



CASE REPORT

Aplastic crisis in sickle cell anemia induced by parvovirus B19

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Abstract

Objective: we report a case of transient aplastic crisis in an 8-month old child with sickle cell anemia and acute 19 parvovirus infection.

Case report: an 8-month old child with sickle cell anemia was admitted to the hospital with fever, profound anemia (HB = 3.8g/dl), and reticulocytopenia (2%). Transient sickle cell aplastic crisis was diagnosed. Laboratory investigation for the presence of parvovirus B19 (PCR) and anti B19 IgM and IgG (ELISA) resulted in positive PCR and IgM, and negative IgG. The patient required erythrocyte transfusion but presented a favorable evolution, and was discharged from the hospital 4 days later.

Conclusion: the clinical and laboratory features in the present case suggest that human parvovirus B19 was the etiologic agent triggering an aplastic crisis in this 8-month old child. Review of the literature shows that this case of parvovirus-associated aplastic crisis is a rare event, due to the child's age.

J Pediatr (Rio J) 2000; 76(6): 458-60: sickle cell anemia, aplastic crisis, parvovirus infection.

Introduction

Sickle cell anemia is the most frequent inherited hemolytic anemia in Brazil. Basically, sickle cell anemia is characterized by an alteration in hemoglobin synthesis. In this type of anemia, glutamic acid is replaced with valine in position 6 of the globulin beta chain, with formation of anomalous hemoglobin, hemoglobin S.

Sickle cell anemia is a chronic disease, characterized by repeated crises, the most frequent being the vaso-occlusive crisis. There may also be sequestration and aplastic crises.¹ It is a consensus that crises are frequently triggered by a process of bacterial or viral infection. According published reports, aplastic crises in sickle cell are associated with some types of viruses, the most common being the parvovirus B19. However, there are few reports of this association in children younger than 1 year of age. Goldstein et al.,² in a study describing the epidemiology of parvovirus-associated aplastic crises in Jamaican children, reported ages varying from 0.5 to 12.5 years. In Brazil, Cubel et al.³ described the occurrence of aplastic crisis induced by parvovirus B 19 in 2-year-old children with sickle cell anemia and in 3 to 8-year-old children with inherited spherocytosis.

The objective of this work is to report a case of aplastic crisis induced by parvovirus 19 in an 8-month-old patient, stressing the rarity of this occurrence in this age group.

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Case report

A brown 8-month old boy, followed at the Service of Pediatric Hematology at Santa Casa de São Paulo since age 5 months, was diagnosed with sickle cell anemia. He was prescribed folic acid daily and prophylactic benzathine penicillin every 15 days. He presented average hemoglobin levels of 7.5 g/dl and reticulocytes of 10-14%.

The child was admitted to the emergency service of this hospital with a history of high fever (39°C) for 2 days, intense irritability when handled, and severe mucocutaneous pallor.

Upon physical examination, he was in regular general state, and interacted with the environment. The paleness of his skin was striking (+++/4+); he was hydrated, feverish, acyanotic, and anicteric. Weight was 7,500 g, height was 69cm, cf=128 bpm, rf= 36 irpm, axillary temperature= 38.7°C. Oropharynx was normal; we observed diffuse rhonchi; heart with rhythmic, tachycardiac noises, without murmurs; his abdomen presented palpable liver at 1.5 cm from the right intercostal space and palpable spleen at 3 cm from the left intercostal space; nervous system with no alterations; skin without exanthemas; normal ganglionic chains.

The clinical diagnosis at admission was sickle cell anemia crisis and undefined infectious process. He was started on venoclysis with maintenance solution and endovenous ampicillin (100mg/kg/day), following the treatment protocol used in our service.

Laboratory tests were as follows:

Hemogram: V.G. 1.37 million/mm³
 Hb 3.8 g/dl
 Ht 11.1% hypochromia+
 MCV 81 fl microcytosis+
 MCHC 34 g/dl anisocytosis+
 MCH 27 pg presence of falcized erythrocytes+
 reticulocytes 2%
 leuk 9,400/mm³ 1% metamyelocyte
 7% rods,
 57% segmented
 1% monocyte
 2% basophils
 30% lymphocytes
 2% atypical lymphocytes
 platelets 326.000/mm³

Urinalysis: normal.

Chest X-ray: discrete bilateral bronchial infiltrated.

Negative hemoculture.

Negative uroculture.

Based on these results - that is, the decrease in red elements, decreased hemoglobin, and decreased number of reticulocytes - sickle cell aplastic crisis was diagnosed. We then collected samples for serological analysis of parvovirus

B19 (research of antibodies IgM and IgG) using the immunoenzymatic method. The presence of B19 antigens was investigated using the PCR technique. The patient received erythrocyte concentrate and presented a favorable evolution. He was discharged on amoxicillin on the 4th day.

Serology results for parvovirus B19 were positive for the presence of IgM, and negative for IgG. PCR results were also positive. A control sample collected after 30 days showed negative IgM and positive IgG, therefore confirming the diagnosis of transient aplastic crisis induced by parvovirus B19.

Discussion

Infection by parvovirus B19 is associated with several clinical manifestations. In children, one of the most common manifestations is infectious erythema, an essentially benign disease. Parvovirus has also been described as the triggering agent in aplastic crises in patients with hereditary hemolytic anemias, such as sickle cell anemia, spherocytosis, thalassemia, pyruvatekinase deficiency, or glucose-6-phosphate-dehydrogenase (G6PD) deficiency.³⁻⁵ More recently, the virus was also correlated with cases of idiopathic thrombocytopenic purpura.⁶

Parvovirus B19 infection in human beings was initially described in 1975 by Cossart et al.;⁷ later on, in 1981, Patisson et al.⁸ and Serjeant et al.⁹ described the virus as the triggering agent in aplastic sickle cell crises.

Parvovirus B19 is the only member of the Parvoviridae family currently known as pathogenic for human beings. It belongs to the Erythrovirus genus due to its tropism for erythroid cells. It is a DNA virus, whose receptor, globoside (Gb4) or antigen P, a neutral membrane glycosphingolipid, is present in red cells in large amounts. It is also present in other 11 human tissues, which would justify some less usual manifestations of this infection, such as myocarditis, hepatitis, arthritis, and thrombocytopenia. In patients diagnosed with hemolytic anemias, a large viral store is found in the medulla due to the strong medullar hyperplasia. As long as antibodies are not formed in sufficient quantity, there will be re-infection of the erythroid cells, which will lead to the interruption of erythropoiesis.¹⁰

An aplastic crisis in a patient who presents hereditary hemolytic anemia is defined as a transient episode of pure red cell aplasia, with virtual absence of erythroid precursors in the bone marrow and absence of reticulocytes in the circulatory system. Generally, leukocytes and platelets are not affected; however, mild leukopenia and/or thrombocytopenia are sometimes present. Atypical lymphocytes, as described in our patient, and eosinophilia may also be observed.¹¹

The viral incubation period in aplastic crisis may vary from 9 to 17 days. Prodromic symptoms include fever,

distress, pain, and mild respiratory and gastrointestinal symptoms. The presence of exanthema in 23% of the patients is also described; however, it is not always diagnosed because most of the patients with sickle cell anemia are black, which makes its visualization difficult. Decreased hematocrit and severe reticulopenia and anemia follow prodromic symptoms, which on average last 6-8 days. The total course of the disease, from the prodromic symptoms to the reappearance of circulating reticulocytes, lasts from 10 to 12 days.¹¹ The occurrence of parvovirus B19 is more common in winter and spring, which was the case with our patient, and there seem to be peaks of higher incidence every 2 to 3 years.¹² B19 transmission may occur through upper airways, blood byproducts, and, in some cases, through vertical transmission during pregnancy. In the case described, we believe that infection was through the upper airways, since the aplastic crisis appeared when the patient was 8 months old and had not received any blood transfusions for about 3 months.

The prevalence of parvovirus B19 infection in the general population increases with age, varying from 2 to 10% in children younger than 5 years of age and from 40 to 60% in adults older than 20 years of age.¹⁰ In the medical literature, there are few reports describing patients younger than 2 years with aplastic crises induced by parvovirus B19, as in our 8-month old patient. In Brazil, Cubel *et al.*³ described three cases of children with aplastic crisis induced by parvovirus B19: a 2-year-old patient with sickle cell anemia, and two siblings (3 and 8 years old) presenting inherited spherocytosis. However, in a cooperative study with Jamaican children, Goldstein *et al.*² studied 67 cases of this association in children whose ages varied from 0.5 to 12.5 years.

The treatment of B19 infection consists of red blood cell transfusions. In severely immunodepressed patients, commercially available endovenous immunoglobulin may also be used; they are a good source of neutralizing antibodies, since most adults have already been exposed to the virus.¹⁰ The recovery of the medulla begins on average 5 to 10 days after the treatment.

As for the specific etiological diagnosis of parvovirus B19, this may be performed through serologic tests and/or visualization of the virus in tissues and blood. The research of IgM and IgG may be performed through enzyme-immunoassay, radioimmunoassay, or immunofluorescence; the antigen, on the other hand, may be detected by DNA hybridization, PCR, or electronic microscopy.¹² In this work, we carried out serologic studies using the immunoenzymatic method. The result in the acute phase of the disease was positive for IgM and negative for IgG. About 30 days later, a positive result for IgG was observed. The presence of antigen was investigated using PCR, with a positive result, thus confirming parvovirus B19 as the etiological agent trigger the aplastic crisis in our patient.

The present report focused on the importance of parvovirus B19 as the triggering agent in transient aplastic crises in sickle cell anemia. This is underscored by the young age of our patient, since there are few reports of B19 parvovirus infection in children in this age group.

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