The case of undiagnosed immunodeficiency in child from mother with leukemia anamnesis

OLEXANDR SMIYAN1, MYKOLA LYNDIN2, OKSANA ROMANIUK1, VLADYSLAV SIKORA2, ARTEM PIDDUBNYI2, ALLA YURCHENKO3, ANNA KOROBCHANSKA4, IRYNA TARASOVA1, NATALIA HYRYAVENKO2, KATERYNA SIKORA5, ANATOLII ROMANIUK2

1Department of Pediatrics, Sumy State University, Sumy, Ukraine
2Department of Pathology, Sumy State University, Sumy, Ukraine
3Department of Neurosurgery and Neurology, Sumy State University, Sumy, Ukraine
4Department of Normal Anatomy, Kharkiv National Medical University, Kharkiv, Ukraine
5Sumy Regional Clinical Perinatal Center, Sumy, Ukraine

*Corresponding author: Vladyslav Sikora, MD, PhD; Department of Pathology, Sumy State University, st. Privokzalnaya 31, m. Sumy 40022, Ukraine; Phone: +380 507 276 193, Fax: +380 0542 33 40 58; E-mail: v.sikora@med.sumdu.edu.ua

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Abstract: Acute lymphoblastic leukemia (ALL) in pregnant women is rare experience, but it can complicate the gestation by increasing the risk of miscarriage and premature birth. However, the adequate carrying of the pregnancy is possible for women who suffered from leukemia in childhood and achieved the remission during the treatment. Furthermore, there are some facts about the possibility of immunosuppression in children whose parents suffer from various immunodeficiency disorders, including ALL. This clinical case demonstrates the importance of correct diagnostics in order to reveal the congenital pathologies of the immune system in children, whose parents suffered from lymphocytic leukemia, even in case of full clinical and laboratory remission for a significant period of time. In the hospital, the thread metric approach was used for sepsis diagnostics. Conducted treatment was ineffective due to the inadequate immune response in the child and lack of the targeted adjusted measures to immunodeficiency disorder. The present case demonstrates the congenital T-cells immunodeficiency in a child who was complicated by the development of acute ulceronecrotic enterocolitis after vaccination. The treatment that was targeted mainly at the agent eradication did not give the desired results due to non-responsiveness of the immune system of the child.

Keywords: acute lymphoblastic leukemia, immunodeficiency, vaccination, immune system, spleen, thymus

Introduction

Acute leukemia is a general malignant disease of hematopoietic system that is characterized by clonal proliferation of dedifferentiated, but functionally active progenitor cells and infiltration in various tissues and organs [1, 2]. Furthermore, although different types of leukemia are distinguished according to the type of tumor cells, acute lymphoblastic leukemia (ALL) (the incidence is 1.28 per 100,000 individuals) is the most common among them [3, 4]. According to the world literature, this nosology is found predominantly in children aged between 2 and 5 years, but can also occur in older age. Although ALL refers to dangerous diseases, the survival rate is about 80% in case of appropriate treatment [5].

Inheritance, impact of physical factors, chemical mutagens, and carcinogen viruses are among the main etiological factors of ALL [6, 7]. In majority of the patients, the clinical picture of ALL is specified by tumor infiltration and dysfunction of the affected organs. Thus, the following syndromes can be distinguished: toxic, hyperplastic, immunodeficiency, hemorrhagic, and anemic [8].

ALL in pregnant women is rare experience, but it can complicate the gestation by increasing the risk of miscarriage and premature birth. However, the adequate carrying of the pregnancy is possible for women who suffered...
from leukemia in childhood and achieved the remission during the treatment. Therefore, lately, in question whether the pregnancy is acceptable in young women with long remissions (over 5 years), it is necessary to consider the possibility of recurrence of the disease [9–11].

In case of ALL recurrence, the pregnancy outcome depends on the effective therapy. The treatment is suspended, since the teratogenic effect of the radiotherapy and chemotherapy is more significant in the first trimester of the pregnancy [12, 13].

Despite many scientific advances, there are some facts about the possibility of immunosuppression in children whose parents suffer from various immunodeficiency disorders, including ALL [14]. Due to this, the children with congenital immunodeficiency disorders have the complications after vaccination in the postnatal period [15]. Rather often such complications occur after tuberculous vaccination that can lead to tuberculosis in various organs and systems due to immunodeficiency [16]. Therefore, it is important to conduct strict selection of children for vaccination, especially the infants, whose mother has complicated anamnesis. These children require additional monitoring in the early period of life in order to prevent the infectious complications.

Case Presentation

A 23-year-old female patient X along with 12-day-old baby was hospitalized to neonatal pathology department with the complaints of low appetite, frequent vomiting mixed with bile, constant crying after breast-feeding, significant abdominal distension, and liquid stool with mucus.

The anamnesis showed that a mother was diagnosed the ALL at the age of 16 years. The diagnosis was verified by the bone marrow biopsy. Physical condition improved after polychemotherapy and radiotherapy. During the past 7 years, she was in complete remission stage.

At the age of 22, the pregnancy occurred. Gestation ran smoothly and ended with the child birth at 38th week of pregnancy (weight: 3,280 g, body length: 51 cm, and Apgar score: 8–10 points). Due to satisfactory condition of the newborn and the absence of clinical and laboratory pathologies, the vaccination against hepatitis B (Engerix-B) and tuberculosis (BCG) was conducted according to the immunization schedule. On the 5th day of life, the baby was hospitalized to neonatal pathology department for the treatment of enterocolitis stages 2–3. Dynamic ileus. Distributive shock Stage 1. Sepsis was made.

Treatment included the arrangement of parenteral nutrition, since the enteral administration of food and medication was impossible, as the necrotizing enterocolitis and enteroparesis were suspected. Fluid maintenance was arranged. Pentoxifylline was prescribed for anticytokine effect, Oktaplexes for hemostatic 10.0 (250 IU), Fenamin (5 mg/kg/h) for pain relief and medication sleep; the passive immunization with Pentaglobin was carried out for immunocorrection, when the oxygen saturation was 83%–94%, providing the breathing support of the child for lung ventilation; mode A/C was established.

Causal therapy was prescribed according to the recommendations to neonatal sepsis treatment — Tsefosulbin (100 mg/kg/day), Ampicillin (150 mg/kg/day), Amikacin (15 mg/kg/day), and Fluconazole (12 mg/kg/day). However, on the next day, the child’s condition changed negatively: gastrointestinal hemorrhage occurred, features of acute renal failure, convulsions, coma, and anemia appeared (erythrocytes — 3.5 mmol/L), and hypoglycemia appeared (15 mg/kg/day).

Despite the conducted treatment, the multiple organ failure syndrome developed on the second day of intensive therapy (day 14 of life) that caused the death of the child.
During the postmortem examination, the attention was paid on the dyscirculatory changes in the central nervous, digestive, urethral, cardiovascular, and hematopoietic systems of the body. Vascular congestion and brain edema, cardiac muscle flabbiness, and features of pulmonary edema were observed.

Increased pneumatosis was observed in intestinal tract. Serous membranes of fused small and large intestines were of a dark red color, and fibrin clots were found on their loops. Serous membrane was smoothed and of a dark red color.

The spleen was slightly enlarged, flabby, and the pulp was of purple-red color, which gave the abundant scraping. Thymus was lobulated, of a milky-white color, soft, and elastic, and slightly enlarged. The kidney surface was uneven, the sections were dull, and the drawings of the cortex and medulla were moderately marked.

Histological examination showed the features of perivascular and pericellular brain edema, interstitial inflammation in lungs, heart, liver, and kidneys (stroma of these organs was swollen, densely infiltrated by lymphocytes and macrophages), severe adipose degeneration, small foci of necrosis in cardiomyocytes and hepatocytes, and focal nephronecrosis. Diffuse necrotic changes, severe leukocytic infiltration, and extensive hemorrhage were observed in small and large intestines (Fig. 1A and 1B). The boundary zone between red and white pulps was rather distinct in the spleen. Red pulp was atrophied and white pulp was represented by dense assemblies of lymphoid cells with the features of perivascular T-cells hypoplasia. Thymus lobules were reduced in size, cortex was thinned due to the loss of lymphocytes and reticular stroma collapse, hyperplasia of epithelial reticular cells was observed. The boundary between the cortex and medulla was smoothed. Thymic corpuscles (Hassall’s corpuscles) were relatively numerous, of various sizes, with the presence of pyknotic leukocytes, a significant number of which were in a state of rhexis (Fig. 1C and 1D).

Immunohistochemical study of spleen and thymus tissues was conducted in order to assess the immunological status of dead child. It included the determination of expression of the following receptors: CD3 (T-cells), CD79α (B-cells), and CK-pan (in epithelial cells). The absence of T-cell zones in the spleen around the central arteries and relative spleen follicle hyperplasia (B-cell zone) was determined (Fig. 2).

In thymus tissue (Fig. 3), a well-defined expression of CK-pan in epithelial reticular cells and Hassall’s corpuscles was observed throughout the whole area, depletion of the expression of CD3-receptors (due to T-cells hypoplasia) and single location of CD79α-positive cells (B-cells) revealed.

Final diagnosis was determined based on the results: Basic disease:

1. Ulceronecrotic enterocolitis Stage III, with the localization in jejunum, ileum, and large intestines.
2. Congenital T-cells immunodeficiency disorder.

Basic disease complications include intoxication, gastrointestinal hemorrhage, acute multiple organ failure, brain edema, and pulmonary edema.

Discussion

In the literature, there are some facts [14] about possibility of the development of immunodeficiency disorder in children, born to women with ALL, that makes
Fig. 2. Spleen tissue. Immunohistochemical study of CD3 (A, B) and CD79α (C, D) expression. Magnification: A, C – 100x; B, D – 400x.

Fig. 3. Thymus tissue. Immunohistochemical study of CD3 (A, B), CD79α (C, D), and CK-pan (E, F) expression. Magnification: A, C, E – 100x; B, D, F – 400x.
impossible to conduct vaccination with live-attenuated vaccines (particularly, tuberculosis, poliomyelitis, etc.) in the first days of life and requires monitoring of the immunological status of children [17–19]. Consequently, in case of immunodeficiency, the BCG vaccine strain becomes “paradoxic agent” of opportunistic infection, despite the high quality of national BCG vaccine. When the vaccination is needed, a question of vaccination rescheduling should be solved, inactivated, or reduced doses of vaccine should be used [20–22].

The present case most likely demonstrates the congenital T-cells immunodeficiency in a child (absence of T-dependent zones of the spleen and thymus hypoplasia) that was complicated by the development of acute ulceronecrotic enterocolitis after vaccination. Due to this, the treatment that was targeted mainly at the agent eradication did not give the desired results due to nonresponsiveness of the immune system of the child.

This clinical case demonstrates the importance of correct diagnostics in order to reveal the congenital pathologies of the immune system in children, whose parents suffered from lymphocytic leukemia, even in case of full clinical and laboratory remission for a significant period of time (7 years). In the hospital, the thread metric approach was used for sepsis diagnostics. As a patient had serious infectious and inflammatory lesion (purulo-ulcerous enterocolitis) with signs of systemic inflammatory response, such as leukocytosis $15 \times 10^9/L$ increase in early forms of neutrophils – more $1.5 \times 10^9/L$, toxic granularity of neutrophils, neutrophilic index more than 0.2. Considering the features of multiple organ failure, it was concluded that there was a high threat of sepsis, and the treatment of neonatal sepsis was prescribed as a therapy. Nevertheless, conducted treatment most likely was ineffective due to the inadequate immune response in the child and lack of the targeted adjusted measures to immunodeficiency disorder. It led to acute enterocolitis and hematosepsis resulting in multiple organ failure that caused death.

**Conclusions**

Children who were born to parents with complicated anamnesis on hemoblastosis require timely monitoring of immune status after birth and individual approach to vaccination. In case of infectious diseases, an individual approach to therapy is required, which is focused not only on agent eradication but also on immune correction.

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