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

### Parwovirus B19 jako przyczyna przejściowej anemii aplastycznej – opis przypadku

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#### Conflict of interest

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None  
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#### Summary

Aplastic anemia is extremely rare type of anemia, especially in children. They are the result of bone marrow failure caused by various factors. 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. Acquired aplastic anemia can be caused by a number of factors, including viruses, EBV, CMV, HIV, varicella zoster, rubella, hepatotropic viruses and parvovirus B19. One of the most common infectious agents causing secondary bone marrow failure from a family *Parvoviridae* is Parvovirus B19. This virus has a particular affinity to erythroblasts and the ability to infect red blood cell precursors, which directly translates into reticulocytopenia peripheral blood. The infection is self-limited and usually after a few weeks the symptoms disappear, and the peripheral blood counts return to normal value.

We present a case 6 years old a boy with spontaneous remission of acquired aplastic anemia.

#### Streszczenie

Niedokrwistości aplastyczne są wyjątkowo rzadkim rodzajem anemii, szczególnie u dzieci. Są wynikiem niewydolności szpiku spowodowanych różnymi czynnikami. Hipoplazja lub całkowita aplazja szpiku może manifestować się izolowanym brakiem jednej linii komórkowej (erytrocytarnej, mieloidalnej lub płytkowej) lub całkowitym wszystkich trzech, z towarzyszącą jej pancytopenią krwi obwodowej. Nabyta anemia aplastyczna może być wywołana przez szereg czynników, w tym wirusy takie jak EBV, CMV, HIV, wirus ospy wietrznej, różyczki, wirusy hepatotropowe oraz parwovirus B19. Jednym z najczęstszych czynników zakaźnych wywołujących wtórną aplazję szpiku jest pochodzący z rodziny *Parvoviridae* parwovirus B19. Wirus ten charakteryzuje się szczególnym powinowactwem do erytroblastów i zdolnością zakażenia prekursorów krwinek czerwonych, co bezpośrednio wpływa się na retikulocytopenię we krwi obwodowej. Infekcja ma charakter samoograniczający się i zwykle po kilku tygodniach objawy ustępują samoistnie, a obraz morfologii krwi obwodowej wraca do normy.

Przedstawiamy przypadek 6-letniego chłopca z nabytą postacią anemii aplastycznej i samoistną 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 Erythrovirus – 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 paediatric 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  $3 \times 10^9/L$  to  $45 \times 10^9/L$ . After several days the platelet count suddenly decreased to  $6 \times 10^9/L$  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 signs 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  $1.03 \times 10^9/L$ , neutrophil count (ANC)  $0.5 \times 10^9/L$ , hemoglobin level (Hb) 10.0 g/dl, red blood cell count  $3.69 \times 10^{12}/L$  and PLT  $32 \times 10^9/L$  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 cytogenetic examination we excluded the hypoplastic phase of the myelodysplastic syndrome. During several next days we carried out wide virological examination. We excluded the hepatitis B and C virus, Epstein-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 Cyclonamine 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  $3.7 \times 10^9/L$ , ANC  $1.9 \times 10^9/L$ , Hb 12.0 g/dl, RBC  $4.14 \times 10^{12}/L$  and PLT  $133 \times 10^9/L$  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 infectiosum 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.

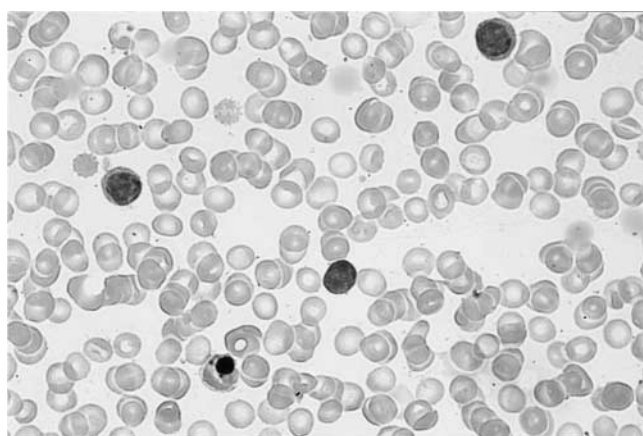


Fig. 1. Peripheral blood smear

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 people 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 reticulocytopenia 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 causes cell death by following the lysis or apoptosis (9, 10, 18). 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 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 hemofagocytic 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 (9, 10).

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.

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