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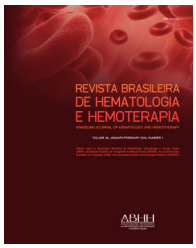

Case Report

Erythrovirus B19 induced persistent bicytopenia in a healthy child

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Introduction

Immune thrombocytopenia (ITP), with an incidence of 3–5 per 100,000 individuals, is diagnosed by exclusion. Erythrovirus B19 (EV19) infection has been reported to be associated with ITP in from 13% to 50% of cases.[1–3] Combined chronic red cell hypoplasia and thrombocytopenia has been rarely reported in otherwise healthy individuals. We report a case of EV19-induced erythroid hypoplasia and thrombocytopenia diagnosed on bone marrow examination.

Case report

An otherwise healthy 4-year-old male child in the month of June presented to us with a history of multiple petechiae and purpura all over his body for three months along with two episodes of melena eight days previously. He had neither history of other bleeding manifestations such as epistaxis, gum bleeding, hematemesis, hematuria, hemoptysis and hemarthrosis, nor were there reports of fever, rash, jaundice, diarrhea, acute abdomen or arthralgia. In addition, no history of recent immunization, drug intake, or transfusions was described. His past history and family history were not significant. On examination, the patient had pallor, petechiae and purpura all over his body. No lymph node enlargement or hepatosplenomegaly was present. His previous investigations from another institution showed a gradual decline in hemoglobin from 12.8 to 8.0 g/dL over a period of one month. His platelet count was low over the entire period ranging from 30×10^9/L to 50×10^9/L.

On routine blood investigation, hemoglobin was 6.6 g/dL. General blood picture revealed normocytic and normochromic red blood cells with no evidence of spherocytes, fragmented cells, schistocytes, polychromatophils or immature cells. The white blood cell count was normal (6.0×10^9/L) along with relative lymphocytosis (58%). The platelet count was markedly reduced to 15.0×10^9 cells/L. His bleeding time was raised to 14 min (by Ivy's method); however, prothrombin time and thromboplastin time were within the normal ranges. His biochemical investigations were also within normal limits including serum urea, creatinine, bilirubin, vitamin B12 and folic acid. Serological tests for human immunodeficiency virus (HIV), hepatitis B and C and Epstein Barr Virus (EBV)

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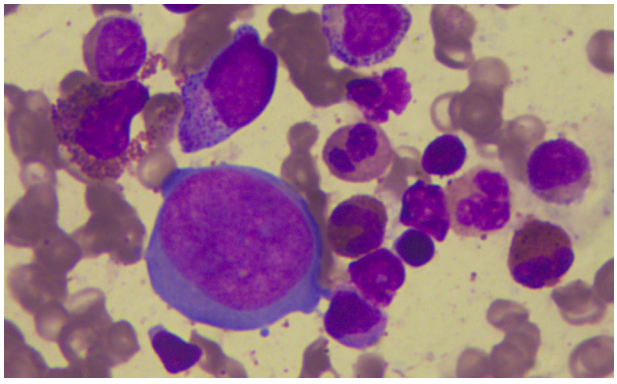

Figure 1 – Bone marrow aspirate (magnification 400×: Leishman stain) giant proerythroblast with intranuclear inclusion and abundant cytoplasm and normal granulocytic precursors.

came out to be negative. Direct antiglobulin test was negative. Reticulocyte count was <1%. Bone marrow aspiration smears were cellular with absolute reduction in erythroid precursors. Granulocytic precursors showed normal morphology and maturation. Giant proerythroblast with prominent intranuclear inclusions and cytoplasmic projections (dog ear) suggested erythrovirus infection (Figure 1). Megakaryocytes were increased in number with numerous cluster formations. Multilobated and hypolobated, and granular and hypogranular forms were seen. However, all of them were non-functional (consistent with ITP). Positive serum immunoglobulin (Ig)M and IgG antibodies against EV19 confirmed our suspicion. A final diagnosis of erythrovirus induced red cell hypoplasia and thrombocytopenia was rendered after detection of erythrovirus DNA by qualitative real time polymerase chain reaction (RT-PCR) using primers for the virion structural protein (VP1). The amplification products were detected on the basis of fluorescent dye labeled probes.[4] The patient was treated with intravenous immunoglobulin (IVIG, 1 mg/kg body weight) approved for use in erythrovirus infections.

Discussion

Yvonne Cossart discovered EV19 (previously called parvovirus B19) in 1974 in London.[5] Infection is most common in late winter and early spring. The virus is transmitted through exposure to respiratory droplets or blood products as well as through vertical transmission from mother to fetus. It is a single stranded DNA virus with marked tropism for erythroid cells via attachment to the globoside P antigen. The antigen is also found on platelets, endothelial cells, cardiac myocytes, and synovium, liver, lung, and kidney tissue. Specificity to infect erythroid lineage may be attributed to preferential expression of the P antigen in erythrocytes and high activity of the viral P6 promoter in these cells.[6]

The clinical manifestations are strongly influenced by the immunological and hematological status of the host. In non-immunocompromised individuals, the infection may range from asymptomatic to mild flu-like illness. The other primary manifestations include erythema infectiosum, arthropathy and hydrops fetalis.[7] Viremia is usually detected 5–10 days after exposure. In a healthy individual, a transient decrease of hemoglobin of up to 1 g/dL may be seen with marked reticulocytopenia during the phase of viremia. Clinically insignificant leucopenia, thrombocytopenia may also be seen. All hematological parameters usually normalize within two weeks. Thus, subclinical erythroid hypoplasia followed by rash or arthralgia is the most common clinical picture in immunocompetent hosts. In immunocompromised hosts, the infection may manifest with aplastic crisis, chronic anemia or ITP.[8] In patients with hemolytic anemia such as sickle cell anemia, EV19 may cause a transient aplastic crisis with sudden drop in hemoglobin. Although the majority of patients recover within two weeks, there is increased risk of congestive heart failure, stroke, and acute splenic sequestration.[9]

Our case was an otherwise healthy child presenting with symptomatic thrombocytopenia and severe normocytic normochromic anemia. Bone marrow examination revealed clues for EV19 infection (Lantern cells) along with megakaryocytic hyperplasia (consistent with ITP). This was further confirmed by positive IgM antibodies (indicating immunocompetency and acute infection). Our case is unique due to persistence of erythroid suppression and immune mediated thrombocytopenia in an otherwise healthy child. Cytokine mediated toxic effects of viral NS-1 (central type) may explain the bi-lineage involvement in this case.[10,11] The second mechanism may be immune-mediated destruction (peripheral type).[12]

Serum IgM antibody testing has 89% sensitivity and 99% specificity.[13] An elevated level of IgM antibodies appears 10–12 days and remains detectable for 3–6 months after acute infection. IgG antibodies presumably persist for life. The diagnostic antibodies are detected against VP1 and VP2 antigens. In immunocompromised hosts, as antibody production is minimal or absent, viral DNA testing by PCR is necessary for diagnosis. PCR is more sensitive than *in situ* hybridization assays.

Our case highlights the importance of the identification of morphological features of EV19 infection. The case also illustrates the variable clinical manifestation of EV19 infection.

Conflicts of interest

The authors declare no conflicts of interest.

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