CASE REPORT

Megaloblastic Anemia Complicated by Parvovirus B19 Induced Erythroblastopenia: A Case Report

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Abstract:

Human parvovirus B19 is a known etiological agent for aplastic crisis in patients with chronic hemolysis and immunodeficiencies. The aplastic state caused in healthy children and adults is usually transient as compared to the more severe form seen in at risk population. Here we present a case of adult immunocompetent male with megaloblastic anemia complicated by aplastic crisis induced by parvovirus B19. A 23 year old male on treatment for megaloblastic anemia, presented with breathlessness, weakness and mild hepatomegaly. Laboratory investigations revealed an Hb-5.7g/dl, reticulocyte count-0.13% and absolute reticulocyte count of $0.00 \times 10^6/\mu L$. His serum vitamin B_{12} levels were 974 pg/ml. Bone marrow studies were done to evaluate the cause. Aspiration smears showed erythroid suppression with large proerythroblasts having vacuolated cytoplasm and eosinophilic intranuclear inclusions (Lantern cells). Biopsy showed proerythroblasts with nucleomegaly, pale chromatin and eosinophilic intranuclear inclusions, morphologically suggestive of parvovirus infection. Parvovirus B19DNA was isolated by TaqMan PCR. Patient was managed by red blood cell transfusion to which he responded well. Aplastic crisis due to parvovirus B19 has been reported in patients with sickle cells anemia, thalassemia, haematological malignancies, transplant recipients and acquired immunodeficiency states. Development of erythroblastopenia due to parvovirus in background of nutritional anemia is unusual. A bone marrow examination in such a scenario helps to exclude causes like myelodysplastic syndrome, lymphoproliferative disorder and provides clues for diagnosis of parvovirus infection which is a treatable etiology.

Keywords: Parvovirus B19, Anemia, Bone Marrow, Erythroid Precursor Cells, Intranuclear Inclusions

Introduction:

Human parvovirus B19 is a single strand DNA virus belonging to the genus Erythrovirus of the family Parvoviridae. It is a known etiological agent for erythema infectiosum (Fifth disease), polyarthropathy syndrome, and rarely hepatitis and myocarditis [1, 2]. The spectrum of a hematological syndrome caused by parvovirus B19 includes transient aplastic crisis in patients with increased erythropoiesis, persistent anemia in patients with immunosuppression, fetal loss due to vertical transmission, and rarely thrombocytopenia, neutropenia, and hemophagocytic syndrome [1, 3]. The spectrum of anemia caused by parvovirus B19 infection ranges from mild with low clinical significance in healthy adults and children; however, it is severe and can become life-threatening in patients with underlying hemolytic disease [2, 4]. Such erythroblastopenia has been widely reported in the literature in patients with hereditary spherocytosis, sickle cell anemia, thalassemia, immunodeficiency syndromes, renal transplant recipients, hematological malignancies,

post-chemotherapy, and bone marrow transplantation [4-9]. We present an unusual scenario of megaloblastic anemia complicated by erythroblastopenia induced by parvovirus B19 in an immunocompetent adult male.

Case Report:

A 23-year-old male presented with complaints of generalized weakness and lethargy, he was found to have anemia (Hb: 11.6 g/dl) with an MCV of 104.4 fl (normal range Hb: 13-17 g/dL, MCV: 83-101 fl). A biochemical assay showed reduced serum vitamin B_{12} levels (114.3 pg/ml) (normal range, serum vitamin B_{12}: 197-1000 pg/ml). The patient was given oral supplements and dietary advice. On follow-up after one-month patient complained of breathlessness, increased weakness, and joint pains. Physical examination revealed pallor and mild hepatomegaly. Complete blood count showed Hb: 5.7 g/dl, along with reticulo-cytopenia (reticulocyte count-0.13 % and an absolute reticulocyte count of 0.00 × 10^6/μL). Serum vitamin B_{12} was normal (974.9 pg/ml) and ferritin was increased (631.2 ng/ml) (normal range, serum ferritin:13-150 ng/ml). Liver function tests revealed raised alanine (ALT: 58 IU/L, normal range: upto 32 IU/L) and aspartate transaminases (AST:60 IU/L, normal range: upto 32 IU/L), but viral markers for Hepatitis B, Hepatitis C, and HIV were negative. Coomb's test and anti-nuclear antibody were negative. He was stabilized with a transfusion of three units of packed red blood cells. Bone marrow studies were done to evaluate anemia. Aspiration smears showed erythroid suppression with giant proerythroblasts having vacuolated cytoplasm and eosinophilic intranuclear inclusions (Fig. 1). Biopsy showed proerythroblasts with nucleomegaly, pale chromatin, and eosinophilic intranuclear inclusions, morphologically suggestive of parvovirus infection (Fig. 2). Bone marrow iron stores were normal and there were no ringed sideroblasts. A TaqMan polymerase chain reaction test was positive for the DNA of parvovirus B19. The patient improved with blood transfusions and had an event-free hospital stay and discharged with a Hb of 12 g/dL and reticulocyte count of 1.2%.

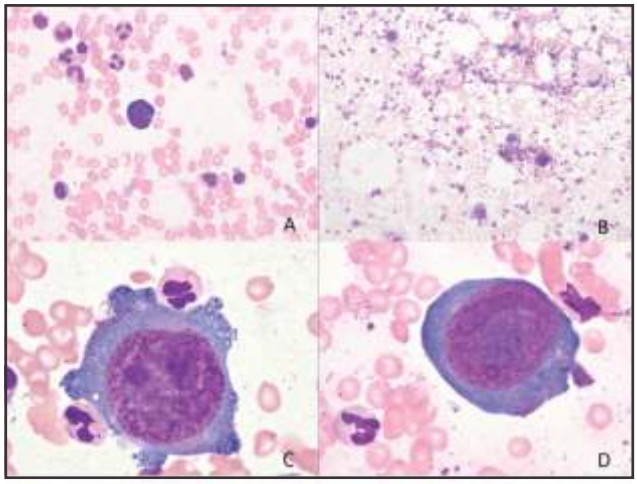

Fig. 1: A) Peripheral Smear Showing Occasional Proerythroblasts, Normal Granulocytes, Lymphocytes and Platelets (Leishman, 400×),B) Bone Marrow Aspirate Smear with Eryhtroblastopenia and Few Giant Proerythroblasts. Other Cells Lines are not Affected (Leishman, 100×),C) Giant Proerythroblast with Intranuclear Inclusion, Cytoplasmic Pseudopodia and Vacuolation, also Referred to as Lantern Cell (Leishman, 1000×),D) Giant Proerythroblast with Cresent Shaped Intranuclear Inclusion (Leishman, 1000×).

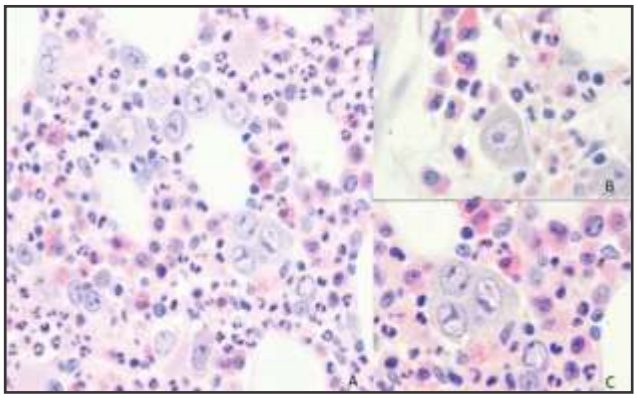

Fig. 2: A) Few Cellular Foci in the Bone Marrow Biopsy with Clustered Giant Proerythroblasts. The Granulocyte Lineage is Preserved (H&E, 400×), B) Giant Proerythroblast with Intranuclear Inclusion (H&E, 1000×), C) A Dyspoietic Tri Nuclear Proerythroblast with Intranuclear Inclusions (H&E, 1000×).

Discussion:

Anemia is the most common hematological manifestation of parvovirus B19 infection. It can range from mild transient form to severe life-threatening forms. Parvovirus B19 shows marked erythroid tropism, owing to the globoside receptors. Globoside is a neutral glycolipid found on the erythroid precursors, where it is referred to as P antigen. Such globoside mediated viral interaction makes the population with P blood group particularly susceptible to infection [1, 2]. In the bone marrow, the replication of parvovirus B19 is dependent on replicating precursors. It shows a particular affinity for the Erythroid Colony-Forming Unit (CFU-E) and Burst-Forming Unit (BFU-E). The pluripotent cells and the Granulocyte and Monocyte Colony Forming Units (CFU-GM) are spared. This selective inhibition of the dedicated erythroid progenitors is the cause of erythroblastopenia in infected patients [3].

The cytopathic effects of the virus include the arrest of the cell cycle in G1 or G2 phase, activation of apoptotic caspases, and the direct toxic effect of the virus. The most characteristic marrow findings include erythroblastopenia along with giant proerythroblasts. Giant proerythroblasts show dark basophilic nuclei, intra-nuclear inclusions, megaloblastoid chromatin, and cytoplasmic pseudopodia are also known as Lantern cells. Other dyserythropoietic forms include bi/multinucleated precursors and intranuclear bridging. The granulocytes and megakaryocytes do not show dysplastic changes [2, 4, 10–12].

Transient Aplastic Crisis (TAC) or erythroblastopenia induced by parvovirus B19 is a self-limiting illness usually seen arising in patients with chronic hemolytic anemia. TAC is characterized by a sudden cessation of erythrocyte production for 10-15 days and a marked fall in the hemoglobin levels [2]. It is seen not only in patients with hemolytic anemia but also in immunocompetent individuals. TAC has been reported associated with hemoglobinopathies, immune hemolytic anemias, malaria, iron deficiency anemia, and in apparently healthy individuals; however, its association with megaloblastic anemia is not widely reported in the literature [3, 4, 10].

Diagnosis of parvovirus B19 can be made by isolation of viral DNA by direct hybridization or polymerase chain reaction. Antibodies both IgM and IgG can be detected against viral antigens like NS1, VP1/VP2. DNA isolation can be done in the acute phase of illness and corresponds with high viremia; IgM also appears during the acute phase

and can persist up to 3 months. IgG can be detected in the sera after 2 weeks of infection; however, the titres decline significantly and are not routinely used for diagnosis [2, 3]. Management of TAC is supportive with blood transfusion and maintenance of suitable hemoglobin levels, and the prognosis is excellent. Persistent infections require intravenous immunoglobulin and is often curative. The patient shows significant improvement in both hemoglobin levels and reticulocyte count [2].

Conclusion:

Transient aplastic crisis due to parvovirus B19 is characterized by peripheral anemia, reticulocytopenia, and bone marrow erythroblastopenia. It can occur in a background of chronic hemolysis and its association with nutritional anemias is rare. It is generally self-limiting and patients respond well to blood transfusion support and intravenous immunoglobulins.

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How to cite this article:

Vijay A, Belurkar S, Harrison A, Singh VK. Megaloblastic Anemia Complicated by Parvovirus B19 Induced Erythroblastopenia: A Case Report. *J Krishna Inst Med Sci Univ* 2021; 10(4):120-123.

Submitted: *04-June-2021* ***Accepted:*** *02-Aug-2021* ***Published:*** *01-Oct-2021*