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Research Article

NEW CORONAVIRUS INFECTION IN A CHILD AT THE AGE OF 2 YEARS 4 MONTHS WITH ACUTE LYMPHOBLASTIC LEUKEMIA (FATAL CASE)

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Children get sick less often than adults with a new coronavirus infection (in the Russian Federation, they account for 7.6% of registered cases of COVID-19), with less severe clinical symptoms, they require hospitalization less often, their disease is milder. The frequency of severe and extremely severe cases of COVID-19 in children does not exceed 1%. A clinical case of the course of COVID-19 in a child aged 2 years 4 months is presented. with acute lymphoblastic leukemia. A feature of the presented case is the development of an extremely severe new coronavirus infection in a child with secondary immunodeficiency caused by a long-term course of malignant, treatment-resistant of acute lymphoblastic leukemia. Slow, within 3 months, the development of the infectious process with long-term preservation of normal indicators of the function of the respiratory system led to the formation of viral-bacterial pneumonia with the development of respiratory distress syndrome. Despite the modern complex of therapeutic measures, severe comorbidity led to the development of DIC and multiple organ failure, which was the direct cause of the child's death. A possible therapy strategy is discussed in a patient with severe comorbidity against the background of secondary immunodeficiency and long-term persistence of SARS-CoV-2 in the presence of IgG antibodies to SARS-CoV-2 in the blood. For the first time, data on morphological changes in the lungs with a long course of COVID-19 (more than 100 days) in a young child are presented.

Keywords: COVID-19; children; acute lymphoblastic leukemia; death.

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Научная статья

НОВАЯ КОРОНАВИРУСНАЯ ИНФЕКЦИЯ У РЕБЕНКА В ВОЗРАСТЕ 2 ЛЕТ 4 МЕСЯЦЕВ С ОСТРЫМ ЛИМФОБЛАСТНЫМ ЛЕЙКОЗОМ (СЛУЧАЙ С ЛЕТАЛЬНЫМ ИСХОДОМ)

© Д.О. Иванов, Ю.В. Петренко, В.А. Резник, Р.А. Насыров, В.Н. Тимченко, Е.Б. Павлова, Н.В. Павлова, С.Л. Баннова, О.Л. Красногорская, Г.В. Кондратьев, Т.М. Чернова, М.А. Шакмаева, А.С. Чепелев, В.А. Галичина

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Новой коронавирусной инфекцией дети болеют реже, чем взрослые (в Российской Федерации они составляют 7,6 % зарегистрированных случаев COVID-19), с менее выраженной клинической симптоматикой, реже требуют госпитализации, заболевание у них протекает легче. Частота тяжелых и крайне тяжелых случаев COVID-19 у детей не превышает 1 %. Представлено клиническое наблюдение течения COVID-19 у ребенка в возрасте 2 лет 4 мес. с острым лимфобластным лейкозом. Особенностью представленного случая стало развитие крайне тяжелой новой коронавирусной инфекции у ребенка со вторичным иммунодефицитом, обусловленным длительным течением злокачественного, резистентного к терапии острого лимфобластного лейкоза. Медленное, в течение 3 мес., развитие инфекционного процесса с длительным сохранением нормальных показателей функции дыхательной системы привело к формированию вирусно-бактериальной пневмонии с развитием респираторного дистресс-синдрома. Несмотря на современный комплекс терапевтических мероприятий, тяжелая сочетанная патология обусловила развитие синдрома диссеминированного свертывания крови и полиорганной недостаточности, что послужило непосредственной причиной смерти ребенка. Обсуждается возможная стратегия терапии пациента с тяжелой коморбидной патологией на фоне вторичного иммунодефицита и длительного персистирования SARS-CoV-2 при наличии в крови антител класса IgG к этому вирусу. Впервые представлены данные морфологических изменений в легких при длительном течении COVID-19 (более 100 сут) у ребенка раннего возраста.

Ключевые слова: COVID-19; дети; острый лимфобластный лейкоз; летальный исход.

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BACKGROUND

Children get sick less often than adults with the new coronavirus infection (NCI) (in the Russian Federation, they account for 7.6% of registered cases of coronavirus disease 2019 [COVID-19]), with less severe clinical symptoms. They less often require hospitalization and had milder disease. The frequency of severe and extremely severe cases of COVID-19 in children does not exceed 1% [3, 4, 8]. The risk group for severe NCI includes patients with premorbid pathology, particularly acute lymphoblastic leukemia (ALL), which is a malignant disease of the hematopoietic system, characterized by uncontrolled proliferation of a tumor clone from hematopoietic precursor cells of lines of lymphoid differentiation with possible involvement of various organs and systems and lethal outcomes [1, 7, 9–12]. NCI contributes to the worsening of the course of leukemia and unfavorable outcomes [2–6, 8]. This study presents a clinical case of NCI a young child with ALL.

CLINICAL CASE

A boy aged 2 years 4 months was hospitalized in the Department for Children with a NCI of the St. Petersburg State Pediatric Medical University (SPbSPMU) with a diagnosis of U07.1 NCI (COVID-19), with the virus identified; C91.0 ALL, T-IV immunological variant, CD1a(–) TCR(+) without significant chromosomal aberrations, very early isolated bone marrow recurrence, active phase II, refractory course; progression; condition after long-term combination restraining palliative chemotherapy.

From the anamnesis, at aged 1 year 11 months (July 2020), the boy had an increase in the cervical lymph nodes, petechial rash, ecchymosis on the skin of the trunk and extremities, and fever of 38.5°C. He was admitted to in a specialized hospital, where he was diagnosed with ALL, T-IV immunological variant, active phase I. Treatment was started according to the ALL-MB2015 protocol, in the course of which extensive necrotizing mucositis of the gastrointestinal tract, moderate enteropathy, and acute pancreatitis developed. In October 2020, a very early isolated bone marrow recurrence of ALL was diagnosed. According to vital indications, anti-relapse polychemotherapy was prescribed, which was accompanied by post-cytostatic depression of hematopoiesis (leukocytopenia, grade IV neutropenia, grade IV thrombocytopenia, and severe anemia) and complications such as bilateral polysegmental pneumonia (*Pseudomonas aeruginosa* was found in the bronchoalveolar lavage), disseminated blood coagulation syndrome, or disseminated intravascular coagulation syndrome (coagulopathy and plasma D-dimer level up to 17800 ng/mL). Despite the ongoing modern antitumor therapy, in January 2021, the tumor was resistant to the treatment, the patient was recognized as incurable, and restraining palliative and symptomatic therapy was prescribed. During the treatment, certain stabilization of the tumor process was achieved. Septicemia (*P. aeruginosa* was isolated from the blood), high-risk febrile neutropenia, steroid myopathy, acute tumor lysis syndrome, hypoproteinemia, and coagulopathy were detected while hematopoiesis was impaired. Modified chemotherapy was planned, with an attempt of bone marrow transplantation; therefore, on January 18, 2021, a COVID-19 test was performed, a positive result was obtained, and the patient was hospitalized at SPbSPMU.

Upon admission to the SPbSPMU, the child's condition was severe and stable. The patient reacted negatively to examination by crying. His appetite was sharply reduced. His skin was pale yellow, with hematoma in the parietal region at the stage of resolution. No recent hemorrhagic elements were found on the skin and mucous membranes. Multiple peripheral lymph nodes were palpated, including cervical and submandibular nodes, enlarged up to 3 cm in diameter, merging into conglomerates, with the inguinal and axillary nodes up to 1.5 cm. His heart rate, respiratory rate, and saturation (SpO_2) were 128 beats per minute, 24 breaths per minute, and 96%–98%, respectively. The liver protruded by 2 cm below the right costal margin, and the spleen protruded by 2 cm below the left costal margin. According to laboratory data, leukopenia (0.1×10^9/L), anemia (erythrocytes 2.31×10^{12}/L, hemoglobin 61 g/L), and thrombocytopenia (10×10^9/L) were detected, and the coagulogram revealed reduced prothrombin index (up to 66.0%, normal 80%–120%), increased prothrombin time (up to 16.3 s, normal 10.6–14.1 s), INR index (up to 1.9, normal 0.9–1.1), C-reactive protein (45.0 mg/L, normal <5 mg/L), ferritin (1697 μg/L, normal 15.0–120.0 μg/L), and D-dimer (498 ng/mL, normal <250 ng/mL). On week 1, the child continued combined antibacterial, antifungal, and maintenance therapy with the necessary hydration against forced diuresis. The material from the nose revealed P. aeruginosa with multiple resistances to antibiotics.

On day 9 of hospitalization (January 26, 2021, was day 9 of the NCI), a gradual deterioration in the child's condition was noted, with the incidence of vomiting (1–3 times daily), fever up to 39.5°C, worsening ALL (hemorrhagic elements on the skin of the lower extremities and back, severe anemia in blood tests, and thrombocytopenia, with blast cells up to 97%). SpO_2 remained within 98%–99%, and the procalcitonin test result was >0.5 ng/mL. This episode was regarded as another stage in the progression of ALL against the course of a NCI without significant clinical manifestations. According to the case conference, blocks of restraining chemotherapy using anthracyclines and cyclophosphamide were initiated. On day 7, an antitumor effect was obtained in the form of a significant decrease in the blast cell count in the peripheral blood test and an improvement in the patient's well-being. Tolerability of chemotherapy was assessed as satisfactory with compensation for vital functions.

From March 01, 2021, (day 43 of NCI) due to the repeated progressions of ALL, which manifested as an increase in intoxication symptoms, appearance of new hemorrhagic elements (on the skin of the abdomen, back, lower extremities, and mucous membranes of the oral cavity), shortness of breath (respiratory rate up to 32 breaths per minute), an increase in the liver size (+3.5 cm below the right costal margin), spleen (+3.0 cm below the left costal margin), increased stool up to 3–5 times a day, and vital indications, another block of combined chemotherapy was started with the administration of a highly selective reversible inhibitor of 26S proteasome activity, bortezomib. The stabilization of hemogram indicators was again achieved, and against the persistent anemia and thrombocytopenia, blast cells were not detected (a short-term antitumor effect on polychemotherapy was achieved).

On March 12, 2021 (day 54 of the NCI), the child had a fever again (38.4°C–38.6°C), increased intoxication symptoms (asthenia and a pronounced decrease in appetite), and serous transparent discharge from the nose, which could be a manifestation of NCI or induced by the anticancer drug cytarabine. After 4 days (after cytarabine cessation), the discharge from the nose became less abundant, and after a week (March 22, 2021, day 64 of the NCI), they disappeared. In the same period, echocardiography revealed a sharp decrease in the left ventricular ejection fraction and an increase in the blood D-dimer to 584 ng/mL, prothrombin time to 20.1 s, and INR to 2.02 and a decrease in the prothrombin index to 51%. The level of brain natriuretic polypeptide significantly increased (nearly twofold), which indicated that the patient had secondary cardiomyopathy combined with chronic heart failure associated with NCI and anthracycline cardiotoxicity. To arrest cardiotoxic manifestations, symptomatic therapy and metabolic support of the myocardium were performed using phosphocreatine. Against the therapy, stable positive dynamics was obtained with a gradual restoration of the left ventricular ejection fraction to normal values.

From April 1, 2021 (day 74 of the NCI), within 2 weeks, the patient had persistent episodes of fever, and the skin-hemorrhagic syndrome progressed. Blast cells reappeared in the blood (25%), with worsening leukopenia and thrombocytopenia. These manifestations indicated the resumption of ALL progression refractory to treatment. Taking into account the presence of IgG to SARS-CoV-2 in the blood without any specific manifestations of NCI and the absence of absolute contraindications for antitumor therapy, an extended case conference decided another course of cytostatic therapy, except for anthracycline antibiotics. During the treatment, symptoms of stomatitis with bleeding and severe pain occurred rapidly, requiring narcotic analgesics. An increase in the indicators of the acute phase of the inflammatory process was noted, with C-reactive protein of 128 mg/L, ferritin of 2161 μg/L, and D-dimer of 1100 ng/mL. The procalcitonin test result was negative. Bacteriological examination revealed a significant amount of *Klebsiella oxytoca* in the feces and oropharyngeal materials. There was infiltration in the paraorbital areas on both sides, with increasing exophthalmos. Anticancer therapy was terminated.

In the period from April 14 to May 02, 2021 (days 87–105 of NCI), the child's condition worsened; he was febrile, had severe asthenia, and had difficulty getting up independently. The labile psyche became severe, with periodic psycho-emotional outbursts, and he did not sleep well (woke up often). The patient's skin acquired a gray tint, and multiple hemorrhagic elements appeared on the trunk, limbs, and visible mucous membranes. He opened his left eye with difficulty; the upper eyelid swelling worsened, which was regarded as lymphostasis against, most probably, leukemic infiltration of the orbit. His blood pressure, respiratory rate, and saturation were 107/72 mm Hg,

36 per minute, and 98%–99%, respectively. Bone marrow hematopoiesis was impaired, leukopenia worsened (0.3×10^9/L), with a significant increase in blast cells in the peripheral blood (87%), deep thrombocytopenia (7×10^9/L), and erythrocyte count of 1.95×10^{12}/L. After another restraining polychemotherapy, no response was obtained. Therapeutic antitumor options have been exhausted, and the patient had absolute contraindications for specific therapy.

During the entire period of stay in the department, SARS-CoV-2 RNA was detected in the oropharyngeal sample. The patient had persistence of NCI (with periodic fluctuations in high cycles of RNA transcription) with secondary immunodeficiency against the cytostatic therapy and refractory ALL.

IgM antibodies to SARS-CoV-2 were not detected (January 25, 2021, March 10, 2021, and April 30, 2021). IgG antibodies were detected on March 10, 2021, and April 30, 2021, which became a contraindication to the use of specific therapy.

In the sputum test on April 26, 2021, *K. oxytoca*, *Staphylococcus epidermidis*, *Streptococcus viridans*, and *Candida* spp. were detected. Repeated bacteriological examinations of the blood did not reveal pathogenic microorganisms. A procalcitonin test was performed repeatedly, and the result remained negative.

On May 03, 2021 (day 106 of NCI) at 15.30, the condition became extremely worse because of cerebral insufficiency and tonic–clonic convulsions. The child was unconscious (10 points according to the Glasgow coma scale). The radial pulse was weak. His heart rate was up to 180 beats per minute, and his blood pressure was 100/80 mm Hg, with sinus tachycardia in ECG monitoring. Spontaneous breathing was ineffective with bradypnea up to 12 breaths per minute, and SpO_2 decreased to 88%. Tracheal intubation was performed, and the child was transferred to the artificial lung ventilation. On May 04, 2021 at 01:19, a sharp deterioration in hemodynamics was noted, with a decrease in blood pressure to 60/30 mm Hg and tachycardia up to 189 beats per minute with the transition to asystole. Cardiopulmonary resuscitation was started with cardiac compressions, with Aira artificial lung ventilation. Despite the measures taken, it was not possible to restore cardiac activity, and at 01:50, he was pronounced dead.

In the hospital, the patient received complex treatment, including infusion therapy with glucose salt solutions with correction of electrolyte and metabolic disorders, enteral and parenteral nutrition, deterrent chemotherapy (cyclophosphan, etoposide, vincristine, mitoxantrone, bortezomib, idarubicin, methotrexate, 6-mercaptopurine, cytarabine, and dexamethasone), antiviral (acyclovir) therapy, antibacterial (ciprofloxacin, sulfamethoxazole/trimethoprim, linezolid, meropenem, fosfomicin, polymyxin B, vancomycin, tigecycline, cefoperazone/sulbactam, and rifaximin) therapy, antifungal therapy (fluconazole, voriconazole, and caspofungin), transfusions of donor blood components (erythrocyte suspension and platelet concentrate), and intravenous immunoglobulins.

PATHOMORPHOLOGICAL RESULTS

The postmortem examination revealed lung tissue with diffuse atelectasis alternating with small emphysematous enlarged areas and small focal hemorrhages in the dilated interalveolar septa (Fig. 1). Most of the alveoli were stellated, focally filled with serous-fibrinous exudate (Fig. 2), desquamated alveolocytes,

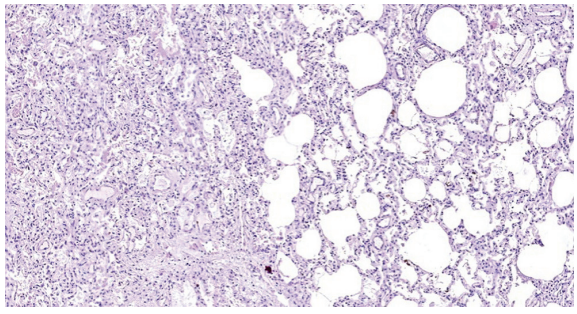

Fig. 1. Alternation of atelectasis with emphysematous altered areas of the lung. Stained with hematoxylin and eosin. Magnification ×100

Рис. 1. Чередование ателектазов с эмфизематозно измененными участками легкого. Окраска гематоксилином и эозином. Ув. ×100

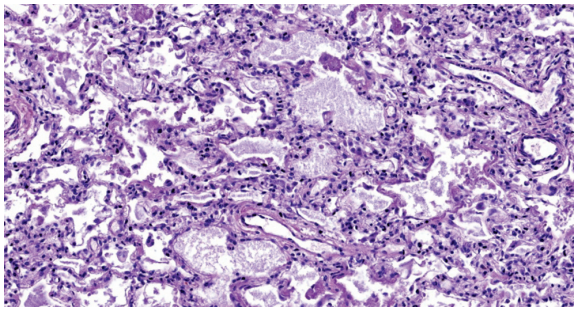

Fig. 2. The alveoli are filled with serous fibrinous exudate. Stained with hematoxylin and eosin. Magnification ×200

Рис. 2. Альвеолы заполнены серозно-фибринозным экссудатом. Окраска гематоксилином и эозином. Ув. ×200

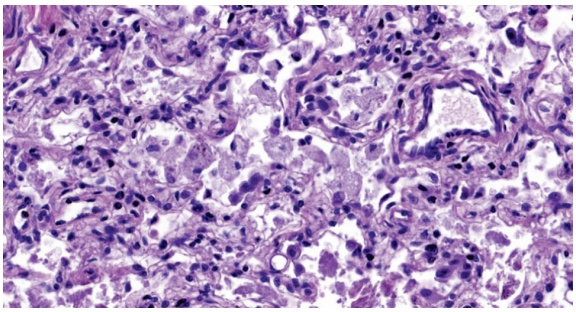

Fig. 3. Alveolar macrophages in the lumen of the alveoli. Stained with hematoxylin and eosin. Magnification ×400
Рис. 3. Альвеолярные макрофаги в просвете альвеол. Окраска гематоксилином и эозином. Ув. ×400

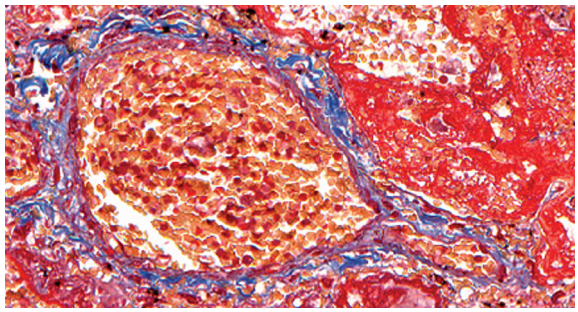

Fig. 4. Part of the alveoli is lined with hyaline membranes. Masson coloring (trichrome). Magnification ×300
Рис. 4. Часть альвеол выстлана гиалиновыми мембранами. Окраска по Массону (трихром). Ув. ×300

and alveolar macrophages (Fig. 3). Part of the alveoli was lined with hyaline membranes (Fig. 4). Microvessels located in the interalveolar septa were round shaped, and fibrin strands were determined in the lumen of most of them. Endothelial cells lining the vessels were swollen, oval in shape, whereas others were more elongated and were not preserved along the entire length of the vessel wall. The medium and larger bronchi were stellated, and the wall was predominantly thickened because of edema and sclerosis of the submucosal layer. The mucous membrane of the bronchi was represented by a cylindrical epithelium with dystrophic changes, desquamated in places, and with a proliferation phenomenon in preserved areas. In the lumen of bronchioles and larger bronchi, desquamated epithelium, single erythrocytes, and macrophages were detected. In addition, predominantly peribronchially, diffuse lymphocytic infiltration with an admixture of a moderate amount of neutrophilic leukocytes, proliferation of connective tissue, and formation of small single lymphoid follicles were noted.

Thus, for the first time, this paper described morphological changes in the lungs with a chronic COVID-19 course (more than 100 days) in a young child with ALL.

CONCLUSION

The case presented is characterized by the development of an extremely severe NCI in a child with secondary immunodeficiency caused by a chronic course of malignant therapy-resistant ALL. The slow development of the infectious process, most probably associated with severe immunosuppression, induced the formation of viral–bacterial pneumonia and respiratory distress syndrome. Despite the complex of modern therapeutic measures, severe comorbidity caused the development of disseminated intravascular coagulation syndrome and multiple organ failure, which became the direct cause of death.

The condition of this patient was repeatedly discussed at extended case conferences with a multidisciplinary approach. Even if the child had palliative ALL status at the time of admission to the infectious diseases hospital, the specialized pediatric oncohematological center offered the possibility of bone marrow transplantation as a salvage therapy, despite the progression of the clonal disease. However, bone marrow transplantation is not possible against the NCI course and at an infectious diseases hospital. The approach for inhibiting the progression of refractory ALL using cytostatics and glucocorticosteroids had an effect on the suppression of active immunological processes characteristic of the SARS-CoV-2 virus, including preventing the development of a cytokine storm, and caused pronounced immunosuppression, which prevented the formation of stable immunity and virus elimination. Thus, IgG antibodies to SARS-CoV-2 detected in the blood at the time of treatment in the infectious diseases hospital limited the use of specific therapy, including donor plasma with IgG antibodies to SARS-CoV-2. For many objective reasons, the use of modern immunobiological drugs was also impossible. Having analyzed this clinical case and summarized global experience, a certain strategy can be formed for managing patients with such comorbidity, i.e., determining the risk ratio of antitumor treatment for a specific malignant neoplasm, taking into account various factors against COVID-19, active use of combined antimicrobial and antimycotic therapy

regimens, accompanying complex and maintenance therapy, timely use of intravenous immunoglobulins, consideration of passive immunization using anti-COVID-19 plasma even if the patient has IgG antibodies to SARS-CoV-2, and active introduction of modern immunobiological preparations into the therapy.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

Competing interests. The authors declare that they have no competing interests.

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Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

REFERENCES

1. Groznova OS, Warriors VA, Donich D, et al. Kawasaki-multisystem inflammatory syndrome in children in the delayed period of coronavirus infection (COVID-19): modern state of the problem and possible new approaches to treatment (plasmapheresis). *Pediatrician (St. Petersburg)*. 2021;12(4):45–57. (In Russ.) DOI: 10.17816/PED12445-57
2. Davydov MI, Gantsev ShKh, Vel'sher LZ, et al. *Onkologiya*. Moscow: GEHOTAR-Media, 2010. 911 p. (In Russ.)
3. Ivanov DO, Petrenko YuV, Reznik VA. *Deti kovidom ne boleyut… Zametki iz krasnoi zony Pediatricheskogo universiteta*. Saint Petersburg: SPbGPMU, 2022. 208 p. (In Russ.)
4. Ivanov DO, Petrenko YuV, Nasyrov RA, et al. Clinical case of COVID-19 course in a child with aplastic anemia. *Journal Infectology*. 2022;14(1):145–151. (In Russ.) DOI: 10.22625/2072-6732-2022-14-1-145-151
5. Ivanov DO, Petrenko YuV, Reznik VA, et al. Characteristics of new coronavirus infection in patients with acute myeloid leukemia. *Clinical Practice in Pediatrics*. 2021;16(3):121–129. (In Russ.) DOI: 10.20953/1817-7646-2021-3-121-129
6. Mazankova LN, Samitova ER, Osmanov IM, et al. COVID-19 and comorbidities in children. *Clinical Practice in Pediatrics*. 2022;17(1):16–23. (In Russ.) DOI: 10.20953/1817-7646-2022-1-16-23
7. Ministerstvo zdravookhraneniya RF. *Profilaktika, diagnostika i lechenie novoi koronavirusnoi infektsii (COVID-19). Vremennye metodicheskie rekomendatsii MZ RF. Versiya 14 (27.12.2021 g.)*. Moscow: Ministerstvo zdravookhraneniya RF, 2021. 232 p. (In Russ.)
8. Chernova TM, Pavlova EB, Timchenko VN, et al. Clinical and epidemiological characteristics and effectiveness of antiviral therapy for COVID-19 in children: The experience of the first year of the pandemic. *Acta Biomedica Scientifica*. 2021;6(6–2):18–28. (In Russ.) DOI: 10.29413/ABS.2021-6.6-2.3
9. Agarwal S, June CH. Harnessing CAR T-cell insights to develop treatments for hyperinflammatory responses in COVID-19 patients. *Cancer Discov*. 2020;10(6):775–778. DOI: 10.1158/2159-8290.CD-20-0473
10. Elzembely MM, Abdelrahman YS, Fadel S, Hafez H. Providing care for pediatric cancer patients in the COVID-19 era: Rapid response recommendations from a developing country. *Pediatr Blood Cancer*. 2020;67(8): e28467. DOI: 10.1002/pbc.28467
11. Hrusak O, Kalina T, Wolf J, et al. Flashsurveyon severe acute respiratory syndrome coronavirus-2 infections in paediatric patients on anticancer treatment. *Eur J Cancer*. 2020;132:11–16. DOI: 10.1016/j.ejca.2020.03.021
12. 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):335–337. DOI: 10.1016/S1470-2045(20)30096-6

СПИСОК ЛИТЕРАТУРЫ

1. Грознова О.С., Воинов В.А., Донич Д., и др. Кавасаки-подобный мультисистемный воспалительный синдром у детей в отсроченном периоде коронавирусной инфекции (COVID-19): современное состояние проблемы и возможные новые подходы к лечению (плазмаферез) // Педиатр. 2021. Т. 12, № 4. С. 45–57. DOI: 10.17816/PED12445-57
2. Давыдов М.И., Ганцев Ш.Х., Вельшер Л.З., и др. Онкология. Москва: ГЭОТАР-Медиа, 2010. 911 с.
3. Иванов Д.О., Петренко Ю.В., Резник В.А. Дети ковидом не болеют… Заметки из красной зоны Педиатрического университета. Санкт-Петербург: СПбГПМУ, 2022. 208 с.

4. Иванов Д.О., Петренко Ю.В., Насыров Р.А., и др. Клинический случай COVID-19 у ребенка с апластической анемией // Журнал инфектологии. 2022. Т. 14, № 1. С. 145–151. DOI: 10.22625/2072-6732-2022-14-1-145-151
5. Иванов Д.О., Петренко Ю.В., Резник В.А., и др. Особенности течения новой коронавирусной инфекции на фоне острого миелобластного лейкоза // Вопросы практической педиатрии. 2021. Т. 16, № 3. С. 121–129. DOI: 10.20953/1817-7646-2021-3-121-129
6. Мазанкова Л.Н., Самитова Э.Р., Османов И.М., и др. COVID-19 и коморбидная патология у детей // Вопросы практической педиатрии. 2022. Т. 17, № 1. С. 16–23. DOI: 10.20953/1817-7646-2022-1-16-23
7. Министерство здравоохранения РФ. Профилактика, диагностика и лечение новой коронавирусной инфекции (COVID-19). Временные методические рекомендации МЗ РФ. Версия 14 (27.12.2021). Москва: Министерство здравоохранения РФ, 2021. 232 с.
8. Чернова Т.М., Павлова Е.Б., Тимченко В.Н., и др. Клинико-эпидемиологическая характеристика и эффективность противовирусной терапии COVID-19 у детей: опыт первого года пандемии // Acta biomedica scientifica. 2021. Т. 6, № 6–2. С. 18–28. DOI: 10.29413/ABS.2021-6.6-2.3
9. Agarwal S., June C.H. Harnessing CAR T-cell insights to develop treatments for hyperinflammatory responses in COVID-19 patients // Cancer Discov. 2020. Vol. 10, No. 6. P. 775–778. DOI: 10.1158/2159-8290.CD-20-0473
10. Elzembely M.M., Abdelrahman Y.S., Fadel S., Hafez H. Providing care for pediatric cancer patients in the COVID-19 era: Rapid response recommendations from a developing country // Pediatr Blood Cancer. 2020. Vol. 67, No. 8. ID e28467. DOI: 10.1002/pbc.28467
11. Hrusak O., Kalina T., Wolf J., et al. Flashsurveyon severe acute respiratory syndrome coronavirus-2 infections in paediatric patients on anticancer treatment // Eur J Cancer. 2020. Vol. 132. P. 11–16. DOI: 10.1016/j.ejca.2020.03.021
12. Liang W., Guan W., Chen R., et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China // Lancet Oncol. 2020. Vol. 21, No. 3. P. 335–337. DOI: 10.1016/S1470-2045(20)30096-6

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