TRANSIENT APLASTIC CRISIS IN THE EVOLUTION OF ACUTE PARVOVIRUS B19 INFECTION IN A PATIENT WITH IRON-DEFICIENCY ANEMIA: A CASE REPORT

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Abstract: *The Parvovirus B19 infection is responsible in children for the fifth disease, also called erythema infectiosum or the slapped-cheek disease. In patients with chronic hemolytic anemia such as sickle-cell disease, spherocytosis, pyruvate kinase deficiency or beta-thalassemia, the parvovirus B19 infection may induce transient aplastic crisis diagnosed by the decreasing of hemoglobin with more than 2g/dL or reticulocytes under 0.2%. The infection in immunocompetent adults is rarely associated with rash, 80% of women present pain in the inter-phalangeal joint of the hands, fist, elbow, knee, occasionally in the cervical and lumbar region and hips, pain that lasts for 2-4 weeks. The Parvovirus B19 infection associated with the first semester of pregnancy may induce miscarriage in 5-10% of cases and hydrops fetalis in the second and third trimester In immunocompromised patients, the parvovirus B19 causes a persistent infection. We report a case of a female patient with aplastic anemia associated with iron-deficiency anemia in the context of parvovirus B19 infection.*

CASE REPORT

Our patient, female Caucasian aged 42, known with iron-deficiency anemia due to repetitive metrorrhagia, anemia that was managed with oral ferrous iron treatment. The patient presents herself to the Infectious Diseases department for a non-itchy maculopapular rash on her trunk and upper limbs with an onset the day before. She began to have pain in her ankles and fists and she had been having occipital headaches for two weeks before her admission into the hospital. The physical examination showed general malaise, paleness, non-itchy maculopapular rash on her trunk and upper and lower limbs, pale mucous membranes; bilateral, painless laterocervical lymph nodes with a diameter of about 1 cm and normal consistency.

Table no. 1. Serum studies

Hemoglobin* (g/dL)	**9.5 – 6.8 – 6.4 – 5.8**
Hematocrit* (%)	32.3 – 24.4 –22.5 – 20.8
MCV* (fL)	66.5 – 62.2 – 63.2 – 66.8
MHC* (pg)	21.1 – 18.5 – 17.7 – 17.8
Reticulocytes (%)	0.32
WBC (/mm^3)	4150
Segmented neutrophils (%)	1
Banded neutrophils (%)	73
Eosinophils (%)	2
Basophiles (%)	1
Lymphocytes (%)	16
Monocytes (%)	6
Limphoplasmocytes (%)	1
Serum iron (µg/dL)	8.9

MCV – mean corpuscular volume, MHC – mean hemoglobin concentration, WBC – white blood cells, * - data presented in dynamics

On admission, she presented a blood pressure of 130/80mmHg, heart rate 84 beats/minute, ventricular extra-systoles and a moderate splenomegaly. Workup included blood test that highlighted in dynamics the exacerbated anemia, which are summarized in table no. 1 (only the pathological results). The pelvic examination confirmed the diagnosis of uterine fibromatosis. Serology for parvovirus B19 was performed, confirming the acute infection, with dynamic growth of IgM to 57.3 U/ml (positive reference value of more than 25 U/ml). The renal and liver functions were normal. Also, the serum ferritin level was normal. The infection with hepatitis A, B, C, human immunodeficiency virus (HIV), cytomegalovirus (CMV), measles and Epstein-Barr virus were excluded.

DISCUSSIONS

Parvovirus B19 was first discovered in 1975 by the Australian virologist Yvonne Cossart.(1,2) It belongs to the *Parvoviridae* family, genus *Erythroparvovirus*. It is a DNA, non-enveloped, icosahedral virus that only measures 23-26 nm in diameter and it is responsible for the fifth disease, also called erythema infectiosum or the lapped-cheek disease. The infection with parvovirus B19 is present in more than 50% of the general population under the age of 15 (3) and has a small incidence in adults. The viral transition is mainly done by the respiratory pathway, but there have been also been described cases of vertical transition.(4) The cellular receptor for B19 is the erythrocyte P (globoside) antigen (5), antigen present on the surface of the erythroid progenitor cells but also in the placenta, myocardial fetal cells, endothelial cells and megakaryocytes; early lysis of erythroid progenitor cells is associated with severe aplastic crisis. Due to the erythroid progenitor cells tropism, especially on pronormoblasts and normoblasts, the cytotoxic action of virus in the host cells induces erythropoiesis suppression during infection, without the possibility of replacement of peripheral erythrocytes with reticulocytes.(5,6) Clinically, the decrease of hemoglobin with 1g/dL does not have repercussions on patients that pass through the infection with parvovirus B19, in the absence of other pathologies such as sickle-cell disease, spherocytosis or thalassemia, in which the decrease of hemoglobin is between 2-6g/dL and leading to aplastic crisis. Recently, there have been described cases of aplastic crisis in previously healthy patients.(7)

The infection with parvovirus B19 has an incubation

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period of 4 to 14 days, sometimes a prolonged one up to 21 days. On the last day of the incubation period and in the first day after the occurrence of the rash, the patient is contagious; for those that developed aplastic anemia – the infectious period extends up to 1 week since onset. The clinical picture in children describes erythema infectiosum (the fifth disease); in adults especially in women, arthropathies, symmetrical arthritis of the interphalangeal joints of the hand and foot, lasting between 1-3 weeks, exceptionally lasting for months, arthritis that can be mistaken for rheumatoid arthritis due to the location and the presence of the rheumatoid factor. The rash in adults might have a purpuric aspect, localized on the hand and foot ("gloves and socks" syndrome).(8) In patients with haemoglobinopathies or hemolytic anemia, the decrease of reticulocytes under 0.1% precipitates the transient aplastic crisis, by transient blocking of the erythrocytes production.(9) In immunocompromised patients due to chemotherapy, immunosuppression therapy or primary or secondary immune deficiency, the parvovirus B19 infection is associated with Pure cell aplasia and chronic anemia. Other manifestations attributable to the infection are: leukopenia, thrombocytopenia (10), Henoch-Schönlein purpura, necrotizing vasculitis (11), Kawasaki disease (12), giant cell arteritis (13), chronic fatigue syndrome (14), hemophagocytic syndrome, myocarditis, pneumonia (15), encephalitis, meningitis (16), ophthalmia. There is no specific antiviral therapy; in immunocompromised patients specific intravenous immunoglobulins are administered, severe anemia is managed with red blood cells concentrates and anti-inflammatory drugs for articular impairment.

Our case is of a woman known with iron-deficiency anemia in whom the infection with parvovirus B19 appeared at the end of July while epidemiologically, the infection is more common for the temperate climate zone in winter or spring. The timeline of the clinical manifestations is unusual: in literature, the onset of the rash is before the articular manifestations, in our case the articular symptoms were present and disappeared 2 weeks prior to the onset of the erythemato-papular rash with a lacy aspect (see figure no. 1). The transient aplastic crisis was associated with iron-deficiency anemia due to metrorrhagia. There was no simultaneous impairment of the leukocyte and megakaryocytic cell lines. In clinical terms, the anemia was relatively well tolerated until the hemoglobin reached the 5.8g/dL, at which point a collapse tendency appeared in orthostatic position and also the heart rhythm disorder – ventricular extra systoles increased.

Figure no. 1. Erythemato-papular rash with a lacy aspect

During the hospitalization period, anti-inflammatory therapy was performed, the patient received 2 red blood cells concentrates, the iron-deficiency was managed with parenteral iron products and continued after discharge for a period of 3 months. One month after the discharge, the blood test highlighted hemoglobin of 12.11g/dL, a MCV 80.73fL and a serum iron of 32 µg/dL.

CONCLUSIONS

Parvovirus B19 infection in association with transient aplastic crisis in adult is not known at its real magnitude, in the cases diagnosed with chronic anemia due to menstruation or repetitive metrorrhagia, as in our case, there is a tendency to accept more easily the etiology of the anemia as a single one. The medical history of the articular impairment, the presence of rash, even without a fever context, should represent enough reasons to check the transition through an acute infection with parvovirus B19.

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