# Case Report

# Human Parvovirus B19 Induced Pure Red Cell Aplasia in a Known Case of Hereditary Spherocytosis; A Bone Marrow Diagnosis

**Tejaswini Priyadarshan Waghmare, Meera T P*, Daksha Piyush Prabhat, Ankita Asthana**

Department of Pathology, Seth GS Medical College and KEM Hospital, Mumbai

***DOI: 10.21276/APALM.3270***

***Corresponding Author**:
*Dr Meera T.P*
*meeratp2511@gmail.com*

*Submitted: 30-Jul-2023*
*Final Revision: 17-Aug-2023*
*Acceptance: 27-Aug-2023*
*Publication: 01-Nov-2023*



## Abstract

Human Parvovirus B19 (HPV B19) is a single stranded DNA virus belonging to parvoviridae family causing an acute self-limiting viral infection transmitted through respiratory droplets. However, in patients with hemolytic anemia, it can cause pure red cell aplasia and eventually aplastic crisis. We report a case of 27-year-old male, who presented with complaints of fever, nausea and body ache for 15 days. Physical examination showed pallor, icterus and splenomegaly. Complete blood count (CBC) revealed pancytopenia. Plasmodium Vivax infection was seen on peripheral blood smear (PBS) and hence was treated with antimalarials, however fever persisted. Bone marrow examination done in view of panytopenia revealed large proerythroblast with eosinophilic intranuclear inclusions. The impression given was hypercellular marrow with erythroblastopenia with parvoviral inclusions. Parvovirus B19 quantitative PCR showed elevated titers. He is also a diagnosed case of Hereditary Spherocytosis and Gilberts syndrome since 2015. Acute onset pancytopenia in individuals suffering from chronic hemolytic anemias should raise a suspicion of viral infection. Timely diagnosis and supportive management is vital.

***Keywords:***

*Human Parvovirus B19, Pure Red Cell Aplasia, Hereditary Spherocytosis, Gilberts Syndrome*

## Introduction

Human Parvovirus B19(HPV B19) is a non-enveloped single stranded DNA virus that is transmitted mainly by respiratory droplets [1]. The virus has an affinity for the erythroid progenitor cells because of their P antigen, which acts as a receptor for the entry of the virus into these cells. Most cases of HPV B19 presents with self-limiting flu like illness and arthropathy in immunocompetent host whereas in patients with inherited hematological disorders such as sickle cell anemia, thalassemia, hereditary spherocytosis etc., it results in pure red cell aplasia (PRCA) that eventually leads to transient aplastic crisis.[2]

## Case Report

A 27-year-old male presented with complaints of fever with nausea and body ache since 15 days. On physical examination pallor

and icterus were present, per abdominal examination revealed splenomegaly. Laboratory investigations revealed pancytopenia with Hb- 5.6 g/dl, Total WBC count 3400 cells/mm3 with differential count of polymorphs 65%, lymphocytes 32%, eosinophil 1% and monocytes 2 %. Platelet count was 80,000/mm3. Peripheral smear examination revealed hypochromia, microcytosis, spherocytes, anisocytosis and few macrocytes. Occasional schizonts of Plasmodium vivax were also seen. Hence the patient was started on antimalarials and later antibiotics were also added owing to persistent fever and pancytopenia. The patient was also given multiple blood transfusions to manage pancytopenia.

Bone marrow examination was advised in view of persistent pancytopenia and fever. Bone marrow examination revealed erythroblastopenia with giant proerythroblasts showing a strongly basophilic cytoplasm with pseudopodia which is highly suggestive of HPV B19 infection. Bone marrow biopsy showed a hypercellular marrow with suppressed erythroid series with few giant erythroblasts with intranuclear eosinophilic virus inclusions. The impression given was hypercellular marrow with erythroblastopenia with parvovirus inclusions. Subsequent parvovirus B19 quantitative PCR showed elevated titers of >5 x 1010 IU which supported the bone marrow diagnosis.

Patient is a diagnosed case of hereditary spherocytosis since 2015. The family screening revealed that father and brother also showed red cell membrane protein defects. He was also diagnosed with Gilbert syndrome in the same year during evaluation for persistent jaundice.

The patient was now advised to start IV immunoglobulins but deferred due to monetary constraints, upon which he was continued on repeated blood transfusions and supportive managements. Patient recovered and the blood investigations at the time of discharge were-Hb-10.6g/dl, TLC- 5600 cells/mm3 and platelet 1.4 lakh/mm3.

Currently the patient is leading an uneventful life and being regularly followed up on clinical hematology OPD every 4 monthly basis.

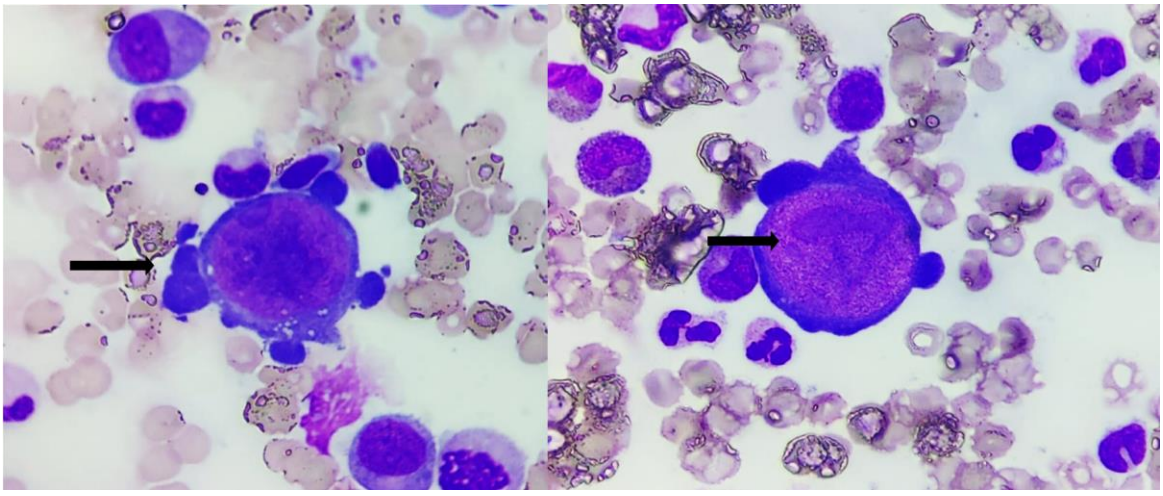

***Figure 1: Bone marrow aspirate, MGG (100X) showing giant proerythroblasts with cytoplasmic projections and prominent nucleoli with no maturing cells.***

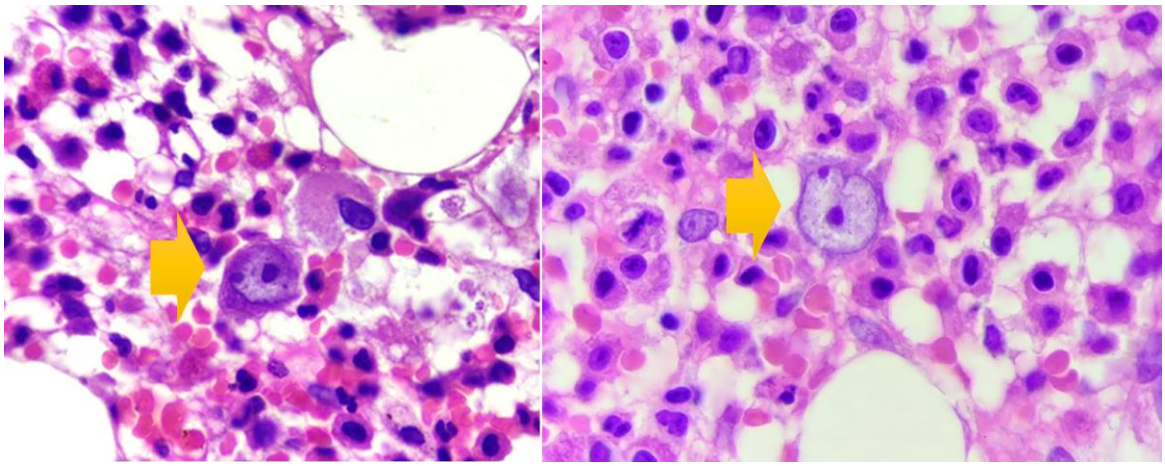

***Figure 2: Bone marrow biopsy, H & E (40x) showing large proerythroblasts with eosinophilic iintranuclear inclusion***

## Discussion

PRCA is a rare disease that presents anemia secondary to the failure of erythropoiesis. It can be constitutional or acquired and either acute or chronic [3]. Constitutional PRCA, also known as Blackfan Diamond Syndrome, is a chronic condition due to an inherited stem cell defect. The acquired causes include transient erythroblastopeina of childhood [4], viral infections by HPV B19, HIV, Hepatitis and drugs like hydantoin, allopurinol, azathioprine, isoniazid, pembrolizumab etc . It is also seen in association with thymoma, Hodgkins lymphoma, Non Hodgkins lymphoma, chronic lymphocytic leukemia, carcinoma, rheumatoid arthritis and systemic lupus erythematosus.[3,4]

Parvovirus B19 is a single stranded DNA virus that shows unique tropism for erythroid progenitor cells due to its attachment to globoside receptor which is expressed on erythroid progenitor cells [5]. The virus is transmitted by respiratory droplets but transmission through transfusion of blood products, vertically from mother to fetus and less commonly as nosocomial infection are also reported. The disease is usually subclinical and self-limiting with mild symptoms that warrant no therapy. The infection is cytotoxic to erythroid progenitor cells followed by arrest of red cell production for 5- 10 days but does not cause significant anemia as their red cell lifespan is 120 days. Common clinical manifestations in immunocompetent individuals include erythema infectiosum in children, polyarthropathy syndrome and other inflammatory disorders in adults [6]. However, in patients with hemolytic anemias whose red ell survival rate is shortened, transient decompensated erythropoiesis leads to severe anemia [7]. In immunocompromised patients the infection can persist leading to chronic anemia. Our patient had Hereditary spherocytosis, which resulted in a shortened lifespan of RBCs and consequently HPV B19 infection resulted in acute PRCA which manifested as fever with pancytopenia.

The characteristic bone marrow finding includes giant pronormoblasts with eosinophilic intranuclear virus inclusions with peripheral condensation of chromatin and cytoplasmic projections [7]. Our patients' bone marrow showed similar findings. Our patient also showed transient pancytopenia. If aplastic crisis sets in, then there is complete absence of maturing erythroblasts.

Green et al in 1984 presented two adult siblings, both diagnosed with hereditary spherocytosis, who developed aplastic crisis following acute febrile illness which was further diagnosed to be HPV B19. They were treated by blood transfusions and supportive treatments and were discharged within 6-8 days. [8].

In a case report by Balaji MD et al, a child with hereditary spherocytosis with a strong family history who developed aplastic

crisis following Parvovirus B19 infection was described [9].

The diagnostic tests for HPV B19 infection include Parvovirus B19 specific antibody testing and viral DNA testing. IgM antibodies are seen from day 10-12 and can be seen for up to 5 months. IgG antibodies are seen from 15 days post infection and can be seen long term. We did Quantitative PCR of viral DNA which showed an elevated titer.[10]

Hereditary spherocytosis is caused by genetic mutation affecting the proteins that make up the RBC membrane including spectrin, ankyrin, band 3 and protein 4.2. This results in loss of stability in the cell membrane and the cell assumes the spherical shape. These RBCs will have shorter lifespan and is prematurely killed by the spleen. In normal individuals' transient cessation of erythropoiesis due to parvovirus B19 can be compensated by increased erythropoietin. But in patients with chronic hemolytic anemia the shorter life span of RBCs aggravates the problem [11]. The concurrent malarial infection in our case also contributed to accelerated hemolysis.

The management includes supportive care like blood transfusion to replace the depleting RBCs. IV immunoglobulin has been shown to be effective in some cases of PRCA.[8] Our patient was also given supportive management with multiple blood transfusions and was advised for IV Immunoglobulins but couldn't comply owing to financial constraints.

## Conclusion

This case report highlights the importance of considering Parvovirus B19 infection as a potential cause of PRCA in individuals with preexisting hemolytic disorders. Bone marrow examination which demonstrates erythroblastopenia and viral inclusions , plays an important role in diagnosis of the disease.

***Acknowledgements :*** *None*
***Funding:*** *None*
***Competing Interests:*** *None*

## References

1. Means Robert T Jr. Pure red cell aplasia. Blood. 2016. 128(21). 2504-2509.
2. Serjeant BE, Hambleton IR, Kerr S, Kilty CG, Serjeant GR. Haematological response to parvovirus B19 infection in homozygous sickle-cell disease. Lancet. 2001 Nov 24;358(9295):1779-80
3. 3.Bain Barbara J, Clark David M, Wilkins Bridget S. Erythropoeisis, Granulopoeisis , thrombopoiesis. Bone Marrow Pathology. Fifth edition. ,Wiley- Blackwell. 2019 February. 558-63
4. Penchansky Land Jordan JA(1997) Transient erythroblastopeina of childhood associated with human herpes virus type 6, variant B, Am J Clin Pathol, 108, 127-132.
5. Remo Leisi, Chiarina Di Tommaso,Christopher Kempf, Carlos Ros, The receptor binding domain in the VP1u region of Parvovirus B19; Viruses ; 8(3)-61
6. Heegaard ED, Brown KE. Human parvovirus B19. Clin Microbiol Rev 2002; 15: 485-505.
7. Fisch P, Handgretinger R, Schaefer HE. Pure red cell aplasia. Br J Haematol.2000; 111: 1010-22.
8. Green DH, Bellingham AJ, Anderson MJ. Parvovirus infection in a family associated with aplastic crisis in an affected sibling pair with hereditary spherocytosis. J Clin Pathol. 1984 Oct;37(10):1144-6.
9. Balaji M. D., Vadlamudy Vinay*, Shankar Vangalpudi V. Aplastic crisis in a child with hereditary spherocytosis with a strong family history resolving with supportive care. nt J Contemp Pediatr. 2018 May;5(3):1150-1152.
10. Jordan JA. Diagnosing human parvovirus B19 infection: guidelines for test selection. Mol Diagn. 2001 Dec;6(4):307-12.