization of patient data.

SINGLE-CENTER EXPERIENCE

COVID-19 among pediatric patients of the hematology department – experience from the University Clinical Hospital No. 1 in Zabrze

Between November 30, 2021, and September 30, 2025, a total of 306 hospitalizations took place in

the Department of Pediatric Hematology and Oncology, of which 165 admissions involved 28 patients with acute leukemias undergoing chemotherapy or presenting bone marrow aplasia following cytotoxic treatment. Among these, SARS-CoV-2 infection was confirmed in 13 children, two of whom experienced reinfection.

Among patients diagnosed with acute lymphoblastic leukemia in the standard-risk group (ALL-SR), four cases of asymptomatic COVID-19 infection were detected during routine pre-admission screening. In the absence of alarming symptoms and with stable hematologic parameters, these patients were referred for home isolation, and the next course of chemotherapy was temporarily postponed.

During another planned hospital admission, a patient with ALL-SR presented with symptoms of upper respiratory tract infection; screening tests confirmed SARS-CoV-2 positivity. The patient did not require hospitalization and was placed under home quarantine, with temporary interruption of chemotherapy. Due to neutropenia and persistent positive viral tests, the patient was hospitalized after five days in the Pediatric Department of University Clinical Hospital No. 1 in Zabrze for observation and supportive management.

In the remaining eight patients, COVID-19 infection was diagnosed during hospital stay. All of them exhibited symptoms of upper respiratory tract involvement. One patient with ALL-SR experienced a second episode of asymptomatic SARS-CoV-2 infection after eight months. Symptomatic patients also included those hospitalized for Wilms' tumor, hepatoblastoma, acute lymphoblastic leukemia—high-risk group (ALL-HR), acute myeloid leukemia (AML), relapse of lymphoma manifesting as ALL, relapse of ALL, and ALL-HR. The following case descriptions illustrate the impact of COVID-19 infection on the clinical course and prognosis of hematologic malignancies in pediatric patients.

Patient 1

Diagnosis

A 16-year-old male was diagnosed in October 2019 with T-cell lymphoblastic lymphoma (clinical stage III – mediastinal mass, involvement of cervical and supraclavicular lymph nodes). The patient was treated according to the EURO-LB 2002 protocol. On October 27, 2021, he was admitted for remission assessment after completion of therapy.

Laboratory, imaging, and bone marrow biopsy findings revealed an early relapse of the primary disease in the form of acute lymphoblastic leukemia (ALL) originating from immature T-cell precursors, with coexistence of immature NK-cell and B-cell precursors.

He was subsequently qualified for treatment according to the IntReALL HR 2010 protocol, including Bortezomib, followed by hematopoietic stem cell transplantation (HSCT). On December 2, 2021, the HIB cycle and the first dose of Bortezomib were initiated.

Clinical course of COVID-19 infection

Following confirmed contact with SARS-CoV-2–positive individuals, an antigen test was performed on December 5, 2021, yielding a positive result. At diagnosis, the patient presented upper respiratory tract infection symptoms, prompting temporary interruption of chemotherapy.

Subsequent antigen tests remained positive, and by December 20, 2021, laboratory studies revealed elevated inflammatory parameters. On December 24, 2021, oxygen saturation dropped to 88–89%. Auscultation revealed fine and medium crackles and rhonchi, predominantly over the right lung.

Chest X-ray showed opacities at the border of the middle and lower fields of the right lung and patchy, streak-like infiltrates in the lower lobe. Chest CT demonstrated bilateral pleural effusion and areas of consolidation involving approximately 50% of pulmonary parenchyma. Laboratory tests showed persistent elevation of inflammatory markers and pancytopenia.

A follow-up CT scan (January 3, 2022) showed near-complete resolution of pulmonary infiltrates, and on the same day the first negative antigen test was obtained.

Laboratory findings during COVID-19 infection

The infection lasted a total of 29 days. At the time of COVID-19 diagnosis, laboratory test results revealed leukocytopenia ($2.02 \times 10^3/\mu L$), with no granulocytopenia ($1.89 \times 10^3/\mu L$) and a normal C-reactive protein (CRP) level.

Inflammatory parameters were closely monitored — C-reactive protein (CRP) dynamics are shown in Figure 1.

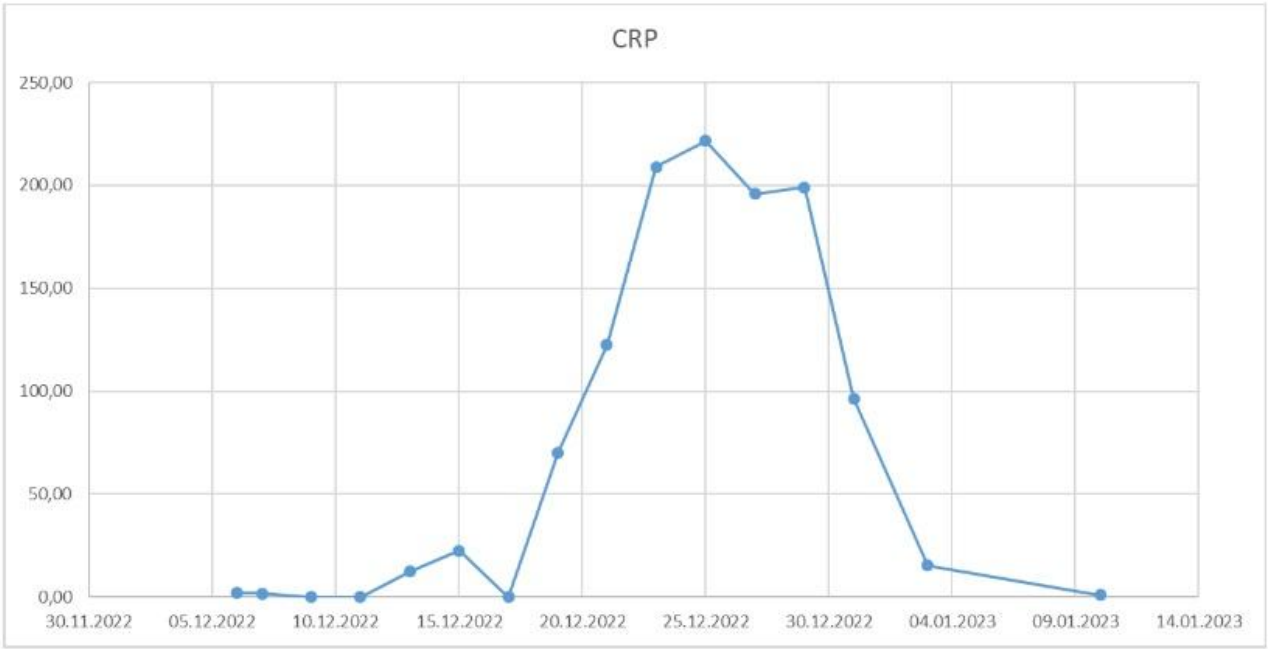

Figure 1. Changes in CRP levels during COVID-19 infection

Interleukin-6 concentration reached 52.18 pg/mL. Considering the clinical picture, a cytokine release syndrome (CRS) secondary to COVID-19 infection was diagnosed.

Therapeutic management

Due to SARS-CoV-2 infection, chemotherapy was discontinued after 3 days of relapse treatment. After clinical improvement, therapy was resumed after 11 days but again interrupted for 3 weeks due to deterioration.

In addition to broad-spectrum antibiotics, antifungal and supportive treatment, the patient received tocilizumab (anti–IL-6 receptor monoclonal antibody).

Subsequent course and outcome

Treatment per IntReALL HR 2010 was completed on October 27, 2021, and HSCT from a 10/10 HLA-matched unrelated donor was performed on May 10, 2022.

On September 15, 2022, bone marrow evaluation confirmed a second relapse of ALL. Two cycles of Vepesid/Cyclophosphamide/Nelarabine were administered, complicated by prolonged bone marrow aplasia. During aplasia, the patient developed pneumonia with increasing right pleural effusion.

Despite intensive treatment, the clinical condition deteriorated, with rising inflammatory markers. On December 26, 2022, the patient presented with respiratory failure and was transferred to the Pediatric Intensive Care Unit, where he died on December 28, 2022.

Patient 2

Diagnosis

A 6-year-old female patient with hypogammaglobulinemia, previously treated for mediastinal T-cell lymphoma with concurrent B-cell leukemia between September 24, 2019, and September 18, 2021, according to the AIEOP BFM 2017 protocol.

On September 18, 2021, a local relapse of mediastinal lymphoma was diagnosed, and the patient was qualified for second-line chemotherapy followed by allogeneic hematopoietic stem cell transplantation after achieving complete or partial remission. Additionally, a PMS2 gene mutation associated with the mismatch repair deficiency (CMMRD) syndrome was detected, indicating defective DNA repair mechanisms.

Between September 23, 2021, and November 1, 2021, the patient received therapy according to the IntReALL 2010 protocol. Due to lack of treatment response, after consultation with the Central Coordinator for NHL relapses, therapy was switched to a nelarabine-based regimen.

A follow-up chest CT performed on January 10, 2022, showed massive tumor progression in all dimensions, with compression of the heart, major vascular trunks, bronchi, and trachea. Administration of a second chemotherapy cycle with nelarabine, modified in phase II by adding high-dose cyclophosphamide (HD-CY) between January 10 and January 18, 2022, resulted in a 55% reduction in tumor volume. However, a subsequent CT scan on February 2, 2022, demonstrated further progression of the primary disease. The patient received another chemotherapy cycle with high-dose cyclophosphamide between February 3 and 4, 2022.

SARS-CoV-2 infection

From February 2, 2022, the patient reported moderate dyspnea with visible respiratory effort, and from February 3, 2022, oxygen saturation drops were observed. On physical examination, increased chest circumference was noted, with complete silence over the left lung field and crackles in the lower segments of the right lung. A chest CT scan performed the same day revealed massive tumor progression, with a twofold increase in tumor volume and the presence of pleural effusion. On February 5, 2022, SARS-CoV-2 infection was confirmed. Laboratory tests showed leukopenia (2.32 $\times 10^3/\mu L$) with severe lymphocytopenia (0.03 $\times 10^3/\mu L$) and markedly elevated inflammatory parameters (CRP 200.45 mg/L) and LDH.

Between February 5 and February 22, 2022, blood counts demonstrated persistent lymphopenia and profound thrombocytopenia.

Treatment of COVID-19 infection

Due to active COVID-19 infection (confirmed February 5, 2022) and features of cytokine release syndrome, the patient was treated with tocilizumab. A decrease in inflammatory parameters was observed (Figure 2).

Figure 2. Graphical representation of CRP concentration changes between February 5 and February 22, 2022.

Further treatment and clinical outcome after COVID-19 infection

The confirmed active SARS-CoV-2 infection precluded continuation of antineoplastic therapy. The patient's condition gradually deteriorated. Pronounced swelling of the upper body was observed, consistent with the development of superior vena cava syndrome. A chest X-ray performed on February 17, 2022, revealed further progression of the neoplastic process. The SARS-CoV-2

antigen test remained positive. On February 22, 2022, a decision was made to administer another cycle of chemotherapy (high-dose cyclophosphamide) as a life-saving measure. Radiotherapy sessions were initiated on March 4, 2022. During treatment, symptoms of superior vena cava syndrome intensified, and further tumor progression was observed, which on March 10, 2022, ultimately prevented continuation of irradiation. Continuous progression of the underlying disease led to sudden cardiac and respiratory arrest on March 14, 2022.

Patient 3

Diagnosis

A 2-year-old boy diagnosed with precursor B-cell acute lymphoblastic leukemia (ALL) without central nervous system involvement (CNS-1), initially treated from September 20, 2021, at the Children's Hospital in Kyiv according to the ALL IC-BFM 2009 high-risk protocol, was admitted on March 1, 2022, to the Department of Pediatric Hematology and Oncology, University Clinical Hospital No. 1 in Zabrze, for continuation of chemotherapy. Due to hypogammaglobulinemia, diagnostic tests for congenital immunodeficiencies were performed, revealing the presence of a variant of uncertain significance (VUS) in a gene associated with dyskeratosis congenita, possibly inherited in an autosomal dominant manner. Since the mutation was not confirmed in family members and the diagnostic criteria for dyskeratosis congenita were not met, the syndrome was not diagnosed. Upon admission, the child's general condition was good, and physical examination and basic laboratory tests showed no significant abnormalities. Treatment was continued according to the Polish version of the AIEOP-BFM 2017 protocol for the high-risk group (third HR block, followed by three cycles of Protocol III, two cycles of Interim Maintenance, and maintenance therapy with six lumbar punctures).

SARS-CoV-2 infection

One day after completing the second Protocol III cycle, the patient developed fever accompanied by elevated C-reactive protein (CRP) levels. Broad-spectrum antibiotic therapy, antifungal prophylaxis, and granulocyte colony-stimulating factor (G-CSF) were administered due to grade 3 neutropenia (according to CTCAE). An antigen test confirmed SARS-CoV-2 infection. The child's condition deteriorated, with persistent fever showing only mild response to antipyretics, tachycardia, and hypotension, though oxygen saturation remained within the normal range. A chest X-ray revealed bilateral perihilar, band-like pulmonary opacities, most pronounced in the upper fields, consistent with inflammatory infiltrates. Due to persistent symptoms suggesting cytokine release syndrome (CRS), dexamethasone and tocilizumab were administered, resulting in significant clinical improvement and normalization of laboratory parameters.

Laboratory findings during SARS-CoV-2

Laboratory results demonstrated progressive elevation of inflammatory markers, particularly CRP, with normalization by day 7. At the time of COVID-19 diagnosis, laboratory tests showed

leukopenia (2.66×10³/μL), granulocytopenia (1.43×10³/μL), lymphopenia (0.53×10³/μL), and elevated inflammatory indices- CRP (9.69 mg/L). Inflammatory parameters were closely monitored — C-reactive protein (CRP) dynamics are shown in Figure 3.

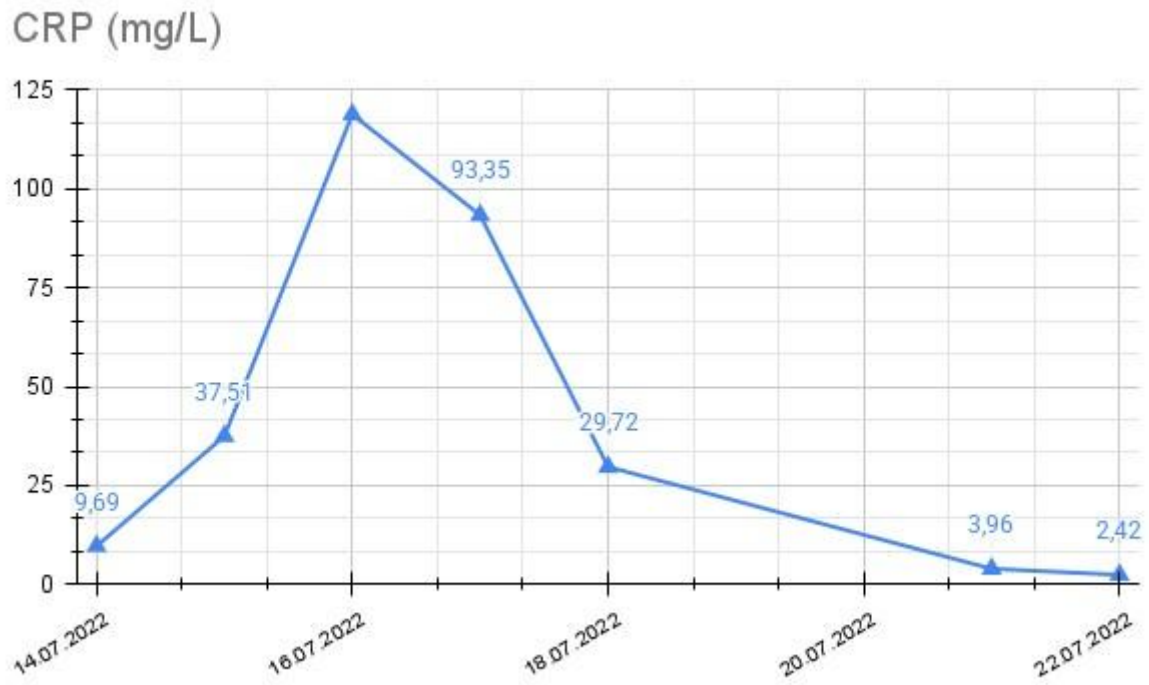

Figure 3. Changes in CRP levels during COVID-19 infection

Clinical course following SARS-CoV-2 infection

Chemotherapy was interrupted for over two months. From September 26, 2022, intensive chemotherapy was resumed without complications, followed by maintenance treatment. Therapy was completed on September 19, 2023. On January 29, 2025, a meningeal relapse of acute lymphoblastic leukemia was diagnosed. The patient was subsequently treated according to the IntReALL 2010 protocol for the standard-risk group and is currently undergoing chemotherapy, having achieved remission.

DISCUSSION

Comparison of COVID-19 course in children with hematologic malignancies and solid tumors

An exploratory systematic review published on January 21, 2021, compared the course of SARS-CoV-2 infection in children with hematologic malignancies and those with solid tumors. The conducted meta-analysis assessed survival outcomes among pediatric oncology patients as well as their hospitalization rates, need for intensive care, and mechanical ventilation [4]. The mortality rate was determined by pooling data from fifteen studies, including 191 young patients. Only one death was recorded—a patient with Burkitt's lymphoma—resulting in an overall mortality rate of approximately 0.6% [4,5,6].

Two studies provided data allowing comparison of hospitalization rates between hematologic and solid tumor patients. Among 29 total patients (16 with hematologic malignancies and 13 with solid tumors), 8 hematologic and 5 solid tumor patients required hospitalization [7,8,9]. Furthermore, three additional studies included data on intensive care unit (ICU) admissions: of 34 hematologic patients, 10 required ICU care, compared with 6 of 25 patients with solid tumors [7,9,10]. Assisted ventilation was necessary in 3 of 22 hematologic patients and 6 of 21 solid tumor patients.

Course of COVID-19 in children with hematologic malignancies

At the Western Ukrainian Specialized Children's Medical Center, an analysis was conducted on 21 cases of COVID-19 among children with hematologic malignancies between March 2020 and May 2021, with a 24-month follow-up period. Among these patients, 15 (71.4%) were diagnosed with acute lymphoblastic leukemia (ALL), 4 (19%) with acute myeloid leukemia (AML), 1 (4.7%) with diffuse lymphoblastic lymphoma (NHL), and 1 (4.7%) with Langerhans cell histiocytosis (LCH). The majority (76%) had mild SARS-CoV-2 infections, 19% were asymptomatic, and one patient (4.7%) developed bilateral pneumonia. These findings are consistent with data obtained in pediatric and adolescent populations without comorbidities [11,12,13,14].

The most frequently reported symptoms were fever (76%), and rhinitis or cough (57%) [32,33,34]. Gastrointestinal symptoms such as abdominal pain and diarrhea were observed in 19% of patients, while 14.3% presented dermatologic manifestations (urticaria, maculopapular rash) [14,15,16,17]. Anosmia occurred in 4.7% of cases, which, together with ageusia, remains one of the most reliable predictors of a positive PCR result in both pediatric and adult populations [18,19,20,21,22]. Interpretation of laboratory findings in this group was challenging due to the variable intensity of chemotherapy, which significantly affected laboratory parameters. Numerous studies confirm the association between severe COVID-19 and the presence of chronic comorbidities, including malignancies, in pediatric patients [11,23,24,25,26,27,28,29,30,31,32].

Situation in Poland

A Polish multicenter retrospective cohort study provided data from 14 domestic pediatric hematology and oncology centers describing the impact of SARS-CoV-2 infection on treatment course and outcomes. The conclusions refer to the period from March 2020 to February 2021, during which approximately 1,200 new childhood cancer cases were diagnosed and around 2,500 patients received chemotherapy. All patients were routinely tested for SARS-CoV-2 upon hospital admission and in cases of suspected COVID-19 [33]. The study demonstrated that, for most pediatric oncology patients, SARS-CoV-2 infection did not lead to severe or life-threatening disease. Nevertheless, data revealed frequent interruptions in anticancer therapy among COVID-19–positive patients, often resulting in delayed chemotherapy or suboptimal treatment. Due to increased susceptibility, since May 2021 vaccination has been recommended for children over 12 years, 3–7 days after chemotherapy, and for patients after hematopoietic stem cell transplantation, according to

guidelines. Vaccination was expected to reduce treatment interruptions and COVID-19–related complications; however, due to the short observation period, definitive results regarding vaccine efficacy are lacking [33,34].

CONCLUSIONS

SARS-CoV-2 infection in immunocompromised pediatric hematology patients undergoing anticancer therapy exerts a measurable impact on the course of treatment of the primary disease. The presented data indicate that COVID-19 infection significantly affects the overall duration of cancer therapy, increasing the likelihood of disease progression and, consequently, worsening prognosis. Furthermore, decreased white blood cell counts resulting from the administration of chemotherapeutic and immunosuppressive agents elevate infection risk and predispose patients to more severe clinical courses.

Summary

A higher risk of severe COVID-19 occurs in immunocompromised patients, particularly those undergoing chemo- and/or radiotherapy. SARS-CoV-2 infection in such individuals frequently leads to interruption of ongoing treatment regimens. The consequences may include difficulties in achieving remission of the primary disease, disease progression potentially leading to death, the need to modify therapeutic protocols, or prolongation of overall treatment duration. The cases of pediatric hemato-oncological patients presented in this study, who contracted COVID-19 during therapy, confirm these conclusions.

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