ABSTRACT

Mucormycosis of the lungs is a severe infectious complication in patients with acute lymphoblastic leukemia, which develops at the stage of high-dose cytostatic therapy. It is characterized by an extremely aggressive, rapidly progressive course and, without specific treatment, is fatal in a short time. Reliable verification of mucor is necessary due to its resistance to the most commonly used antifungal drugs, particularly to voriconazole.

The article presents a clinical case of pulmonary mucormycosis in a 12-year-old child at the stage of diagnosis of acute lymphoblastic leukemia. The first symptoms of the disease (headaches, malaise and weakness, pallor), changes in the general blood count (hyperleukocytosis up to 200 thousand cells/μl, single platelets). Based on the results of the examination, the main diagnosis was verified for acute lymphoblastic leukemia L2, IFT T-II, CD1a-. At the stage of diagnosis of acute lymphoblastic leukemia, the underlying disease was complicated by the development of right-sided pneumonia according to X-ray examination. To verify the etiology of infiltration of lung tissue, broncho-alveolar lavage was directed to microbiological diagnostics, which included studies: enzyme immunoassay, microscopic and cultural. On the aggregate of all the results obtained, invasive mucormycosis was diagnosed and antifungal therapy was started immediately.

Keywords:
acute lymphoblastic leukemia, invasive mycosis, oncohematology, mucormycosis, diagnosis of mucormycosis, treatment of invasive mycosis
РЕЗЮМЕ

Мукормикоз легких – тяжелое инфекционное осложнение у больных острым лимфобластным лейкозом, которое развивается на этапе высокодозной цитостатической терапии. Оно характеризуется чрезвычайно агрессивным, быстро прогрессирующим течением и без специфического лечения заканчивается летальным исходом в короткое время. Достоверная верификация мукора необходима в связи с устойчивостью к наиболее часто используемым противогрибковым лекарственным средствам, в частности, к вориконазолу.

В статье представлен клинический случай легочной формы мукормикоза у ребенка 12 лет на этапе диагностики острового лимфобластного лейкоза. Первые симптомы заболевания (головные боли, недомогание и слабость, бледность), изменения в общем анализе крови (ОАК) (гиперлейкоцитоз до 200 тыс. кл/мкл, тромбоциты единичные). По результатам обследования верифицирован основной диагноз острый лимфобластный лейкоз L2, ИФТ Т-II, CD1a-. На этапе диагностики острого лимфобластного лейкоза, основное заболевание было осложнено развитием правосторонней пневмонии согласно рентгенологическому исследованию. Для верификации этиологии инфильтрации легочной ткани на микробиологическую диагностику был направлен бронхо-альвеолярный лаваж (БАЛ). Исследование включало методы: иммуноферментный, микроскопический и культуральный. На совокупности всех полученных результатов был диагностирован инвазивный мукормикоз и начата незамедлительно противогрибковая терапия.

Ключевые слова:
острый лимфобластный лейкоз, инвазивный микоз, онкогематология, мукормикоз, диагностика мукормикоза, лечение инвазивного микоза
RELEVANCE

The continuing increase in the number of infections caused by fungi (micromycetes) remains one of the urgent problems of both global and domestic healthcare. Diseases caused by microscopic fungi (mycoses) have become an urgent clinical problem. Mycoses are a serious danger for people with an immunosuppressive condition. Especially in acute leukemia, taking into account the initial hyperleukocytosis and the development of life-threatening complications against this background, the increasing severity of the patient’s condition, requiring immediate initiation of specific treatment. The optimization of high-tech medicine, the active use of cytostatic and immunosuppressive drugs, the use of broad-spectrum antibiotics in the prevention and treatment have led to an increase in the number of immunocompromised patients with a high risk of developing not only superficial, but also invasive mycotic infectious complications with severe clinical manifestations and very high attributable mortality [1–4].

Invasive mycoses (IM) are a common complication in oncological and hematological patients. The most common pathogen of IM in oncohematological patients is *Aspergillus* spp. Early diagnosis, prevention and treatment with voriconazole significantly reduced the incidence of invasive aspergillosis. At the same time, the frequency of IM caused by mucormycetes (*Rhizopus* spp., *Rhizomucor* spp., *Mucor* spp., *Lichtheimia corymbifera*) and other rare pathogens such as *Fusarium* spp. increased. These and other mucormycetes are resistant to the most commonly used antifungal drugs, in particular, voriconazole. Due to the difficulty of diagnosis (there is no clear picture during X-ray examinations, an invasive procedure is required to obtain a biopsy or bronchoalveolar lavage (BAL), the absence of specific tests to detect antigen or specific antibodies), the number of publications on rare pathogens caused by IM in cancer patients is limited [5–7].

The possibilities of high-tech methods of diagnosis, prevention and treatment are increasing, but at the same time, invasive mycosis remains the dominant cause of infectious mortality in patients with cancer [8–10].

CLINICAL CASE DESCRIPTION

The article presents a clinical case of the pulmonary form of mucormycosis in a child at the stage of diagnosing of acute lymphoblastic leukemia. There is an informed consent of the patient for research.

A 12-year-old patient has been ill since January 2020, when the first symptoms of the disease appeared (headaches, malaise and weakness, pallor) during the examination, changes in the clinical blood count (CBC) were revealed (hyperleukocytosis up to 200 thousand cells / µl, single platelets). To clarify the diagnosis, the child was sent to the SBI of the RO "ODKB" in Rostov-on-Don. According to the results of the examination in the Department of Pediatric Oncology and Hematology with chemotherapy, the main diagnosis of acute lymphoblastic leukemia L2, IFT T-II, CD1a- was verified in the child. At the stage of diagnosis of acute lymphoblastic leukemia, the underlying disease was complicated by the development of right-sided pneumonia. According to the CT scan of the chest organs, infiltration of lung tissue was detected in S8, S9 on the right, located subpleurally with bronchial lumens and a cavity with fuzzy, uneven hyperintensive edges measuring 11 × 4 mm and a hypointensive center of an inhomogeneous structure; areas of centrilobular emphysema in S 1/2 on the right in the basal zone measuring 10 × 7 mm were determined. To verify the etiology of lung tissue infiltration, it was decided to conduct an invasive procedure in order to obtain a BAL. The BAL and blood serum were sent for research to the Laboratory of Clinical Microbiology of the National Medical Research Centre for Oncology of the Ministry of Health of Russia.
Microbiological diagnostics included studies: enzyme immunoassay, microscopic and cultural.

The presence of galactomannan (GM) in blood serum and BAL was determined by enzyme immunoassay using diagnostic test systems (XEMA GalMAg EIA kit, Russia). The GM level was regarded as positive at values ≥ 0.59 OD (optical density). Microscopic examination of BAL was carried out using light and fluorescence microscopy with white calcofluor in order to identify fungal hyphae. The cultural study was carried out by a generally accepted microbiological method. On the first day, the following results were obtained: the level of galactomannan in the blood optical density index (IOP) – 0.12 (negative), in the IOP score – 0.17 (negative). The study using light microscopy did not reveal the pathogen, and with the help of fluorescence microscopy with white calcofluor, an unsepted mycelium branching at right angles was found in the material (Fig. 1).

It’s worth pointing out that during the cultural mycological examination, the result was negative – the absence of growth for 2–5 days.

Thus, based on the totality of all the results obtained, invasive mucormycosis was diagnosed and antifungal therapy (amphotericin At 50 mg/day) was started immediately. Taking into account the positive dynamics on CT two weeks after the start of treatment, they decided to continue antifungal therapy with the rotation of the drug to posaconazole at a dose of 200 mg 4 times a day, lasting up to 2 months. When assessing the child’s condition in dynamics, a month after the start of treatment with MI, a positive effect was noted on CT of the chest organs in the form of a decrease in the focus of inflammation.

CONCLUSION

Mucormycosis is characterized by an extremely aggressive, progressive course with a very rapid destruction of all tissue barriers and, without specific treatment, ends in death in a short time from the moment of the appearance of clinical signs. The causative agents of mucormycosis are resistant to azoles and echinocandides used in clinical practice. It was not typical that the child developed mucormycosis of the lungs in the initial stage of the disease (at the stage of diagnosis) before the use of high-dose cytostatic therapy. The development of pneumonia in immunocompromised patients requires caution in diagnosis in order not to miss mycosis. The results of the current review should help the doctor to establish a connection between the various manifestations of mucormycosis, the corresponding predisposing factors and pathogens.

References


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