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Morphological Evaluation of Bone Marrow in Red Cell Aplasia: A Case Series

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1. Introduction

Red cell aplasia is a disorder characterized by normocytic normochromic anaemia with marked reticulocytopenia and absence or marked reduction of erythroid precursors in the bone marrow (1) . Red cell aplasia are due to different causes which are divided into primary and acquired (1) (2) . Due to rarity of red cell aplasia, studies of many cases are not done. Red cell aplasia can mimic other disease which present solely as anaemia (1) . Bone marrow examination is required to establish the diagnosis of red cell aplasia and to establish the cause (1) .

2. Case Series

In our study, 5 cases of red cell aplasia due to different causes were evaluated and their bone marrow findings and peripheral blood were analysed to reach to a definitive diagnosis.

Case 1
A 9 months old male patient with complaint of fever for 14 days & epistaxis was referred from paediatric ward for bone marrow examination. On examination pallor, hepatosplenomegaly and gum hyperplasia were present.

On investigation, hemoglobin was 6.4g/dl, TLC - 7110/cu. mm, DLC - Neutrophils - 17%, Lymphocytes - 80%, Monocytes - 2%, Eosinophil - 1%. Platelets - 1.1lakh/cu. mm**,** Reticulocyte - 0.02%. General blood picture showed normocytic normochromic red cells. Bone marrow aspiration smears showed particulate and normocellular marrow with increased M: E ratio {75: 1} DLC - Blasts - 1%, Promyelocyte - 2%, Myelocyte - 14%, Metamyelocyte - 13%, Neutrophils - 42%, Lymphocytes - 23%, Monocytes - 2%, Eosinophils - 2%, Erythroid - 1%. Erythopoiesis was reduced and cells were megaloblastic**.** Giant Proerythroblasts were present (Fig 1). Megakaryopoiesis was adequate with normal morphology. Impression was given as normocellular bone marrow with marked erythroid hypoplasia possibly due to parvo B19 infection.

Case 2
A 65 years old male patient who is a known case of renal dysfunction with type 2 diabetes mellitus and HCV Infection who came with complaint of weakness and backache was referred from medicine ward for bone marrow examination.

On investigation, hemoglobin was 7.9 g/dl, TLC - 5510/cu. mm, DLC - Neutrophils - 67%, Lymphocytes - 23%, Monocytes - 8%, Eosinophil - 2%. Platelets - 1.29lakh/cu. mm**,** Reticulocyte - 0.04%. General blood picture showed predominantly normocytic normochromic red cells. Bone marrow aspiration smears showed particulate and normocellular marrow with increased M: E ratio{42: 1}. DLC - Blasts - 1%, Promyelocyte - 2%, Myelocyte - 12%, Metamyelocyte - 11%, Neutrophils - 58%, Lymphocytes - 13%, Monocytes - 0%, Eosinophils - 0%, Plasma cell - 1%, erythroid - 2%. Erythopoiesis was reduced**.** Megakaryopoiesis was adequate. Trephine biopsy showed normocellular bone marrow (Fig 2) with erythroid hypoplasia and 1%plasma cells. Erythroid hypoplasia may be due to HCV infection.

Case 3
A 3 years old male patient who is a known case of primary hemophagocytic lymphohistiocytosis (HLH) with ANA positive who came with complaint of fever with rash for 1 week was referred from paediatric ward for bone marrow examination. On examination pallor and cervical lymphadenopathy were present.

On investigation, hemoglobin was 9.6 g/dl, TLC - 4610/cu. mm, DLC - Neutrophils - 70%, Lymphocytes - 29%, Monocytes - 1%, Eosinophil - 0%. Platelets - 1.1lakh/cu. mm**,** Reticulocyte - 0.01%. General blood picture showed predominantly normocytic normochromic red cells. Bone marrow aspiration smears showed normocellular marrow with increased M: E ratio {68: 1}. DLC - Blasts - 2%, Promyelocyte - 2%, Myelocyte - 2%, Metamyelocyte - 8%, Neutrophils - 48%, Lymphocytes - 29%, Monocytes - 8%, Eosinophils - 0%, Erythroid - 1%. Erythopoiesis was markedly reduced**.** Megakaryopoiesis was adequate. Trephine biopsy showed normocellular bone marrow (overall cellularity 80 - 90%) with adequate representation of the granulocytic lineage elements and megakaryocytes. Impression is that of normocellular bone marrow (overall cellularity 80 - 90%) with erythroid hypoplasia and features of hemophagocytosis. (Fig 3 & 4).

Case 4
A 79 years old female who is a known case of chronic kidney disease on erythropoietin therapy with hypertension and hypothyroidism who came with complaint of shortness of breadth, generalized weakness and backache was referred

from medicine ward for bone marrow examination. On examination pallor and bone tenderness were present.

On investigation, hemoglobin was 3.4 g/dl, TLC - 4820/cu. mm, DLC - Neutrophils - 53% Lymphocytes - 37%, Monocytes - 5%, Eosinophil - 5%. Platelets - 1.1lakh/cu. mm**,** Reticulocyte - 0.05%. General blood picture showed normocytic normochromic red cells. Bone marrow aspiration smears showed particulate and normocellular marrow with increased M: E ratio {53: 1}. DLC - Myelocyte - 4%, Metamyelocyte - 3%, Neutrophils - 45%, Lymphocytes - 45%, Monocytes - 0%, Eosinophils - 0%, Plasma cell - 2%, erythroid - 1%. Erythopoiesis was reduced**.** Megakaryopoiesis was adequate. Trephine biopsy showed normocellular marrow spaces (overall cellularity 25 - 35%) with marked reduction in erythroid precursors Impression is that of normocellular marrow with marked erythroid hypoplasia.

Case 5

A 53 years old female patient with complaint of shortness of breath, generelised weakness and loss of appetite was referred from medicine ward for bone marrow examination. On examination pallor was present.

On investigation, hemoglobin was 3.7 g/dl, TLC - 4300/cu. mm, DLC - Myelocyte - 1% Neutrophils - 58%, Lymphocytes - 30%, Monocytes - 10%, Eosinophil - 1%. Platelets - 1.29 lakh/ cu. mm, Reticulocyte - 0.02%. General blood picture showed normocytic normochromic red cells with few microcytes and spherocytes. Bone marrow aspiration smears showed particulate and normocellular marrow with increased M: E ratio{39: 1}. DLC - Blasts - 2%, Promyelocyte - 2%, Myelocyte - 15%, Metamyelocyte - 20%, Neutrophils - 34%, Lymphocytes - 18%, Monocytes - 5%, Eosinophils - 1%, Plasma cell - 1%, Erythroid - 2%. Erythopoiesis was reduced**.** Megakaryopoiesis was adequate with 26% hypolobation (Fig 5 &6). Trephine biopsy showed normocellular marrow spaces (overall cellularity 40 - 50%) with megakaryocytic and granulocytic preponderence. The erythroid precursors are reduced. Macrophages are increased.

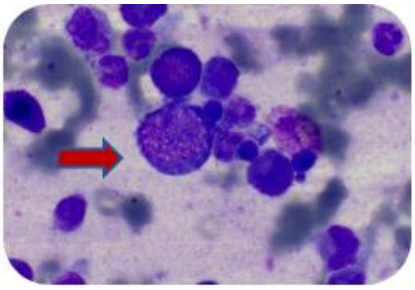


Figure 1: Bone marrow picture showing giant proerythroblast

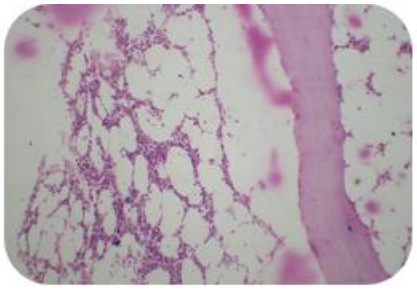


Figure 2: Bone marrow trephine biopsy in low power

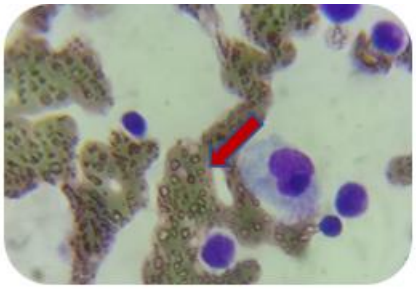


Figure 3: Histiocytes showing hemophagocytosis

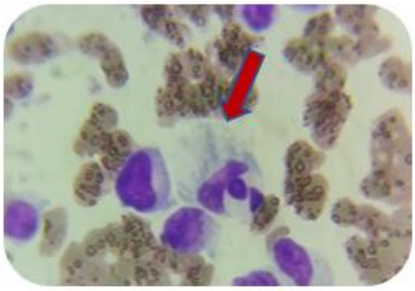


Figure 4: Histiocytes showing hemophagocytosis

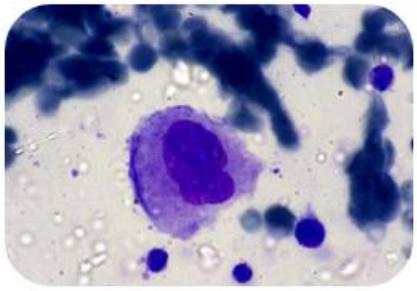


Figure 5: Bone marrow piture showing hypolobated megakaryocyte

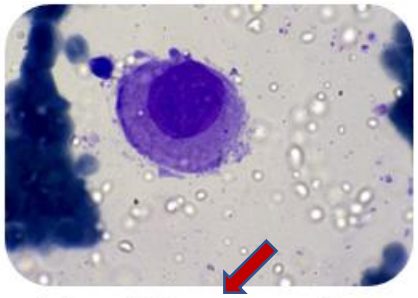


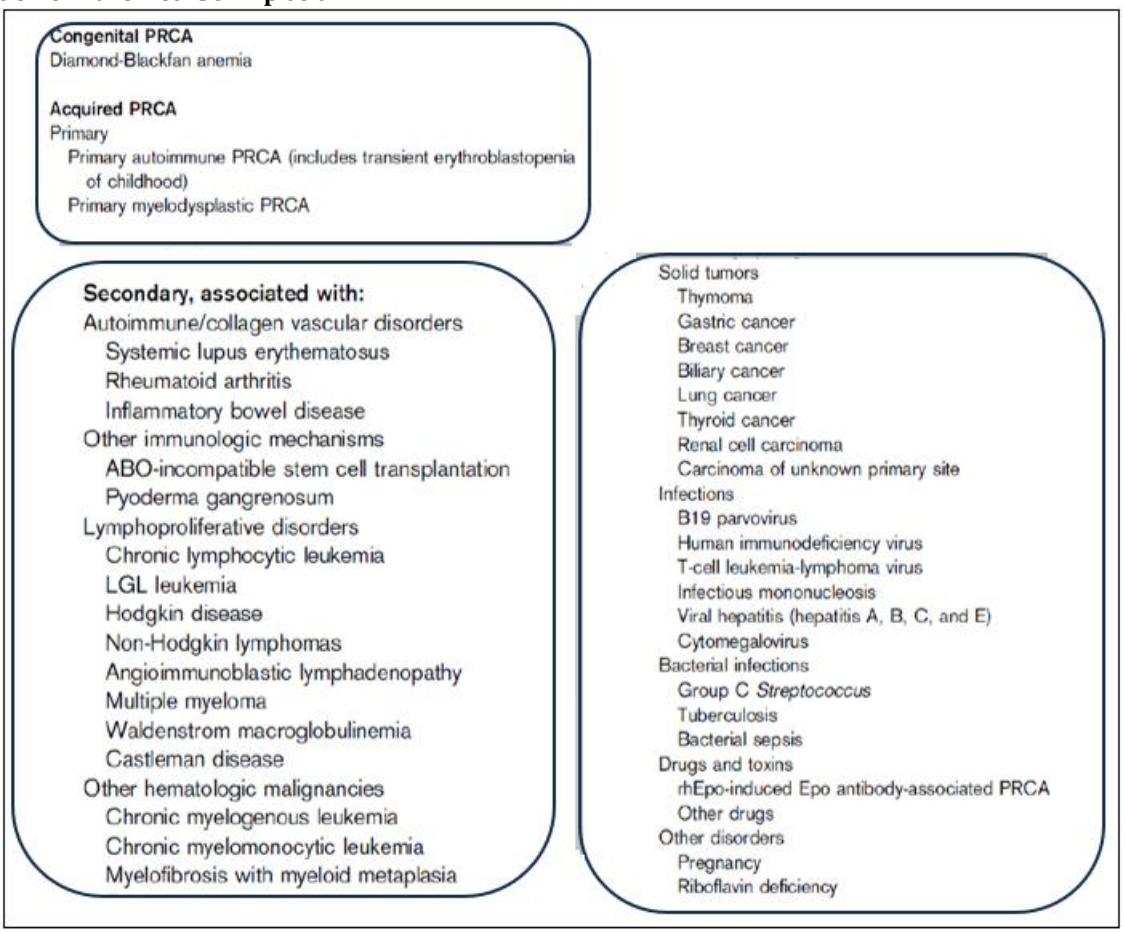
Figure 6: Bone marrow piture showing hypolobated megakaryocyte

3. Discussion

PRCA is a rare disorder which is due to isolated depression of erythroid series and is characterized by normocytic normochromic anaemia, reticulocyte count of <1% and marrow erythroblasts < 0.5% (1) . In some cases, few proerythroblasts and/or basophilic erythroblasts <5% of the differential count can be seen. Large proerythroblasts with vacuolated cytoplasmic pseudopodia called giant proerythroblasts if present are suggestive of B19 Parvovirus infection, but are not diagnostic (3) .

Extensive study of literature has been done but exact incidence of PRCA could not be ascertained. The etiology of PRCA is heterogenous (4) .

Classification of Pure Red Cell Aplasia



Clinical Presentation

There is no specific clinical presentation of primary acquired PRCA but can present with signs and symptoms of anaemia (5) . Patients with secondary PRCA manifest the symptomatology of the associated syndrome

Diagnostic Evaluation

Diagnosis of PRCA requires bone marrow examination (1) . In primary acquired (autoimmune) PRCA there is normal marrow cellularity with normal myeloid and megakaryocyte maturation. The diagnosis of PRCA is based on absence or near absence of erythroblasts in otherwise normal marrow. In some cases, there can be increase in lymphocytes, lymphoid aggregate and plasma cells indicating immune/inflammatory activation (6) . Iron stains will be normal. Ring sideroblasts are difficult to see because of the paucity of erythroid precursors. If ring sideroblasts are seen along with marked hypercellularity, it indicates myelodysplastic syndrome (7) . In Chronic kidney disease, Erythropoietin therapy due to the production of erythropoietin antibodies may induced Pure red cell aplasia (8) . The clinical presentation includes severe anaemia and low reticulocyte count and characterized by the absence of erythroid precursors in the bone marrow (9). Pure red cell aplasia may be acquired following Hepatitis C infection possibly due to autoimmune destruction (10) . PRCA may be associated with still's disease in adults due to autoimmune cause (11) .

In our cases, erythroid hypoplasia leading to red cell aplasia are due to? Parvo B19 infection in the 1st case due to the presence of giant proerythroblast, 2nd case due to HCV infection, 3rd case possibly due to autoimmune cause and related HLH , 4th case possibly due to Autoimmune and EPO antibody induced in CKD patient. Myelodysplasia associated PRCA in the 5th case.

Bone marrow examination is necessary to make a diagnosis of PRCA and also to guide for relevant investigations.

4. Conclusion

PRCA should be suspected in patients with an isolated anemia associated with marked reticulocytopenia. Evaluation of acquired PRCA should focus on identifying patients with myelodysplastic syndrome presenting with erythroid hypoplasia or PRCA associated with drugs, Parvovirus B19 infection, thymoma, or lymphoproliferative disorders for whom syndrome - specific management is required. Morphological evaluation of bone marrow is a necessity to reach to a definitive diagnosis of red cell aplasia and to guide for further necessary follow up.

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