Case Report

Refractory Pure Red Cell Aplasia Secondary to Parvovirus B19 in an Immunocompetent Patient : A Challenging Case Report

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This report presents a case of acquired Pure Red Cell Aplasia (PRCA) of a 36-year-old immunocompetent woman after parvovirus B19 infection. Following the fever, she developed severe anaemia and dyspnoea which necessitated frequent blood transfusions. Despite extensive diagnostics, including bone marrow biopsy, initial oral prednisolone and recombinant erythropoietin yielded limited results. Subsequent Intravenous Immunoglobulin (IVIG) treatment did not show significant improvement, challenging the traditional understanding of Parvovirus B19-related PRCA. This case emphasizes the necessity for further research into its diverse clinical manifestations and optimal management strategies.

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Pure Red Cell Aplasia (PRCA) is a disorder of Red Blood Cells characterized by severe anaemia, reduced reticulocytes in peripheral blood and virtually absent mature erythroblasts in the bone marrow. However, other cell lineages usually remain unaffected. Paul Kaznelson first described it in 1922. The congenital form of PRCA was described by Diamond and Blackfan in 1938.

PRCA is classified as congenital and acquired. The former is a lifelong disorder associated with congenital abnormalities; the acquired type can be further classified as primary and secondary PRCA. Primary-acquired PRCA is idiopathic, while secondary-acquired PRCA is associated with autoimmune diseases, lymphoprolife rative disorders, infections (parvovirus B19), neoplasms (thymoma being the best-known), pregnancy and drugs[1].

Case Report

A 36-year-old, regularly menstruating homemaker without any co-morbidities, addiction, or high-risk behaviour, presented to the OPD with a history of Acute-onset Fever (101-102°F) with chills and myalgia without diurnal variation, which occurred 6 months ago and lasted for 7 days,resolved with over-the-counter medications. The fever was not associated with headache, sore throat, productive cough, abdominal pain, burning sensation during micturition, rashes, and joint pain.

After ten days of fever resolution, she gradually developed Shortness Of Breath (SOB), initially occurring on exertion. Over three months, her SOB worsened from mMRC grade I to grade III, without cough, orthopnea, or paroxysmal nocturnal dyspnea. SOB was associated with regular palpitations during exertion without a history of syncope and chest pain. She was evaluated elsewhere and diagnosed with severe anaemia (haemoglobin 2g/dL) and received multiple blood transfusions every 15-20 days due to the recurrence of similar symptoms.

Editor's Comment :

- Diagnosis of PRCA should be considered in the case of treatment-resistant anaemia. Acquired PRCA is commonly associated with Parvovirus B19 infection and usually has a good prognosis. However, in a handful of cases it may not respond to the conventional treatment including oral prednisolone and IVIG. Refractory cases necessitate patient counselling, intermittent blood transfusions, and long-term follow-up for comprehensive care.

On examination, her vital signs were stable, heart rate of 98 beats per minute, blood pressure of 100/60 mmHg, respiratory rate of 20 breaths per minute, temperature of 98.5°F and oxygen saturation of 99% on room air. Her general physical examination was unremarkable except for severe pallor.Cardiovascular, respiratory, gastrointestinal and neurological examinations were non-contributory.

Upon further evaluation, a complete hemogram revealed severe anaemia and the peripheral smear showed normocytic normochromic anaemia. Subsequent investigations demonstrated decreased reticulocyte count despite adequate levels of vitamin B12, folic acid and ferritin (Table 1). These findings raised concerns regarding the possibility of acquired PRCA. To confirm the diagnosis, a bone marrow biopsy was done, which revealed cellular marrow (Fig 1) with reduced erythroid precursor, along with the presence of a few giant proerythroblasts (Fig 2). To determine the aetiology of PRCA, Anti-nuclear Antibody (ANA) was negative, High-resolution Computed Tomography (HRCT) thorax was

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Table 1 — *Various relevant laboratory parameters*

Laboratory parameters									
Investigations	Reference range	D 01	D 19	D 23	D 30	D 32	D 35	D 45	D 48
Haemoglobin	11.5 – 15 gm/dL	4.5	3.4	9.4	9.24	8.3	7.7	7.7	8
Total Leucocyte Count	4-11 x 10^3/L	5.8	5.3	7.1	7.4	9.85	7.4	7.30	13.30
Differential Count (N/L/M)	40-80/20-40/2-10 %	44/47/6	53/40/4	49/43/6	73/22/4	54/28/12	49/42/6.1	79/5.7/16	65/27/5
Platelets	150-450 x 10^3/mm^3	433	276	321	371	410	371	458	337

Peripheral blood smear : Normocytic normochromic RBCs with mild anisocytosis, Normal counts with mild lymphocytosis. Adequate platelets. No blood parasites were seen.
Bone marrow aspiration and biopsy : Cellular bone marrow with reduced erythrocyte component with occasional giant pronormoblasts seen ;
Vitamin B12: >2000 pmol/L (156-672 pmol/L) ; **Folic acid:** 12ng/mL(> 5.38 ng/mL) ;
Reticulocyte count: <0.2% ; **Ferritin :** 364 ng/mL (10-291 ng/mL) ;
DAT & IAT: negative ; **ANA- IFA:** negative (<1:80) ; **Viral markers:** Non-reactive ;
Stool occult blood: Negative ; **Parvovirus IgG:** 0.95 (< 0.9) ; **Parvovirus IgM:** 3.84 (< 0.9)

N Neutrophils; L Lymphocytes; M Monocytes; DAT Direct antiglobulin test; IATIndirect antiglobulin test; ANA Antinuclear antibody; IFA Immunofluorescence assay; IgG Immunoglobulin G; IgM Immunoglobulin M

done for the possibility of thymoma and was ruled out. Viral markers were found to be negative, while parvovirus serology was positive. Hemoglobinopathies were ruled out by performing haemoglobin high-performance liquid chromatography.

She was treated with oral prednisolone (1mg/kg) along with subcutaneous recombinant EPO. The patient did not exhibit improvement and necessitated blood transfusions every fortnight. Consequently, IVIG was given (0.4mg/kg/day) for 5 days. Despite these therapeutic interventions, there was no significant improvement and the patient currently requires recurrent blood transfusions at intervals of every 3 to 4 weeks.

Discussion

Multiple cases were reported in the literature of parvovirus B19-associated PRCA in immuno-compromised patients. To the best of our knowledge, this is the first case of parvovirus B19-associated chronic PRCA in an immunocompetent non-pregnant adult.

Parvovirus is a compact, non-enveloped, single-stranded DNA virus that exhibits an affinity for erythroid progenitor cells. Parvovirus B19 member of the *erythrovirus* genus belongs to the *Parvoviridae* family. It is the only known parvovirus pathogenic to humans and can cause fifth disease in immunocompetent individuals[2], transient aplastic crisis in patients with haemolytic disorders[3], chronic infection in immuno-compromised patients can lead to chronic pure red cell aplasia. In pregnant women leads to congenital infections and hydrops fetalis[4]. Rarely, immuno-competent adults may manifest with symmetric polyarthropathy mimicking rheumatoid arthritis.

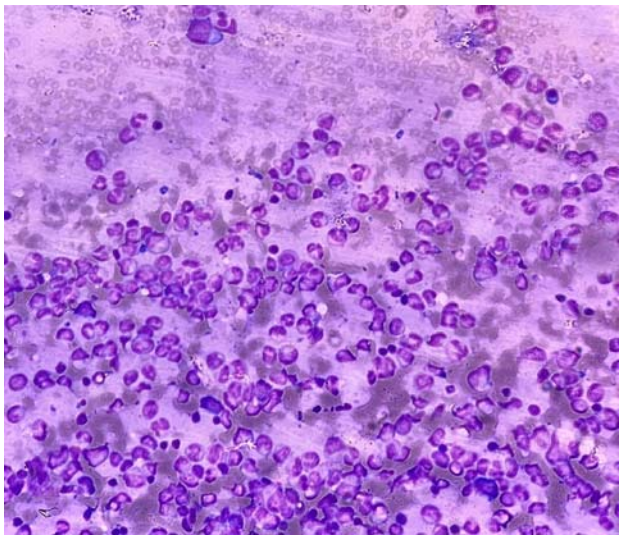

Fig 1 — Bone marrow aspirate showing adequate myeloid series with all stages of maturation. No erythroid lineage cells are seen. Magnification x200 (Leishman stain)

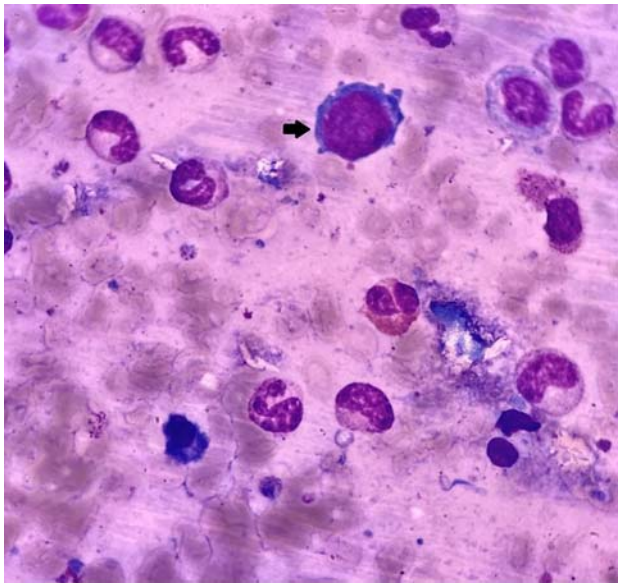

Fig 2 — Bone marrow aspirate showing giant proerythroblast displaying high nucleocytoplasmic ratio, round nucleus, fine chromatin, prominent nucleoli with scant basophilic cytoplasm showing cytoplasmic protrusion. Magnification x400 (Leishman stain)

Parvovirus primarily transmits through the respiratory route and infrequently via blood transfusions and vertical transmission. Following infection in healthy adults, viremia occurs after one week, accompanied by mild symptoms such as pyrexia, malaise, myalgia and pruritus. In the 2nd week of infection peak viremia and production of IgM followed by IgG antibodies occur. Around 3rd week, a second symptomatic phase occurs which manifests as rash, pruritus or arthralgia. PRCA is a self-limiting condition. IgM antibodies typically persist for about 3 months but can be detected for an extended duration, while IgG antibodies provide lifelong protection against secondary infections[6-7].

PS shows normocytic normochromic anaemia with reticulocyte count <10000/µL. WBCs and platelets are normal, sometimes relative lymphocytosis, thrombocytosis or thrombocytopenia[1]. Diagnosing PRCA requires a bone marrow examination, there are absence or near absence of erythroblasts (<1% on marrow differential count). Rarely, a few proerythroblasts or basophilic erythroblasts (up to 5%) may be present. "Giant proerythroblasts" with vacuolated cytoplasm and pseudopodia may suggest parvovirus B19 infection but are not definitive for diagnosis[8]. Confirmation involves anti-parvovirus B19 IgM presence and positive peripheral blood PCR for high parvovirus B19 load.

Management of PRCA depends on the treatment of the underlying cause. Initially, supportive care is given to maintain haemoglobin levels above 7 gm/dL. Definitive treatment is IVIG at 0.4 g/kg/day over five days. Alternatives include corticosteroids, cyclosporin A, cyclophosphamide, anti-thymocyte globulin, alemtuzumab and rituximab[9].

Conclusion

An atypical presentation of PRCA following Parvovirus B19 infection in an immunocompetent adult may not respond to the conventional therapeutic interventions including oral prednisolone and IVIG.This warrants further research to refine management strategies for this uncommon manifestation of PRCA.

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