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A Case Study of Child with Acute Lymphoblastic Leukemia Treated in Intensive Care

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Abstract

The most common childhood cancer is acute lymphoblastic leukemia, which, thanks to medical progress, achieves up to 95% of complete remission and 80% of cures with appropriate treatment among patients diagnosed with ALL.

A less than three-year-old boy treated for an infectious disease and progressively worsening symptoms was transferred by the Emergency Department to the Department of Hematology and Oncology of Children after revealing leukocytosis and thrombocytopenia. In a short time, the child's condition deteriorated, and it was decided to transfer the patient to the Children's Intensive Care Unit. Due to respiratory failure, the boy was intubated, and mechanical ventilation was started. Catecholamines and sedatives were introduced. Due to increasing edema and anuria, diuretics were administered without diuresis. Hemodialysis was used. In spite of transfused group compatible blood products and exchange transfusion, coagulation disorders occurred. On the tenth day of hospitalization in the intensive care unit, the procedure of confirming brain death was performed.

Both the prevention and treatment of hyperleukocytosis syndrome and the development of treatment methods do not reduce the risk of this syndrome among children diagnosed with acute lymphoblastic leukemia. The determination of permanent and irreversible cessation of brain function is possible only after the proper execution of the procedure for determining brain death.

Key words*: Acute lymphoblastic leukemia, T-cell leukemia, hyperleukocytosis syndrome, neurological disorders, declaration of brain death, brain death, death*

Introduction

Acute lymphoblastic leukemia is considered the most common childhood cancer. The peak incidence of ALL is between 2 and 5 years of age [1–5]. Despite the high progress of medicine, which achieves even 95% of complete remission and as much as 80% of cures with appropriate treatment [2, 6, 7, 8], such a result cannot always be expected. When using anticancer treatment, one should take into account the high risk of complications, including the serious ones, such as hemorrhagic episodes, thromboembolic episodes, systemic disorders, or death [9, 10, 11].

This article describes the case of a child, from the first symptoms, through the diagnosis and treatment due to acute lymphoblastic leukemia, who developed significant hemostatic disorders which led to a quick death.

A case report

Due to the suspicion of otitis, the parents brought their 33-month-old son to the outpatient clinic, where laboratory tests (morphology, iron, IgE, giardia) were performed as a standard. A few days later, swelling of the parotid area appeared on both sides, as well as enlarged retroauricular and cervical lymph nodes, and fever up to 38.2°C. On the first day, tonsillitis was diagnosed, and antibiotics were administered. At the next visit, the child was consulted in the infectious diseases ward and diagnosed with mumps, and the antibiotic was changed. The boy began to be sleepy and lethargic, without fever during the day. In the following days vomiting occurred, and the parents noticed petechiae on the left upper eyelid and a crack in the upper lip. The parents brought the child to the ER, where laboratory tests were performed, showing significant leukocytosis 212,000/ul and thrombocytopenia 84,000/ul. As a matter of urgency, the child with a suspected hematopoietic proliferative disease was referred for further treatment to the Department of Pediatric Hematology and Oncology.

The boy was admitted to the Department of Hematology and Pediatric Oncology in a serious condition, with increasing shortness of breath. On

admission, the child was pale, sleepy, apathetic, dehydrated, with enlarged cervical nodes, with significant hepatosplenomegaly with single petechiae on the mucosa and skin, and with severe abdominal pain. Laboratory test results showed hemoglobin 9.3 g/l, platelets 74,000/µl, leukocytes undetectable in the apparatus, after dilution 1,300,000, lactate dehydrogenase (LDH) 4,900, high uric acid, elevated creatinine, normal urea, elevated liver tests, coagulation disorders, hypoxia with hypercapnia and hypokalemia. Hydration with alkalization and potassium was started, as well as antibiotic therapy; analgesics were administered, and due to the increasing shortness of breath, and shallow and heavy breathing, passive oxygen therapy was implemented.

A chest X-ray was performed (at the Th4 level, the mediastinal shadow was enlarged with nodules, especially on the left side) and an abdominal ultrasound (hepatomegaly, thickened gallbladder wall, spleen enlargement with a polycyclic internal contour or with hypertrophied accessory spleens present), and later, under general anesthesia, also a myelogram and lumbar puncture were performed. This was followed by high non-invasive blood pressure (148/81 mmHg) and anuria; despite being highly hydrated, only small amounts of urine were obtained from the patient. Due to the very serious condition, increasing shortness of breath, life-threatening hyperleukocytosis in the course of T-cell leukemia, and the need to perform a life-saving procedure, i.e., exchange transfusion, it was decided to transfer the child to the Pediatric Intensive Care Unit.

On admission to the intensive care unit, the boy's condition was severe; his breathing was spontaneous with significant respiratory effort on passive oxygen therapy, and shallowing of consciousness was observed. Asymmetric vesicular murmur over the lung fields with numerous wheezes and crackles was also noticed. On the neck, large bundles of lymph nodes were located laterally symmetrically. The oral mucosa was dry with petechiae and hemorrhagic changes. Abdomen was soft with organomegaly. Intestinal peristalsis was audible. The results of additional tests showed massive leukocyturia (717,000), thrombocytopenia, hypokalemia and coagulation disorders (mainly prolonged PT, high d-dimers). The child was intubated, and mechanical

ventilation of the lungs was started. Due to significant coagulation disorders, blood products (FFP, NuRBCz) were transfused, and exchange transfusion was performed according to hematological indications. The procedure was repeated the following day. In the first days, the boy's condition was metabolically and hemodynamically unstable. He required pharmacological support of the circulatory system, kidneys, compensation of electrolyte and coagulological disorders. On the next day, hemodialysis was performed. The incorporation of steroids brought a positive effect in the treatment of leukemia – organomegaly disappeared, and the lymph nodes decreased. Unfortunately, neurological disorders progressed. Sedation and painkillers were discontinued. Despite this, the boy was still unconscious (GCS 3 points). The absence of trunk reflexes and self-respiratory drive was observed. The pupils were equal, wide, and unresponsive to light. Magnetic resonance imaging of the head was performed to establish the diagnosis. The examination showed invagination of the cerebellar tonsils into the foramen magnum and changes suggesting irreversible brain damage. Considering the clinical condition – apnea, areflexia, lack of trunk reflexes, difficulties with maintaining a normal body temperature – brain death was suspected. Preparations for tests confirming the diagnosis were initiated. Two tests were performed that confirmed the suspicion. The child was pronounced dead by the commission, and he was disconnected from the ventilator. The autopsy results confirmed cerebral edema with almost complete softening of the brain tissue and intussusception of the brain stem into the foramen magnum, i.e. changes in the course of acute leukemia.

Discussion

The most common cause of failure in the treatment of acute lymphoblastic leukemia in children is the recurrence of the disease, which occurs in about 20–30% of patients, but death rarely occurs shortly after such a diagnosis is made [14].

Hyperleukocytosis syndrome among patients treated for acute lymphoblastic leukemia occurs in about 9-13% of patients with a white blood cell

count greater than 300,000/µl. The syndrome is more common among male children, as in the case described above [15].

In the course of ALL, the incidence of CNS involvement is more frequent than in the course of acute myeloid leukemia, both in children and adults [11–13]. In the case discussed above, the symptoms that grew the fastest were breathing disorders, shortness of breath (asymmetrical vesicular murmur with numerous wheezes and crackles in the auscultation examination over the lung fields) resulting in shallowing of consciousness. These are the features of hyperleukocytosis syndrome [16]. Later on, in addition to the lungs, other parenchymal organs such as the liver and kidneys became inefficient due to the increased number of white blood cells. In the case discussed, the kidneys ceased to function, which could be observed by anuria, which resulted in the use of hemodialysis. In this case, other characteristic symptoms indicating the occurrence of leukostasis in the child could also be observed, such as: increasing circulatory failure (tachycardia, high blood pressure), central nervous system disorders, and organomegaly [4, 8].

In acute lymphoblastic leukemia, the disease process is the main cause of the increased risk of thromboembolic complications. This is due to the stimulation of the coagulation system [17]. Treatment in intensive care is dictated by quick and often long-term medical assistance to patients diagnosed with an acute or chronic, but also often incurable disease entity. It should be remembered that the indications for hospitalization and the treatment itself at each stage of the disease should not take on the characteristics of persistent therapy. Therefore, children in particular should be protected, as far as possible, from inflicted and prolonged suffering resulting from the disease itself, but also from the applied therapy [18, 19]. Due to the deteriorating clinical condition of the boy, sedatives were discontinued, and despite this, the lack of consciousness, breathing and trunk reflexes persisted, which was confirmed by the results of magnetic resonance imaging of the head.

Establishing brain death diagnosis depends on the patient's age group. The first age group comprises newborns – up to 28 days of age, and the second – children between 29 days of age to the age of 18 years. In the case discussed, it was of course the second age group that was taken into account.

The initial observation time was not less than 24 hours from the moment of finding the basic trunk areflexia. The first stage (initial observation) was performed after the appropriate patient's temperature had been reached (external active heating) due to difficulties in maintaining the proper body temperature. The second stage was attended by a specialist in anesthesiology and intensive care, and a doctor specializing in pediatric neurology, who independently performed the analyses of statements and exclusions twice using the tests confirming trunk areflexia and persistent apnea. Electrophysiological tests (electroencephalography and multimodal evoked potentials/ auditory brainstem response and SEP – somatosensory evoked potentials) and cerebral blood flow tests were performed. Due to the patient's age (below 12 years), computed tomography angiography were not performed. The clinical examination was carried out in accordance with the regulations [18, 19]. Brain areflexia was confirmed on the basis of two examinations, where the following were not observed: pupillary reaction to light, corneal reflex, spontaneous eye movements, eye movements during the caloric test, motor reactions to a pain stimulus, vomiting and cough reflexes, and oculocerebral reflex. At the end of each series of examinations, an apnea test was performed with the use of CPAP using a ventilator. After the stabilization of the partial pressure of carbon dioxide in the arterial blood, a 10-minute ventilation of the patient with 100% oxygen was introduced, and then arterial blood samples were collected for gasometric examination according to recommendations. Before returning to baseline ventilation, an alveolar recruitment maneuver was performed. In the case discussed, and thus in children over 28 days of age, both series (analysis of findings and exclusions and clinical trials) must be performed after the initial observation period at intervals of at least 24 hours (if instrumental tests are not performed), or of at least 3 hours (if instrumental examination was performed). In newborns, instrumental examination does not shorten the period between the series, and it should be 24 hours [18, 19]. After confirming brain death, a Brain Death Protocol is issued and signed by physicians actively participating in the procedure. On the basis of the protocol, a death certificate is then issued [18–20].

Conclusions

Both the prevention and treatment of hyperleukocytosis syndrome and the development of treatment methods do not reduce the risk of the syndrome in children diagnosed with acute lymphoblastic leukemia. It is one of the most serious reasons for patients being transferred to the intensive care unit with a hematological diagnosis, and their death. The determination of permanent and irreversible cessation of brain function is possible only after the proper execution of the procedure for determining brain death.

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