CASE REPORT

JIACM 2024; 25 (4): 230-31

Pure Red Cell Aplasia

Heli Kapoor, Varun Shahi**, Rajesh Satyapal Taneja***, Praveen Malik*****

Abstract

Pure Red Cell Aplasia (PRCA) is an uncommon haematological disorder characterised by normocytic anaemia with reticulocytopaenia and preserved leucocyte and platelet counts. PRCA may be congenital or acquired. Acquired PRCA can be primary or secondarily associated with thymoma, lymphoproliferative diseases, infections, autoimmune disorders and certain drugs. Very rarely, it can be idiopathic. We report a case of chronic acquired idiopathic PRCA in a 60-year-old male. The patient had severe anaemia for which he had received multiple blood transfusions in last three months. The bone marrow aspiration and biopsy were done which revealed isolated depression of erythroblasts with final impression of acquired PRCA. A battery of tests and CT (chest and abdomen) were done to rule-out possible aetiologies but none were found. Hence, a diagnosis of idiopathic PRCA was established. Treatment was initiated with cyclosporin A and steroids in combination; remarkable improvement in haemogloblin and reticulocyte count was achieved.

Introduction

Pure Red Cell Aplasia (PRCA) is an exceedingly rare bone marrow disorder with an incidence of 1.06 patients per million per year[1]. It was first reported by Paul Kaznelson in 1922[2]. This condition manifests as isolated depression of erythroid series and is characterised by normocytic normochromic anaemia, reticulocytopaenia (reticulocyte count <1%) and diminished marrow erythroblasts (<0.5%)[2]. It can occur at any age with equal prevalence in both genders. PRCA may be congenital or acquired. Acquired PRCA may be primary or secondarily associated with Thymoma, Lympho-proliferative diseases (chronic lymphocytic leukaemia, lymphoma), solid organ malignancy, Infections (Parvovirus B19 infection, HIV, hepatitis, tuberculosis), Autoimmune disorders (SLE, Rheumatoid Arthritis) and Drug-induced (Erythropoietin)[3]. This case report delves into a unique instance of acquired PRCA, where the aetiology remained elusive, and was ultimately labelled as idiopathic.

Case report

A 60-year-old male, presented to the medicine emergency with complaints of generalised weakness, progressive exertional dyspnoea and swelling of feet over the past one year, which had worsened over last three months. There were no complaints of fever, jaundice, weight loss, loss of appetite, skin rash, joint pains, blood loss from any site or prolonged drug intake. The patient had a medical history of hypertension. Past history was notable for multiple blood transfusions in last 3 months.There was no significant family history. Physical examination revealed severe pallor, bilateral pedal oedema (pitting) and tachycardia without any lymphadenopathy and hepatosplenomegaly. On routine haemogram, his haemoglobin was 5.9 gm/dL, Reticulocyte count was 0.6%, RBC count - 1.82 million/cumm, haematocrit 18%, total leucocyte count - 9,010/cumm, DLC-Neutrophils - 38.50%, Lymphocytes - 40.1%, Eosinophils - 6%, platelets - 3.87 lac/cumm. On peripheral blood film examination, normocytic normochromic RBCs were seen. His liver function tests and renal function tests were within normal range. Stool for occult blood was negative. Bone marrow aspiration and biopsy was suggestive of significant erythroid suppression with an M: E ratio of 30:1. Erythroid series showed maturation arrest, few in early megaloblast phase with only 3% erythroid cells in marrow. Myeloid series showed normal differentiation and maturation with adequate and functional megakaryocytes. Differential count of the non-erythroid series showed myeloblasts - 00%, myelocyte - 06%, metamyelocyte - 3%, neutrophil - 80%, lymphocyte - 06%, eosinophil - 1%, plasma cells - 1%. Keeping in view the clinical presentation, examination, laboratory and bone marrow biopsy findings, a diagnosis of acquired PRCA was made. To find the underlying cause of acquired PRCA, blood samples were sent for infectious (Parvovirus B19, Hepatitis B, C, A, EBV, CMV virus) and autoimmune aetiologies (RF, ANA); all of which were negative. His CECT Chest and abdomen was normal which ruled-out the possibility of thymoma. Extensive work-up eliminated known causes, leading to the diagnosis of idiopathic PRCA. The patient was started on combination therapy of cyclosporin A and steroids. His haemoglobin increased to 9.8 gm/dL with significant improvement in reticulocyte count on follow-

**Assistant Professor, **Post-Graduate Resident, ***Professor, ****Professor and Head, Department of Medicine, ESIC Medical College and Hospital, NIT-3, Faridabad - 121 001, Haryana.*

Corresponding Author: Dr Rajesh Satyapal Taneja, Professor, Department of Medicine, ESIC Medical College and Hospital, NIT-3, Faridabad - 121 001, Haryana. Tel: 9971258295, E-mail: rajeshtaneja25@gmail.com

up after about four weeks of therapy.

Discussion

PRCA is an uncommon single lineage cytopaenia characterised by decreased RBC precursors with normal granulopoiesis and megakaryopoiesis in the bone marrow, presenting clinically as anaemia[4]. The aetiology of PRCA is as follows[5]:

- Congenital PRCA (Diamond-Blackfan anaemia)
- Acquired PRCA
- Primary

I. Primary autoimmune PRCA (includes transient erythroblastopenia of childhood)

II. Primary myelodysplastic PRCA

- Secondary (associated with)

I. Autoimmune/collagen vascular disorders (SLE, RA)

II. Lymphoproliferative disorders (CLL, Lymphoma, Angioimmunoblastic lymphadenopathy)

III. Solid Tumours (Thymoma)

IV. Infections (Parvovirus B19; Hepatitis A, B, C, E; HIV; EBV; CMV; TB)

V. Drugs and toxins (Erythropoietin)

The pathogenesis is heterogeneous and involves immune dysfunction with antibodies directed against erythroid precursor cells or erythropoietin[6], or due to T-cell-mediated suppression of erythropoiesis[7]. Clinical presentation of patients of acquired PRCA can be variable; severe anaemia, fever, anorexia, nausea, vomiting, headache and abdominal pain. Bone marrow examination reveals a complete absence of erythroblasts but normal granulocytic and megakaryocytic series.Thorough investigation is crucial to identify underlying causes, including a viral screen, serological studies for autoimmune diseases and CT thorax to rule-out thymoma.

Majority of acquired PRCA cases show clinical and haematological improvement on removal of the underlying offending agent. However, in Idiopathic PRCA most effective first-line treatment is Cyclosporin A (CsA) administered at a starting dose of 2 to 6 mg/kg per day (in divided doses) combined with steroid (prednisone at 30 mg/day) with a rapid taper, yielding an overall response rate (ORR) of about 65% to 87%[2]. The second-line therapy includes antithymocyte globulin (ATG) and cyclophosphamide. Following treatment, response to therapy is assessed by serial evaluation of reticulocyte count and haematocrit. The goal of treatment is to induce remission to attain an optimal haemoglobin concentration with the recovery of erythropoiesis, without any requirement for blood transfusion and associated problems.

In our case, even after extensive investigations none of the established causative factors for PRCA could be established; thus the case was labelled as idiopathic PRCA. The patient was then started on treatment with cyclosporin A and steroids, which induced remission and a significant increase in haemoglobin concentration after 4 weeks of therapy.

Conclusion

Any anaemia of prolonged duration, not responding to conventional therapy should be evaluated by bone marrow studies to rule-out ineffective erythropoiesis, dysplastic syndromes, a selective erythroid suppression/PRCA or infiltrative diseases of the bone marrow. PRCA is a rare disorder with varied aetiology. Whenever a diagnosis of PRCA is made, an underlying cause should be sought. A rapid response follows treatment of the underlying cause or withdrawal of the incriminating drug. In cases where no cause can be established, idiopathic PRCA may be treated with Cyclosporin A and steroids.

Reference

1. Nakazawa H, Sakai K, Ohta A *et al*. Incidence of acquired pure red cell aplasia: a nationwide epidemiologic analysis with 2 registry databases in Japan. *Blood Adv* 2022; 6282-90.
2. Sawada K, Fujishima N, Hirokawa M. Acquired pure red cell aplasia: updated review of treatment. *Br J Haematol* 2008; 505-14.
3. Fisch P, Handgretinger R, Schaefer HE. Pure red cell aplasia. *Br J Haematol* 2000; 1010-22.
4. Kaznelson P. Zur Entstehung der Blutpla Èttchen. Verhand lungen der Deutschen Gesellschaft. *Fur Innere Medizin* 1922; 34: 557-8.
5. Lipton J, Glader B, Means B. Red cells aplasia: acquired and congenital disorders. In: Greer JP, Arber DA, Glader B *et al.* (eds). *Wintrobe's Clinical Hematology*. 13th ed. Lippincott Williams & Wilkins 2014; 975-6.
6. Rahbar M, Chitsazian Z, Abdoli F *et al*. Pure red cell aplasia due to antibody against erythropoietin in haemodialysis patients. *J Nephropathol* 2017; 6 (1): 25-9.
7. Wilson HA, McLaren GD, Dworken HJ. Transient pure red-cell aplasia: cell-mediated suppression of erythropoiesis associated with hepatitis. *Ann Intern Med*.