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Case report

Molecular and clinical evaluation of the acute *human parvovirus* B19 infection: comparison of two cases in children with sickle cell disease and discussion of the literature

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ABSTRACT

Human parvovirus B19 is a well-known cause of severe conditions in patients with sickle cell disease, but the molecular mechanisms of the infection are insufficiently understood. The different clinical outcome of the acute parvovirus B19 infection in two pediatric patients with sickle cell disease has been examined. One of them developed life-threatening condition requiring emergency transfusions, while the other had asymptomatic infection, diagnosed occasionally. Both cases had high viral load and identical subgenotype, indicating that the viral molecular characteristics play a minimal role in the infection outcome.

Introduction

Human parvovirus B19 (B19V) causes a broad spectrum of clinical conditions, ranging from mild to life-threatening.[1] The acute infection in healthy children leads to *erythema infectiosum*, which is a mild febrile exanthema, but pediatric patients with hemoglobinopathies often develop transient aplastic crisis (TAC).[2] The progression of TAC can lead to severe and even fatal anemia resulting in congestive heart failure, cerebrovascular collapse,[3] and acute splenic sequestration.[4] Myocarditis, arthritis, nephrotic syndrome[5] and fatal bone marrow embolism[6] due to B19V have also been reported in patients with sickle cell disease (SCD).

On the contrary, some SCD patients can develop subclinical B19V infection. The reason why they do not represent clinical symptomatology is obscure, but different factors like aplasia duration and severity, fetal hemoglobin concentrations and

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Table 1 – Changes of the hematological parameters of the examined children during the acute parvovirus B19 infection.

Case report number	Blood parameters	Baseline values	Sample no. 1	Sample no. 2
Case report no. 1	Hemoglobin	11.0 g/dL	10.5 g/dL	10.6 g/dL
	Hematocrit	35%	33%	33%
	Leukocytes	12,300	6700	6500
	Neutrophils	5700	2400	2000
	Lymphocytes	4500	2500	2600
	Platelets	201,000	122,000	201,000
	Reticulocytes	1%	0.3%	1%
Case report no. 2	Hemoglobin	7.8 g/dL	4.4 g/dL	8.1 g/dL
	Hematocrit	26%	14%	28%
	Leukocytes	11,900	18,200	9300
	Neutrophils	6900	2900	4000
	Lymphocytes	3900	14,400	4500
	Platelets	232,000	398,000	434,000
	Reticulocytes	11.27%	0.65%	4.5%

genetic modifiers have been implicated.[7] Moreover, the elevated high substitution rates of B19V have also been regarded as infection modifiers.[8]

This case report comparison examines the contrasting outcome of B19V infection in two children with SCD during a nosocomial B19V outbreak in the Hemotherapy Center of Ribeirão Preto, Brazil. Despite the identical B19V subgenotypes and high viral load, the patients presented different clinical and laboratory pictures. B19V molecular and genotypic features during acute infection were examined.

Case report 1

A four-year-old Afro-Brazilian girl with SCD type SC was subjected to routine blood screening during her visit as an outpatient at the transfusion unit of the Hemotherapy Center of Ribeirão Preto, Brazil (September 3rd, 2010). The patient was asymptomatic and her mother reported no complaints during the past week. The physical examination did not reveal signs of acute infection, such as fever, adenopathy or spleen enlargement.

From the laboratory results (Table 1) three findings were observed: the baseline hemoglobin had stable values (10.5 g/dL, baseline 11.0 g/dL) on the background of a profound reticulocytopenia (0.3% reticulocytes, range 0.66–2.19%) and thrombocytopenia (122×10^3 μL, baseline 201×10^3 μL). B19V was suspected as a cause for the reticulocytopenia, although the patient was asymptomatic. Therefore, the sample was also quantified for B19V by *in-house* developed TaqMan PCR (see Methods). The result was positive with $1.2 \times 10/10$ viral copies/mL, and although hospitalized for two days the patient remained asymptomatic without development of TAC. The patient was anti-B19V IgG negative (OD = 0.115).

One month later (November 10th, 2010), the patient returned to the Hemotherapy center for a medical evaluation. Her mother did not report complaints or indisposition and the physical examination remained unchanged. Nevertheless, a second blood sample was tested for B19V. The result was negative (rapid viral clearance) and the baseline hemoglobin remained unchanged (10.6 g/mL). The platelets and the reticulocytes showed stabilization (Table 1). The phylogenetic analysis of two partial viral genes (VP1 and NS1) revealed that the detected viral isolate belongs to subgenotype 1A of the main genotype 1 (97% bootstrap probabilities for VP1 and 93.6% for NS1, $^{**}p < 0.01$) (Fig. 1A and B).

Case report 2

A 10-year-old boy with $S\beta^0$-SCD suddenly developed serious hypoplastic anemia on November 8th, 2010 and acute B19V infection was suspected. The patient was pale and as the condition deteriorated progressively, he was hospitalized and treated by emergency blood transfusions (10 mL/kg of packed red cells). Additional symptoms included five-day history of pain in the arms and the legs, lethargy and malaise. The day before seeking medical care, the patient had episodes of fever and vomiting. The physical examination showed cervical adenopathy, left upper quadrant tenderness and an enlarged spleen. Post-transfusion, the spleen decreased in size and the blood counts improved.

At the time of the acute infection a blood sample was collected for evaluation of the blood parameters, and for B19V detection. The hematological parameters displayed a significant drop of the hemoglobin (4.4 g/dL), reticulocytopenia (0.65%, baseline 11.27%), lympho- (14.4×10^3, baseline 3.9×10^3) and leukocytosis (18.2×10^3, baseline 11.9×10^3) (Table 1). The B19V TaqMan PCR was positive and demonstrated 1.6×10^7 viral copies/mL. Although, high this viral load was significantly lower than that of case report no. 1. Nevertheless, this patient developed severe TAC, life-threatening anemia and needed emergency transfusions. After blood transfusion, the hemoglobin was stabilized from 4.4 g/dL (November 8th, 2010) to 8.1 g/dL (November 10th, 2010) but the TAC continued approximately one week. In this comparative case, the acute infection was connected with severe anemia, as well as life-threatening drop of the hemoglobin and hematocrit on the background of lymphocytosis, leukocytosis and reticulocytopenia. The serologic detection of anti-B19V IgG at the time of the collection of the molecular diagnosis demonstrated negative result (OD = 0,201 U/mL).

The phylogenetic analysis of partial VP1 and NS1 gene sequences demonstrated that the isolate belongs to subgenotype 1A of genotype 1 (97% bootstrap probabilities by the VP1 and 93.6% by the NS1 gene). This sequence formed one cluster