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Parvovirus B19 as a cause of transient aplastic anemia – case report

Parwowirus B19 jako przyczyna przejściowej anemii aplastycznej
– opis przypadku

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Streszczenie

Przedstawiamy przypadek 6-letniego chłopca z nabytej postaci anemii aplastycznej i spontaniczną remisją choroby.

INTRODUCTION
Aplastic anemia is an extremely rare type of anemia, especially in children. It is a result of bone marrow failure caused by various factors (1-3). Hypoplasia or total bone marrow aplasia can manifest lack of isolated single cell line (red blood cell, myeloid or platelet) or complete all three of its accompanying peripheral blood pancytopenia (1-3). The lack of normal hematopoietic system may be due to the depletion of stem cells, and/or to the decrease their capacity for renewal and differentiation of hematopoietic cells of individual rows. In a typical clinical picture they are: pale skin and mucosal, tachycardia, signs of bleeding diathesis (petechiae, ecchymosis, mucosal bleeding) and recurrent or difficult treating infections. Symptoms may increase gradually over many months or occur suddenly. Bone marrow aplasia may be either congenital or acquired. The most common congenital disorders of hematopoiesis include: Fanconi anemia, Diamond Blackfan anemia, dyskeratosis congenital, Shwachman-Diamond
syndrome and severe congenital neutropenia, which occur at different times after birth (1-3).

Acquired AA in children is diagnosed after excluding congenital marrow failure usually between 6 and 9 years of age, rarely younger than 3 years of age. The cause of acquired AA is unknown in about 50-70% of cases, but activation of the immune system or bone marrow cells directly by damaging, may be initiated by viral, bacterial, exposure to chemical and physical agents (drugs, chemical compounds, toxic, radiation) (1-4).

One of infectious agents causing aplasia bone marrow comes from a family *Parvoviridae*, genus *Erythroivirus* – Parvovirus B19 (B19V). Research on adults and children with AA suggests a significant association of this infection with the development of aplasia (5-8).

Here we present a boy with aplastic anemia due to parvovirus B19 infection.

**CASE REPORT**

The six-year-old boy was admitted to a local pediatric unit with thrombocytopenia. Before the hospitalization he had suffered from an acute respiratory tract infection. The symptoms had included fatigue, cough, runny nose and sub febrile temperature. The medical history, physical examination and blood count indicated the immune thrombocytopenia. The treatment included an intravenous immunoglobulin G infusion at a total dose of 2 g/kg bodyweight. Moreover the boy was being treated with antibiotic (cefuroxime) due to the respiratory infection. Initially the platelet count (PLT) increased from 3 × 10^9/L to 45 × 10^9/L. After several days the platelet count suddenly decreased to 6 × 10^9/L and the normocytic anemia, leucopenia with neutropenia appeared. The child was transferred to the Hematology and Oncology Department because of the suspicion of a cancer. During hospital admission the boy was in a good general condition and without sings and symptoms of bleeding. The physical examination showed no abnormalities except several bruises on the legs and the upper respiratory tract infection. The laboratory studies produced a pancytopenia. The white blood count (WBC) was 1.03 × 10^9/L, neutrophil count (ANC) 0.5 × 10^9/L, hemoglobin level (Hb) 10.0 g/dl, red blood cell count 3.69 × 10^{12}/L and PLT 32 × 10^9/L and reticulocyte count 2 promiles. The C-reactive protein level was low. Both the lactate dehydrogenase activity and the uric acid concentration were low. No disturbances of iron, folic acid and B12 vitamin metabolism were detected. There were no significant abnormalities in the chest X-ray, mediastinum and abdomen ultrasound. There were significant changes in the boy’s blood smear, and that is: red blood cells anisocytosis and poikilocytosis and Pelger-Huet anomaly. The boy was twice subject to the bone marrow aspiration. At the beginning we observed a aplastic (fig. 1), then after 2 weeks a hypocellular marrow (especially low granulocyte and megakaryocyte count). In the bone marrow trepanobiopsy we found hypocellularity (only 15% cells, mainly red blood cells). It was characteristic feature of the severe bone marrow aplasia. In the cyto genetic examination we excluded the hipoplastic phase of the myelodysplastic syndrome. During several next days we carried out wide virological examination. We excluded the hepatitis B and C virus, Ebstein-Barr virus, human immunodeficiency virus, cytomegalovirus infection. We found the high antibodies IgG titre of parvovirus B19 using ELISA test. This was probably evidence for the infection with the parvovirus B19, which had taken place several weeks before the incidence of thrombocytopenia. During the hospitalization there was the necessity of platelet transfusion on two occasions because of the platelet count under 20 thousands per microliter and the epistaxis. The antibiotic therapy was continued. Moreover the boy was treated with Clonamine and Rutinoscorbin. After several days there was some improvement. The patient was discharged. He was monitored periodically and the trend was upward. After two months from the hospital admission the improvement was significant: WBC was 3.7 × 10^9/L, ANC 1.9 × 10^9/L, Hb 12.0 g/dl, RBC 4.14 × 10^{12}/L and PLT 133 × 10^9/L and reticulocyte count 14.5 promiles. We gave up next marrow aspiration because of a blood count improvement and a good general condition. These days (after six months) the blood count is normal and the boy is in remission of the aplastic anemia.

Parvovirus B19 infection is global, due to the widespread presence of IgG antibodies in the serum of patients from Europe, North America and Asia (9-11). Most often in patients with acute B19V infection have no symptoms at all or are mild flu-like symptoms. In children, it causes symptoms of erythema infectious called “fifth disease”. A red rash first appears on the cheeks and often spreads to the arms, legs, and trunk of the body within a few days. **Fig. 1. Peripheral blood smear**

In adults acute B19V infection giving lymphadenopathy, malaise, fever, joint pain and rare myocarditis (9-11). In patients with chronic hematological such as: hereditary spherocytosis, sickle cell anemia, thalassemia acute infection with this virus results in transient aplastic crisis (12-15).
Also in patients without any chronic disorders transient or permanent marrow aplasia may occur. Experimental studies have shown that infection in healthy volunteers can lead to anemia and neutropenia and thrombocytopenia (16, 17).

B19V has a particular tropism for erythroblasts and the ability to infect red blood cell precursors, which directly translates into retikulocytopenia peripheral blood. This pathogen has an affinity for erythroid progenitor cell lines by binding to the surface glycoprotein Gb4 erythroblasts (VP2). In contrast, the NS1 protein genitor cell lines by binding to the surface glycoprotein.

The result of this mechanism could be the onset bone by the action of cytokines induced by the infection. The result of this mechanism could be the onset of hemophagocytic syndrome, pancytopenia with marrow hypoplasia and aplasia (1). The second hypothesis is based on the immunological damage to the individual cell lines in the bone by the action of cytokines induced by the infection. The result of this mechanism could be the onset of hemophagocytic syndrom, pancytopenia with marrow hypoplasia and aplasia (1). Achieving remission after use of immunosuppressive therapy, may confirm this mechanism. There is no specific treatment of this infection beyond the administration of immunoglobulins Ig G, which can reduce the viral replication.

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Mishra et al. detected the presence of immunoglobulin IgM and B19V DNA in 40.7% of adults patient with aplastic anemia (6). In the paediatric population with AA also statistically more often the presence detection infection with B19V compared to healthy children (7, 8). Gupta et al. B19V showed a B19V infection in 18 of 66 children with AA (27.2%), which was significantly higher than in the healthy population of 2.2% (8). Similar data are the result of another a study conducted on a group of 30 paediatric patients with AA in the this infection was found in 20% of patients (7).

There is no specific antiviral therapy B19V infection (9, 10). Intravenous infusions of immunoglobulin IgG (IVIG) are used in immunocompromised patients, but frequently may need to re-applications. IVIG is not recommended for arthritis induced by B19V. The majority of patients who develop aplastic anemia due to infection B19V not receive IVIG and are treated as standard hematopoietic cell transplantation or immunosuppressive therapy with the use of anti-thymocyte globulin (1, 7).

CONCLUSIONS

It seems that the cause transient bone marrow aplasia in our patient could be B19V infection and the administration of immunoglobulin IgG contributed to the rapid spontaneous remission.

BIBLIOGRAPHY