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Severe thrombocytopenia and anemia in a child with parvovirus B19 infection (a case report)

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Parvovirus B19 (PVB19) is a common viral pathogen associated with various hematological disorders, particularly in pediatric patients. This case report highlights a rare presentation of severe thrombocytopenia and anemia in an immunocompetent child after PVB19 infection.

Aim – based on a clinical case, analyze the course of severe thrombocytopenia and anemia in a child with parvovirus infection to raise awareness among physicians about hematological complications associated with PVB19.

Clinical case of severe thrombocytopenia in a 3-month-old Ukrainian boy. The disease began with the appearance of a petechial rash after a mild respiratory illness. Before the boy's illness, his two siblings were diagnosed with PVB19 infection. The child had persistent thrombocytopenia and anemia. In blood PVB19 DNA was revealed, positive immunoglobulin (Ig) G to PVB19 was detected. The child received platelet concentrate transfusions, pulse therapy with prednisolone, and immunoglobulin. There was no stable response to treatment. No immunodeficiency or systemic hematological disease was detected. No genetic predictors of anemia were identified. The final diagnosis was established: Acute parvovirus infection, severe course. Acute thrombocytopenic purpura. Anemia of complex genesis, severe form. Complications: Hypofibrinogenemia. The child was discharged home on day 72 with normal levels of thrombocytes and hemoglobin.

Conclusion. Hematological complications determine the severity of the course and prognosis of PVB19 infection. For these reasons, in young children, considering the likelihood of thrombocytopenia and anemia, for timely diagnosis, it is recommended to determine IgM to PVB19 and verify the diagnosis of PVB19 infection. Severe hematological complications, in particular, transient aplastic crisis, develop after 3–4 weeks, so it is essential to monitor the indicators of a complete blood count in children after PVB19 infection.

The study was conducted according to the principles of the Declaration of Helsinki. Parents' agreement has been received for it.

The authors declare no conflict of interest.

Keywords: thrombocytopenia, anemia, parvovirus B19 infection, infectious erythema, children.

Тяжка тромбоцитопенія та анемія у дитини з парвовірусною інфекцією B19 (випадок із практики)

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Парвовірус B19 є поширеним патогеном, що асоціюється з різними гематологічними розладами, особливо в дітей. Висвітлено рідкісний випадок тяжкої тромбоцитопенії та анемії в імунокомпетентної дитини після інфікування парвовірусом B19.

Мета – на підставі клінічного випадку проаналізувати перебіг тяжкої тромбоцитопенії та анемії в дитини з парвовірусною інфекцією для підвищення обізнаності лікарів про гематологічні ускладнення, пов'язані з парвовірусом B19.

Наводимо **клінічний випадок** тяжкої тромбоцитопенії у 3-місячного українського хлопчика. Захворювання почалося з появи петехіального висипу після легкого респіраторного захворювання. Перед тим як хлопчик захворів, у його брата і сестри було діагностовано парвовірусну інфекцію B19. У дитини спостерігалися стійкі тромбоцитопенія та анемія. В крові виявлено ДНК парвовірусу B19 та позитивні IgG до парвовірусу B19. Дитина отримувала переливання тромбоконцентрату, пульс-терапію преднізолоном, імуноглобулін. Стабільної відповіді на лікування не було. Імунодефіциту чи системного гематологічного захворювання не виявлено. Генетичних предикторів анемії не виявлено. Встановлено заключний діагноз: Гостра парвовірусна інфекція, тяжкий перебіг. Гостра тромбоцитопенічна пурпура. Анемія складного генезу, важка форма. Ускладнення: Гіпофібриногенемія. Дитина виписана додому на 72 добу з показниками тромбоцитів та гемоглобіну в межах норми.

Висновок. Гематологічні ускладнення визначають тяжкість перебігу та прогноз парвовірусної інфекції B19. Із цих причин у дітей раннього віку, з урахуванням ймовірності тромбоцитопенії та анемії, для своєчасної діагностики рекомендовано визначати IgM до парвовірусу B19 та проводити верифікацію діагнозу парвовірусної інфекції. Тяжкі гематологічні ускладнення, зокрема, транзиторний апластичний криз, розвиваються через 3–4 тижні, тому необхідно контролювати показники загального аналізу крові в дітей після інфікування парвовірусом B19.

Дослідження виконано відповідно до принципів Гельсінської декларації. На проведення дослідження отримано згоду батьків дитини.

Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: тромбоцитопенія, анемія, парвовірусна інфекція B19, інфекційна еритема, діти.

Cases of parvovirus B19 (PVB19) infection in adults and children have increased in Ukraine, particularly in 2024. PVB19 infection can result in a disease known as infectious erythema (IE), or the «fifth disease» (ICD-10: O98.5). It can be asymptomatic or mild with manifestations of acute respiratory viral infection. The severity of PVB19 infection is determined by the risk of

complications. In some patients, PVB19 infection causes arthralgia and arthritis, and in people with chronic hemolytic anemia – transient aplastic crisis (TAC). Severe anemia, thrombocytopenia, and neutropenia in people with blood disorders or immunodeficiency may result from PVB19 infection [8]. In pregnant women, the virus can cause spontaneous abortion, non-immune hydrops fetalis, and fetal anemia, especially when infected between 9 and 20 weeks of pregnancy. In addition, the pathogen is associated with damage to other organs and systems, namely the heart, liver, nervous system, and kidneys [3].

In childhood, 50–80% of people are infected with PVB19, and the percentage of seropositive adults reaches 70% [1].

Infectious erythema is characterized by the appearance of red erythema on the face (slap symptom), and on the body and extremities – a spotted papular rash, and mesh spots in the form of lace. Exanthema is accompanied by fever, often preceded by moderate catarrhal syndrome [6,9].

The hematologic manifestation of PVB19 infection can occur in the form of TAC. Through the blood group P antigen receptor, the virus infects and destroys erythroid progenitor cells, suppresses erythropoiesis, and leads to acute erythroblastopenia and reticulocytopenia. This is mainly in patients with chronic hemolytic anemia (sickle cell disease, hereditary spherocytosis, thalassemia) or cytopenias (iron-deficiency anemia, immunodeficiency [3].

According to the current classification, thrombocytopenia is a condition in which the platelet count is below 100×10^9/L. In severe thrombocytopenia, the platelet count is below 50×10^9/L [4]. The causes of thrombocytopenia are diverse [12]. A differential diagnosis of primary immune thrombocytopenia and secondary thrombocytopenia should be done. Secondary thrombocytopenia is caused by infections, ethanol abuse, certain medications, and liver disease. Primary immune thrombocytopenia (PIT) in 55% of children was preceded by an infectious disease [11].

Diagnosis of PIT after viral infection requires a thorough evaluation of the patient's history, physical examination, and laboratory data to exclude other causes. Serologic tests are performed to diagnose viral infections, which allow to differentiate PIT from secondary thrombocytopenia [13].

Immune thrombocytopenia in infants and young children has certain clinical features compared to older children. As a rule, in this age group, PIT is acute and self-limiting, with a spontaneous remission rate of approximately 70–80% within the first six months after diagnosis. If the child does not have severe bleeding symptoms, observation is the main approach in management. When treatment is necessary, intravenous immunoglobulin (IVIG) and corticosteroids are used. Differential diagnosis in this age group is crucial, as it is necessary to exclude other causes of thrombocytopenia, such as congenital platelet disorders or infections [13].

The infectious causes of thrombocytopenia are diverse: Epstein-Barr virus (EBV), cytomegalovirus (CMV), influenza viruses, measles, hepatitis C, human immunodeficiency virus (HIV), enteroviruses, herpesviruses of type 6–7, etc. [12]. The pathogenetic mechanisms of thrombocytopenia in patients with PVB19 infection include chronic inflammation, autoantibody production, and molecular mimicry [12].

PVB19 infection is considered one of the triggering factors of PIT. In 6 out of 35 (17%) patients with diagnosed PIT, immunoglobulins (Ig) M to PVB19 were detected. In 6 out of 47 (13%) children with newly diagnosed PIT, PVB19 DNA was detected in the blood [7].

During infection of erythroid cells, the cytotoxic non-structural protein (NS) 1 of the virus can inhibit other cell types. Infection of human bone marrow cells with PVB19 blocks the formation of megakaryocyte colonies, which is associated with a low level of PVB19 genome expression. Other studies have confirmed this low level of expression in non-permissive megacaryoblastoid cells [7].

After acute infection, PVB19 DNA persists throughout life in many tissues, including bone marrow, colon, heart, skin, liver, thyroid, testicles, lymphoid, and synovial tissues [6]. PVB19 is one of the triggers of autoimmune pathology [7]. PVB19 DNA was detected in bone marrow in 2% of healthy people [1].

Aim: based on a clinical case, analyze the course of severe thrombocytopenia and anemia in a child with parvovirus infection to raise awareness among physicians about hematological complications associated with PVB19.

The study was conducted at the Ivano-Frankivsk Regional Children's Clinical Hospital of the Ivano-Frankivsk Regional Council. The clinical examination results, laboratory, and instrumental tests of a 3-month-old child were analyzed. The research was carried out in accordance with the principles of the Declaration of Helsinki. The research protocol was approved by

the Local Ethics Committee of the institution. The informed consent of the child's parents was obtained for the research.

Written informed consent was obtained from the legal guardian to participate in this study and for the publication of any potentially identifiable data included in this article.

Clinical case

The 3-month-old Ukrainian boy fell ill acutely on the 20th of May 2024, when his mother noticed a hemorrhagic rash on the skin of the face, torso, upper, and lower extremities. In 2 weeks (on the 5th of June 2024, Day 16), the boy's mother referred him to the family physician, who examined the child. In the complete blood count (CBC), thrombocytopenia was detected (thrombocytes 20×10^9/L) (Table 1). The child was referred to the regional hospital and hospitalized in the intensive care unit (ICU). Considering clinical and laboratory data (severe thrombocytopenia, hypofibrinogenemia), the diagnosis was made: Acute thrombocytopenia. Hypofibrinogenemia.

A week before the onset of the petechial rash, the child had rhinitis. The mother claims that the child's illness was caused by the fact that her two older children had PVB19 infection, which was confirmed by laboratory tests.

The child was born after the third pregnancy, which was uncomplicated. At 37 weeks of pregnancy, the mother contracted a mild form of COVID-19, confirmed by a polymerase chain reaction (PCR) test. The delivery was on time and without complications. The Apgar score – 10 points. The birth weight is 3200 g. The height is 50 cm. The child was not ill until the age of 3 months. He was on mixed feeding. Vaccinations were carried out according to age.

Objective examination (June 6th, 2024; Day 16): the child's general condition is severe. The body temperature is 36.6°C. The child is active, stretches, and periodically is restless. Body weight is 5600 g. The skin and mucous membranes are moist, pale, single petechiae on the skin of the face, trunk, and extremities. Tissue turgor is preserved. Anisocoria D>S. The large fontanelle is at the level of the skull bones. The oropharynx is not hyperemic, and the tonsils are not visible. Peripheral lymph nodes are not enlarged. Auscultatory breathing is vesicular, respiratory rate is 32/min. The heart rate is 78/min, heart sounds are rhythmic and audible. The abdomen is soft and not painful. The liver is 1 cm beyond the right costal arch; the spleen is not enlarged. Meningeal symptoms are negative. Pathological Babinski reflexes are negative on both sides. There are no seizures. The diuresis is sufficient; the urine color is not changed. The stool is without abnormalities.

To determine the cause of thrombocytopenia, the child underwent additional tests (Table 1).

Biochemical blood test (day 17, 6th June 2024): Total protein – 56.2 g/L; urea – 2.2 mmol/L; creatinine – 38.7 mcmol/L; C-reactive protein – 9.48 mg/L; total bilirubin – 25.2 mcmol/L; direct bilirubin – 10.00 mcmol/L; indirect bilirubin – 15.20 mcmol/L; potassium – 4.20 mmol/L; sodium – 137.4 mmol/L; chlorides – 108.7 mmol/L; glucose – 5.0 mmol/L; calcium – 2.28 mmol/L; alanine transaminase (ALT) – 14 IU; aspartate transaminase (AST) – 28 IU.

Coagulogram (day 17, 6th June 2024): prothrombin time – 13.8 seconds; prothrombin index – 90.5%; international normalized ratio (INR) – 1.16; activated partial thromboplastin time (APTT) - 32.3; fibrinogen – 1.60 g/L; D-dimer – 570 ng/mL.

Stool culture (day 19, 8th June 2024): no pathogenic enterobacteria were detected.

Nasopharyngeal smear culture (day 19, 8th June 2024): no pathogenic microorganisms detected.

The child was consulted by a neurologist: no other neurological symptoms were detected except for anisocoria. The child was examined by an ophthalmologist: OD=OS. Optical media are transparent. Fundus: optic discs are pale pink, monotonous, more pale; borders are clear. Physiological escalation is present. Vessels 2:4. The macula is without abnormality.

The child had persistent two-line cytopenic syndrome (thrombocytopenia, anemia). In this regard, a differential diagnosis was made with autoinflammatory syndrome, Multisystem Inflammatory Syndrome (MIS-C), and viral and bacterial infection – sepsis – was not excluded.

Because of bradycardia of 84–96 beats/min, rapid fatigue of the child during breastfeeding, carditis was suspected. Echocardiographic examination on day 16 (5th June 2024): descending aorta pressure gradient 12 mmHg. Abdominal aorta – pulsatile blood flow. Pericardial layers: separation along the front wall is slit-like. The course of the main vessels is normal. Myocardial walls are not thickened. Contractility is good. Patent foramen ovale is 4.0 mm without overloading of the right heart, tachycardia was noted: heart rate – 177 b/min. Ejection fraction – 64%.

Table 1

Results of CBC performed at the ICU

Day of the illness	Hemoglobin (g/L)	RBC ($\times10^{12}$/L)	WBC ($\times10^{9}$/L)	Thrombocytes ($\times10^{9}$/L)	Basophils (%)	Eosinophils (%)	Band neutrophils (%)	Segmented neutrophils (%)	Lymphocytes (%)	Monocytes (%)	ESR (mm/hour)
Day 16 (5th June 2024)	91	3.73	13.08	single	0	2	2	22	68	6	-
Day 21 (20th June 2024)	101	3.62	5.99	20	0	0	6	49	38	7	5

Table 2

Results of CBC performed at the hematological department

Day of the illness	Hemoglobin (g/L)	RBC ($\times10^{12}$/L)	WBC ($\times10^{9}$/L)	Thrombocytes ($\times10^{9}$/L)	Basophils (%)	Eosinophils (%)	Band neutrophils (%)	Segmented neutrophils (%)	Lymphocytes (%)	Monocytes (%)	ESR (mm/hour)
Day 32 (July 2, 2024)	108	3.54	11.68	48	0	0	2	50	34	13	14
Day 45 (July 15, 2024)	99	3.39	12.2	276	0	0	3	32	58	6	12
Day 48 (July 18, 2024)	96	3.43	8.62	62	0	1	4	18	68	8	6
Day 61 (August 1, 2024)	139	5.13	8.0	139	0	0	8	34	55	5	-

Pulmonary artery valve pressure is 4 mmHg. Tricuspid valve: physiological regurgitation.

As treatment was poorly effective, tests were prescribed to exclude cytomegalovirus, herpes simplex, and parvovirus infections.

Day 29, June 18th, 2024: PCR test of blood: PVB19 DNA was detected; CMV DNA was not detected.

Day 29, June 18th, 2024: Western blot analysis of anti-PVB19 antibodies: antibodies to viral antigen VP1 (anti-VP1) – positive; antibodies to viral antigen VLP (anti-VLP) – doubtful; antibodies to viral antigen VP2 (anti-VP2) – negative; anti-NS1 – negative; Conclusion: Immunoglobulins G (IgG) to PVB19 by immunoblot method are positive.

Day 29, June 18th, 2024: Antinuclear antibodies – 1.3.

Serologic tests (IgG) were positive for the following infections: toxoplasmosis, rubella, and herpes simplex virus type ½. It is explained by transplacental transmission of maternal antibodies and gives grounds to exclude congenital infection.

The following immunological tests were performed to exclude immunodeficiency:

Day 29, June 18th, 2024: Granulocytes – 28.7; Monocytes – 14.9%; Lymphocytes – 56.4%; Lymphocytes – 5.73×10^9/L; Total T-Lymphocytes – 53.2%; T-helpers – 39.0%; T-helpers – 2.24×10^9/L; T- cytotoxic lymphocytes – 12.8%; T-cytotoxic lymphocytes activated – 0.49%; T-helpers / T-cytotoxic lymphocytes – 3,05; Double-Positive T lymphocytes (DPT-L) –0,1%; Double-Negative T lymphocytes (DNT-L) – 1,6%; T-cells with NK-like cytotoxic phenotype (TNK-cells) – 1.9%; Activated T-cells – 1%; ab-T-cells – 98.22%.

Naive T-helpers (CD45+CD4+CD45RA+CD45RO-) 80.73%; Memory T-cells (CD45+CD4+CD45RA- CD45RO+) 13.08%; Activated T-helper cells (CD45+CD4+CD45RA+CD45RO+) – 6.02; Activated T-helper cells (late activation) (CD45+CD4+HLA-DR+) – 0.72; Activated T-helper cells (early activation) (CD45+CD4+25+) – 10.49; Regulatory T-cells (CD45+CD4+CD25brightCD127neg) – 10.7; T-cytotoxic lymphocytes (CD45+CD3+CD4-CD8+) – 0.73; yd-T-cells (CD45+CD3+TcRab-TcRyd+) – 1,55; Total B-lymphocytes (CD45+CD19+) – 43,3%; Total B-lymphocytes (CD45+CD19+) – 2.480%; B1-cells (autoreactive) (CD45+CD19+CD5+) – 19.7%; B2-cells (naive) (CD45+CD19+CD5-CD27-) – 78.6; memory B-cells (CD45+CD19+CD5-CD27+) – 1.7; General NK-cells (LGL) (CD45+CD3-CD16+56+) – 2.3%; General NK-cells (LGL) (CD45+CD3-CD16+56+) – 0.132%.

25-hydroxyvitamin D (25(OH)D) (Day 28, June 17th, 2024): 17.7 ng/mL.

Blood culture (Day 30, June 19th, 2024): negative.

Day 30, June 19th, 2024: Autoantibodies to double-stranded DNA, IgG (ADNA II) – 12.6 (negative); Triglycerides – 0.93 mmol/L (normal).

Day 36, June 25th, 2024: Cryoglobulin – 279 units (normal – 0-16 units).

Day 37, June 26th, 2024: Reticulocytes – 1.8% (normal – 0.2–1.0%).

Urine culture (Day 38, June 27th, 2024): negative.

Results of instrumental examinations

Chest X-ray (day 25, June 14th, 2024). The lung fields are homogeneously pneumatized. The sinuses are empty. The borders of the heart are within normal limits. The distal end of the catheter is in the projection of the superior vena cava.

Chest X-ray (Day 50, July 9th, 2024). Pulmonary fields without clear signs of focal and diffuse changes. The sinuses are empty. The heart shadow is within normal limits.

Ultrasound examination of lungs (day 31, June 20th, 2024). Right lung: the pleural layers are not compacted. The excursion of the visceral pleura is observed between the pleural layers; no fluid is detected in the places accessible for inspection. In the intercostal spaces, single B lines are visualized, up to 3 (normal up to 3). No consolidation foci are detected. Left lung: the pleural layers are not compacted. Excursion of the visceral pleura is observed between the pleural layers; no fluid is detected in the places accessible for inspection. In the intercostal spaces, single B lines are visualized, up to 3 (normal up to 3). There are no foci of consolidation. Conclusion: No signs of interstitial edema, no subpleural consolidation foci were found. Access to the subclavian area is partially restricted. In the places accessible for examination, no additional formations are detected. The blood flow in the subclavian vein at the level of the sternoclavicular junction is not impaired.

Echocardiographic examination (day 31, June 20th, 2024): descending aorta pressure gradient 6 mmHg. Blood flow is pulsating. Pericardial layers are without abnormalities. The course of the main vessels is normal. Myocardial walls are

not thickened. Total contractility is good. Patent foramen ovale is 2.5 mm. Ejection fraction is 64%. Pulmonary artery valve pressure is 4 mmHg.

Multidetector computed tomography of the head (MDCT) (day 25, June 14th, 2024): The examination was performed without contrast enhancement. No bone integrity disorders or bone-destructive changes were detected. The median structures of the brain are not displaced. The differentiation of gray and white matter of the brain is preserved. Spaces containing cerebrospinal fluid are not extended. No additional masses in the brain and orbits were found. Nasal passages are free. Pneumatization of the paranasal sinuses is preserved. The pneumatization of the mastoid cells of the temporal bones and middle ear cavities is unchanged. The auditory ossicles are differentiated.

Neurosonography (day 25, June 14th, 2024): The echogenicity of brain tissue is normal. No displacement of median structures was detected. Gyri and sulci are clear and well-formed. The thalamus and subcortical ganglia have homogeneous, normal echogenicity. The 3rd ventricle is 4.2 mm wide. The 4th ventricle is not dilated. Lateral ventricles: normal. Vascular plexuses: symmetrical, smooth contours, homogeneous structure. The right ventricle is homogeneous, and the contour is clear. Left ventricle – homogeneous, clear contour – Large cistern is normal (5–14 mm). The interhemispheric gap is normal. Subarachnoid spaces along the convexal surfaces: right – 3 mm, left – 3 mm. Subependymal zones – echogenicity is not changed. Periventricular areas – echogenicity slightly increased. Cerebellum – echogenicity not changed, structure preserved.

The child stayed in the ICU for 6 days (from June 6th, 2024, till June 12th, 2024), after that he was transferred to the hematology department with platelets 20×10^9/L.

Results of the CBC during hospitalization in the hematology department are summarized in Table 2.

The child received pathogenetic therapy for immune thrombocytopenia (pulse-therapy with prednisolone for 1 week, with a gradual dose reduction of prednisolone dose to 2 mg/kg/day); intravenous infusion of Ringer's solution, normal saline, and glucose. There was no response to treatment. The thromboconcentrate was transfused.

The intravenous immunoglobulin 10% was administered: 25 mL (1.25 g) on June 6th, 2024, and on June 7th, 2024, 50 мл (2.5 g) – on July 1, 2024. The platelet count increased slightly and remained at 50×10^9/L.

Biochemical blood test July 7th, 2024 (Day 37): iron – 17.26 mcmol/L; ferritin – 177.0 ng/mL; C-reactive protein – 154.5 mg/L (normal <5 mg/L).

Anti-SARS-CoV-2 IgG against the S Protein – >200, this was interpreted as maternal antibodies. PCR from the oropharynx for SARS-CoV-2 DNA was negative.

Immunological blood test (July 12th, 2024 (day 42): IgG – 8,1; IgA – 0,9; IgM – 0,2. IgE total – 15.2 IU/mL. July 18th, 2024 (day 48): IgE total – 3.97 IU/mL; Antinuclear antibodies – 0.5; Potassium – 3.36 mmol/L; folic acid – 17.9 ng/mL; ferritin – 33.2 ng/mL.

Blood group test July 7th, 2024 (Day 37): A (II) Rh (+) – positive.

Coombs test July 12th, 2024 (day 42): negative.

Biochemical blood test (July 31 2024, day 61): Total protein – 72.3 g/L; urea – 1.9 mmol/L; creatinine – 35 mcmol/L; C-reactive protein – 7.17 mg/L; total bilirubin – 13.80 mcmol/L; direct bilirubin – 2.25 mcmol/L; indirect bilirubin – 11.55 mcmol/L; potassium – 4.12 mmol/L; sodium – 135.4 mmol/L; chlorides – 111.3 mmol/L; glucose – 5.1 mmol/L; lactate dehydrogenase (LDH) – 378 U/L; iron – 11.48 mcmol/L; ALT – 24 IU; AST – 29 IU.

Coagulogram (July 31, 2024, day 61): prothrombin time – 11.9 sec; prothrombin index – 105.0%; INR - 0.99; APTT – 24.9; fibrinogen – 2.22 g/L. D-dimer – 180.9 ng/mL.

Immunological blood test (July 31, 2024, Day 61): IgG – 5.8 g/L; IgA – 0.2 g/L; IgM – 0.3 g/L.

Blood test (July 31, 2024, Day 61): Procalcitonin – 1.1 ng/mL.

There was no consistently positive response to pathogenic therapy, so a bone marrow puncture was performed: *Bone marrow aspirate* (July 18th, 2024, day 48): The preparations are hypocellular (all cell lines are proportionally narrowed, the content of lymphocytes is increased, fragments of bone marrow reticulum are not detected). The blast cells are heteromorphic, megakaryocytes of 2–3 stages of maturation, without signs of functioning. Dyspoesis is not expressed. Hemophagocytosis is not detected. Anaplastic cells are not detected.

Immunocytological test July 23rd, 2024 (day 53): No evidence of systemic hematologic disease was found in the material provided. The evalua-

tion of the megakaryocytic germ is inadequate due to the blood in the aspirate. An immunocytologic study of peripheral blood lymphocyte populations may be appropriate.

Myelogram (July 23rd, 2024, Day 53): ***Conclusion:*** Granulocytic cell line is preserved, with signs of dyspoiesis (hypogranularity, vacuolization of the cytoplasm of cells of the maturing and mature granulocytes). The erythroid cell line is narrowed, of normoblastic type. Megakaryocytic cell line is narrowed, single megakaryocytes, microforms are determined, and platelet aggregation in preparations. With a low number of cellular elements in the bone marrow preparation, the preservation of the granulocytic cell line of hematopoiesis with expressed signs of dyspoiesis is determined. The number of monocytes is increased. The relative number of blast cells is 1.0%.

Wiskott–Aldrich syndrome was suspected, but diagnostics were not performed in Ukraine. To identify genetic predictors of anemia, the child was tested in the medical genetics laboratory of the National specialized children's hospital «OHMATDYT». A molecular genetic study was conducted using the method NGS (type of analysis Custom-panel Congenital anemias on the platform Ion GeneStudio S5), result: variants of pathogenic significance identified: gene HFE NM_000410.4 (gene-associated phenotype – hemochromatosis type I), a variant of reconstruction c.187C>G (p.His63Asp), heterozygous status. According to the test results, no genetic predictors of anemia were identified.

Based on complaints, medical history, clinical and laboratory data, the following ***final diagnosis*** was established: Acute parvovirus infection (DNA of PVB16 positive by blood PCR), severe course. Acute thrombocytopenic purpura. Anemia of complex genesis, severe form. Complications: Hypofibrinogenemia.

After examination and treatment, the child was discharged home on day 72 with improved condition under the supervision of a family doctor. At discharge, hemoglobin was 139 g/L, thrombocytes 139×10^9/L.

3 months after discharge from the hospital (Day 107, November 5th, 2024), the overall condition of the boy was good, platelets were 130×10^9/L, hemoglobin 135 g/L, erythrocytes 4.2×10^{12}/L. 5 months later (Day 167, January 2nd, 2025), test results are as follows: thrombocytes 190×10^9/L, hemoglobin 142 g/L, erythrocytes 4.5×10^{12}/L.

Our case is notable for the severe course of acute parvovirus B19 infection in a previously healthy 3-month-old infant, presenting with profound anemia and refractory thrombocytopenia. Given the early age of onset, congenital infection had to be excluded, and immunological testing confirmed the absence of immunodeficiency. The child's thrombocytopenia did not respond to pathogenetic therapy, which argues against primary ITP and supports its secondary nature, triggered by PVB19 infection. The positive ANA test suggests an autoimmune contribution to the hematologic abnormalities.

In our case, the unusually severe thrombocytopenia and lack of treatment response may be associated with age-related immaturity of the immune system in the first six months of life. The elevated antinuclear antibody level further indicates the possible involvement of an autoimmune mechanism in this complication.

In the review by Kerr JR. (2015) cases of thrombocytopenia in patients with PVB19 infection, including those with experimental infection with PVB19, have been described [7]. B19-associated thrombocytopenia can occur in isolation or simultaneously with the involvement of other blood cell lines in children and adults. The incidence of thrombocytopenia in PVB19 infection is higher in immunosuppressed individuals. Thrombocytopenia was detected in 21% of cases among 98 patients with PVB19 infection after kidney transplantation [2,5,7,10].

The frequent hematological manifestations of PVB19 infection are due to the presence of a large number of PVB19 receptors in the bone marrow. Since the infection affects early precursors in the bone marrow (especially erythrocyte precursors), there is a progressive decrease in the production of affected cells until an immune response is formed, neutralizing the virus and restoring bone marrow function. The duration and intensity of hematological manifestations depend on the half-life of the affected precursors, bone marrow reserves, the patient's immune status, and the presence of other hematological diseases. In immunocompetent individuals without bone marrow diseases, the immune response develops 10–14 days after infection, after which bone marrow function is restored. In patients with impaired immune response (e.g., HIV patients) or concomitant hematological diseases (e.g., hemolysis patients), the course of the disease is more severe, with prolonged vire-

mia, expressed bone marrow dysfunction, leading to delayed bone marrow recovery and corresponding clinical consequences [1].

Although PVB19 infection is mostly asymptomatic in immunocompetent patients, it can manifest as ITP. PVB19 can trigger thrombocytopenia through two mechanisms: central and peripheral. Central thrombocytopenia is associated with PVB19 suppression of bone marrow through the NS1 protein, which inhibits megakaryocytic colony formation. Whereas peripheral thrombocytopenia is an immunological phenomenon explained by antiplatelet antibodies, leading to platelet sequestration in reticuloendothelial organs [1].

Conclusion

Hematological complications determine the severity of the course and prognosis of PVB19 infection. For these reasons, in young children, considering the likelihood of thrombocytopenia and anemia, for timely diagnosis, it is recommended to determine IgM to PVB19 and conduct a PCR test to verify the diagnosis of PVB19 infection.

Severe hematological complications, in particular, TAC, develop after 3-4 weeks, so it is essential to monitor the indicators of a complete blood count in children after PVB19 infection.

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