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Pure Red Cell Aplasia- A Case Report

Medical Science

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ABSTRACT

Pure red cell aplasia(PRCA) is a rare condition. Cardinal findings are a low hemoglobin level, reticulocytopenia, and absent or extremely infrequent erythroid precursor cells in the marrow. We report a case of 25 year old man who presented with transfusion dependent anemia to our centre. After being investigated he was diagnosed with PRCA and started on glucocorticoids as underlying cause could not be established. He was advised to follow up with cytogenetic studies to rule out myelodysplasia or other lymphoid malignancies.

INTRODUCTION:

Pure red cell aplasia is a rare disorder in which maturation arrest occurs in the process of formation of erythrocytes. Erythroblasts are virtually absent in bone marrow; however, WBC and platelet production is normal. The anemia due to PRCA is usually normocytic but can be macrocytic. In 1922, Kaznelson recognized that this condition was a different entity from aplastic anemia, which presents with pancytopenia. The characteristics of PRCA include a severe anemia, a reticulocyte count of less than 1%, and the presence of less than 0.5% mature erythroblasts in the bone marrow. The bone marrow is usually normocellular. . Pure red cell aplasia in adults is usually acquired. Most often no underlying cause is identified and hence idiopathic PRCA is the most common variety of acquired PRCA. Life expectancy in idiopathic PRCA is 1-2 decades. Prognosis of acquired PRCA depends on the underlying cause.

CASE HISTORY:

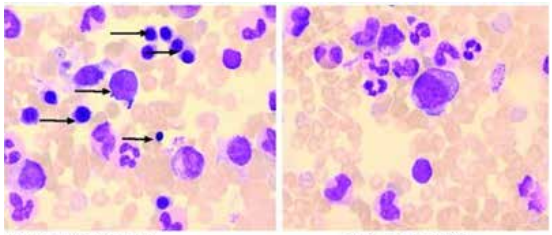
25 year old male patient presented with chief complaints of weakness, dyspnoea on exertion and a history of multiple transfusions in 1 year. . There was no history of chronic illness, drugs exposure or any other prior medical or surgical illness, skin lesions or multiple joint swelling. There was no prior history of hemolytic anemia. There was no family history of hematolological diseases. On examination, the patient was vitally stable with sinus tachycardia, normal blood pressure and respiratory rate. Marked pallor was observed. Respiratory system examination was normal with bilateral air entry and clear chest. Findings in Cardiovascular system examination were loud first heart sound, hyperdynamic apex beat and functional flow murmur was heard. There were no palpable lymph nodes. Only significant finding was that spleen was palpable about 4 cm below the left costal margin. Investigations are presented in Table 1

Inspite of all efforts and investigations, cause remained elusive. Cytogenetic study was advised by haematologist to rule out myelodysplastic disorder. Patient was managed by transfusing P.C.V as and when required and giving pulse steroid therapy along with immunosuppressant i.e. azathioprine. Patient was discharged after hematologist's opinion on oral steroids and advised to follow up with cytogenetic study report.

Table 1: List of investigations done.

Sr.No.	Investigation	Findings	Conclusion
1.	Complete blood count with peripheral smear	Hb-3gm%, Normal leukocyte and platelet count, Microcytic RBCs	Only erythropoietic lineage involvement
2.	Liver function tests and renal function tests	Normal	Ruling out anemia of chronic disease
3.	Serological tests-HIV,HbsAg,HCV	Non reactive	Ruling out immunocompromised state due to HIV and PRCA secondary to these viral infections
4.	S.Iron,S.Ferritin	Slightly increased	Probably due to recurrent blood transfusion & ruled out iron deficiency as a cause
5.	Sickling, NESTROFT, Direct and Indirect Coomb's test	Negative	Ruling out hemolytic anemia
6.	S.LDH	Normal(104)	Ruling out hemolytic anemia
7.	Retic count	0.5%	Hypoproliferative cause suspected
8.	Bone marrow biopsy	Normocellular marrow with erthroid hypoplasia	PRCA confirmed.
9.	ANA profile	Negative	Autoimmune etiology unlikely
10.	DNA PCR for Parvovirus B19	Negative	Ruling out PRCA secondary to Parvovirus infection.
11.	CECT thorax and Abdomen	Hepatosplenomegaly	No evidence of Thymoma. Hepatosplenomegaly leading us to suspect lymphoproliferative disorders, MDS.

BONE MARROW SMEAR IN A PATIENT WITH PRCA
FIGURE 1



DISCUSSION:

Pure red cell aplasia (PRCA) is a rare diagnosis. Commonly, PRCA presents as macrocytic or normocytic anemia. This case presented as microcytic anemia thus confounding diagnosis. Reduced retic count and erythroid hypoplasia in bone marrow however supported our diagnosis. Hepatosplenomegaly however lead us to suspect underlying lymphoproliferative disorder or myelodysplastic disorder. The diagnosis of MDS should be considered in any patient with unexplained cytopenia(s) or monocytosis. Hence, cytogenetic studies were advised by hematologist to rule out malignancies and myelodysplastic syndromes.

A later age of onset ruled out congenital PRCA which routinely presents in early childhood. A careful search for etiology of PRCA was undertaken as management differs in primary idiopathic and secondary PRCA In general, PRCA is due to a selective injury, often immunological, that affects the early phase of erythrocyte maturation.

Diamond-Blackfan syndrome is a rare congenital PRCA that is usually detected at birth, or later during the first 18 months of childhood. Affected individuals usually have a macrocytic anemia. The expression of hemoglobin F and surface "I" antigen in erythrocytes is increased, indicating erythrocyte immaturity. About one third of these patients have developmental defects, including cleft palates, macroglossia, craniofacial defects, thumb or upper limb abnormalities, cardiac defects, and urogenital malformations. Growth is often retarded. A modest increased risk for leukemia and neoplasms is noted. De novo cases of Diamond-Blackfan syndrome are believed to be caused by intrauterine damage to early erythroid stem cells. A familial history of PRCA is evident in approximately 10% of patients.

Transient erythroblastopenia of childhood (TEC) is a self–limiting, benign disorder. A history of a recent viral infection is usually noted. Parvovirus B19 infection should be ruled out.

Acquired primary (idiopathic) PRCA is the most common form of red cell aplasia in adults. However, PRCA can be secondary to underlying disorders. For example, autoimmune disorders (eg, type 1 diabetes, thyroiditis, rheumatoid arthritis, Sjögren syndrome) can be responsible. PRCA has been shown to be secondary to T-cell inhibition of marrow erythroid cells. PRCA can also be secondary to and is associated with the Thymoma, hematological malignancy, T-cell granular lymphocyte leukemia and solid tumors, Infections, Drugs, Pregnancy, Systemic lupus erythematosus, Renal failure, Good syndrome(thymoma with combined B and T cell deficiency. PRCA can occur following ABO-mismatched marrow transplantation. . In patients with PRCA in whom a plasma inhibitor of erythropoiesis cannot be demonstrated, lymphocyte-mediated inhibition of erythropoiesis is the most probable mechanism of pathogenesis.

The incidence of PRCA has increased in patients with chronic renal disease who have received epoetin therapy. This has been ascribed to the generation of antiepoetin antibodies, which occurs more often with epoetin-alpha than with epoetin-beta. This complication may be avoided by using an erythropoietin-mimicking human antibody, which stimulates erythropoiesis but does not appear to induce antiepoetin antibodies and PRCA.

An initial work-up should include a drug and medical history, a physical examination, and a complete blood count and blood smear. Chest x-ray or computed tomography to rule out thymoma, lymphocyte immunophenotype, and or T-cell gene rearrangement studies, marrow cytogenetic studies, and serum Southern analysis for presence of HPV B 19 are generally indicated. Specific therapies (ie, drug withdrawal, IgG for chronic HPV B19, thymectomy) should be pursued where appropriate. If the work-up for concomitant disease is unhelpful, immunosuppressive therapy should be employed. In patients with PRCA in whom a plasma inhibitor of erythropoiesis cannot be demonstrated, lymphocyte-mediated inhibition of erythropoiesis is the most probable mechanism of pathogenesis.

Acquired PRCA is not usually a preleukaemic disorder if cases with dysmyelopoiesis and cytogenetic abnormalities are carefully excluded. Diagnostic difficulties may arise in patients with parvovirus infection where bone marrow histology may vary depending on the stage of the disease, in patients with PRCA in remission who are in the process of relapsing and whose bone marrow may show signs of dyserythropoiesis, and in occasional patients in whom erythroid aplasia or hypoplasia precedes the development of abnormalities in the other haematopoietic lineages The presence of one of the characteristic chromosomal abnormalities is presumptive evidence of MDS in patients with otherwise unexplained refractory cytopenia and no morphologic evidence of dysplasia(-7/del(7q,)-5/del(5q),del(13q),del(11q),del(12p) or t(12p),del(9q)).

Primary, or secondary PRCA not responding to treatment of the underlying diseases, is treated as an immunologically mediated disease, based on a number of studies implicating a pathological role of serum auto-antibodies, natural killer (NK) cell-mediated or T lymphocyte-mediated effects impairing various stages and mechanisms of erythropoiesis. The major objective in the treatment of PRCA is to induce a remission with the recovery of erythropoiesis, thus providing relief from transfusions and avoiding transfusion-associated problems. The therapeutic plan usually focuses on the sequential use of various immunosuppressive therapies until a remission is obtained. Remissions have been achieved by treatment with corticosteroids(CS), cyclophosphamide (CY), cyclosporine A (CsA), antithymocyte globulin (ATG), splenectomy, and plasmapheresis. More recently, the efficacies of the anti-CD20 monoclonal antibody, rituximab, and anti-CD52 monoclonal antibody, alemtuzumab, to induce remissions of therapy-resistant PRCA have also been reported. However, these drugs are double edged swords with serious side effects. They also lead to immunocompromised state and susceptibility to infections which may aggravate the primary problem of anemia. Steroids can lead to Secondary Diabetes and Osteoporosis.

CONCLUSION:

Pure red cell aplasia (PRCA) is a syndrome characterized by a severe normocytic anaemia usually transfusion dependent, reticulocytopenia, and absence of erythroblasts from an otherwise normal bone marrow. Cytogenetic study should be conducted in every case of PRCA when etiol-

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ogy is unknown to rule out myelodysplastic syndromes and hematological malignancies. Primary PRCA, or secondary PRCA which has not responded to treatment of the underlying disease, is treated as an immunologically-mediated disease. Although vigorous immunosuppressive treatments(mainly glucocorticoids) induce and maintain remissions in a majority, they carry an increased risk of serious complications. Successful management should also include managing secondary infections and other complications related to treatment.

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