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Pure Red Cell Aplasia – A Rare Case Report.

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ABSTRACT

PRCA is a rare disorder that can affect any age and both genders equally. PRCA may be congenital or acquired. Acquired PRCA can be primary or secondarily associated with thymoma, chronic lymphocytic leukemia, lymphoma, solid organ malignancy, parvovirus B19 infection, HIV, hepatitis, tuberculosis, autoimmune disorders, SLE, rheumatoid arthritis, due to some nutritional deficiency, drug induced or may present as an idiopathic disorder. We report a case of chronic acquired PRCA in a 40 year old male. Any anaemia of prolonged duration, not responding to conventional therapy should be evaluated by bone marrow studies to rule out ineffective erythropoiesis, dysplastic syndromes, infiltrative diseases of the bone marrow or a selective erythroid suppression. PRCA is a rare disorder with varied etiology, where no cause can be established, it is labeled as idiopathic PRCA, treatment is done with corticosteroids (first line of therapy), which show a response by 4 weeks. Other agents that can also be used are cyclosporine, cyclophosphamide, azathioprine, rituximab.

Keywords: Anaemia, idiopathic, PRCA.

INTRODUCTION

PRCA is a rare disorder. It is the result of isolated depression of erythroid series and is characterized by normocytic normochromic anaemia, reticulocyte count < 1%, marrow erythroblasts < 0.5%. It is a rare disorder that affects any age and both male and females equally. PRCA may be congenital or acquired. Acquired PRCA may be primary or secondarily associated with thymoma, chronic lymphocytic leukemia, lymphoma, solid organ malignancy, parvovirus B19 infection, HIV, hepatitis, tuberculosis, autoimmune disorders, SLE, rheumatoid arthritis, due to some nutritional deficiency, drug induced or may present as an idiopathic disorder.[1] We report a case of chronic acquired PRCA in a 40 year old male.

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CASE REPORT

A 40 year old male, electrician by occupation presented to the Medicine OPD, Rajindra Hospital Patiala with complaints of generalized body aches, dyspnoea on exertion for the past one year and history of exacerbation of symptoms for past three months. There was no complaint of fever, jaundice, weight loss, loss of appetite, body rash, joint pains or any drug intake of long duration. 12 years back patient had a history of infection with mycobacterium tuberculosis (tubercular pleural effusion) and subsequent treatment with anti-tubercular drugs for 6 months following which the patient recovered. No significant family history was available. On examination breath sounds on left side of chest were decreased (attributed to past pleural tubercular infection), no remarkable finding was seen in any other system clinically. No organomegaly was noted. On investigation, his hemoglobin was 3.9g%, total leucocyte count - 5800/cumm, DLC- Neutrophils-32%, Lymphocytes-56%, Eosinophils-12%, platelets – 1.5lac/cumm, RBC count - 1.25million/cumm, hematocrit 12%, reticulocyte count - 0.1%, ESR-18mm/hour. On peripheral blood film examination normocytic normochromic picture of RBCs was seen with no polychromasia, no nRBC. His LFTs and RFTs were within normal range. Stool for occult blood was negative. Sputum for AFB was negative. Patient was RA factor negative, ANA negative. His chest X ray showed left pleural thickening, no other abnormality was seen. Bone marrow aspiration was performed in Bhupindera Clinical Laboratory, Clinical Pathology department, Rajindra Hospital Patiala. The bone marrow aspiration smears revealed a moderately hypercellular marrow [Figure 1] with increased M:E ratio(19:1) and depression of erythroid series. Only 5% proerythroblasts were seen with absence of mature normoblasts [Figure 2], no features of

dyserythropoeisis or giant erythroblasts were seen. Myeloid series showed normal differentiation and maturation. Megakaryocytes were adequate and functional. Differential count of non-erythroid series showed myeloblasts-00%, promyelocyte-10%, myelocyte-19%, metamyelocyte-13%, neutrophil-27%, lymphocyte-15%, eosinophil-10%, plasma cells-6%. Keeping in view the clinical history and examination, laboratory findings and bone marrow aspiration findings,a diagnosis of acquired PRCA was made.

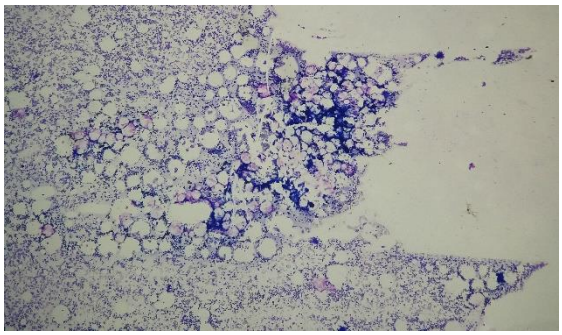

Figure 1: Bone marrow aspiration smears showing moderately hypercellular marrow. (Leishman Stain 40X)

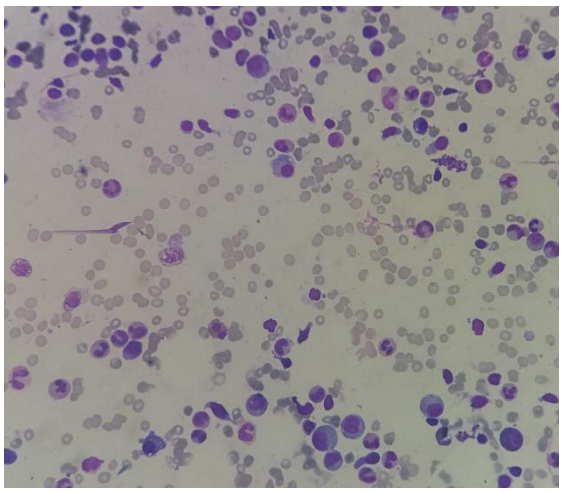

Figure 2: Erythroid series show only proerythroblasts, no mature form seen. (Leishman stain 400X)

DISCUSSION & CONCLUSION

PRCA is characterized by decreased RBC precursors with normal granulopoiesis and megakaryopoiesis in the bone marrow presenting clinically as anaemia.[2] Even after extensive study of literature, exact incidence of PRCA could not be ascertained.
The etiology of PRCA is heterogenous [Table 1][3]

Table 1 – Etiology of PRCA

I. Congenital form (Diamond-Blackfan anaemia)
II. Acquired PRCA
(a)Parvovirus B19 infection
1.Transient aplastic crisis (TAC) in patients with shortened erythrocyte life span
2.Chronic type of bone marrow failure in immunosupressed patients
(b)Immunological suppression of erythropoiesis
1.Antibody mediated
i.Antibody against red-cell progenitors
-Transient erythroblastopenia in childhood (TEC)
-Adult form
-ABO-incompatibility following bone marrow transplantation
ii.Antibody against erythropoietin
2. αβ or γδ T cell-mediated
-T-helper cell-mediated antibody production
-MHC-restricted, recognition of red-cell progenitors
-MHC-unrestricted recognition of red-cell progenitors
3. NK cell- or T cell-mediated
-MHC-unrestricted cytotoxicity
(c)Associated with pregnancy
(d)Associated with certain drugs and toxins
(e)Initial manifestation of a pre-leukaemic syndrome

In adults, PRCA may be associated with systemic autoimmune disease, drugs, toxins, solid organ transplantation, malignancy, systemic infections like tuberculosis.[4] HIV, CMV, out of these, of particular interest is, infection with Parvovirus B19. Such patients present with severe anaemia, fever, anorexia, nausea, vomiting, headache, abdominal pain and chills. The haemoglobin concentration is low.[5] It was seen that this crisis was a result of cessation of RBC production. BMA showed large proerythroblasts with large vesicular nuclei with loosely distributed chromatin and prominent, inclusion body-like nucleoli, surrounded by a basophilic cytoplasm.[6] which is a characteristic finding.
PRCA presenting in conditions such as collagen vascular disease, autoimmune disease, tuberculosis, post transplantation, assosciated with thymoma seem to have an immunologically mediated suppression of erythropoeisis which may be antibody mediated,[7] T cell mediated,[8] or NK cell mediated.[9]
Patients of autoimmune disease show IgG antibody directed against erythroblasts leading to a complement mediated lysis of RBC progenitors. Anti-erythroblast antibodies that are not directly cytotoxic may inhibit RBC maturation by inhibiting erythropoeitin receptors.
It has been seen that T cells in patients with B-CLL suppress erythroid colony formation in vitro probably by secretion of inhibitory lymphokines.[10]
In addition to more than 30 drugs have been implicated in the etiology of PRCA with only phenytoin, isoniazid and azathioprine having a proven causative role.[11] Pathogenesis include direct effect on RBC precursors as well as induction of autoimmunity.
Majority of the PRCA cases show clinical and hematological improvement on removal of the underlying offending agent. Conventionally PRCA

has been treated with corticosteroids. Understanding the pathophysiology of PRCA has provided us with novel therapeutic options including cyclosporine, cyclophosphamide, rituximab, anti thymocyte globulin.[12] Following treatment response to therapy is assessed by serial evaluation of reticulocyte count and hematocrit.

In the case discussed above although the patient had history of infection with mycobacterium tuberculosis 12 years back and subsequent treatment with isoniazid and rifampicin, no temporal relationship could be established to implicate any causation. Even with extensive investigations none of the proved causative factors for PRCA could be established thus the case was labeled as idiopathic PRCA.

The patient was started treatment with predenisone 1mg/kg body weight/day. On follow up after one month the reticulocyte count and hematocrit of the patient had improved.

Any anaemia of prolonged duration, not responding to conventional therapy should be evaluated by bone marrow studies to rule out ineffective erythropoiesis, dysplastic syndromes, infiltrative diseases of the bone marrow or a selective erythroid suppression. PRCA is a rare disorder with varied etiology. Whenever a causative agent can be established, rapid response follows with the treatment of underlying cause or withdrawal of incriminating drug. In cases where no cause can be established, labeled as idiopathic PRCA, treatment is done with corticosteroids (first line of therapy), which show a response by 4 weeks. Other agents that can also be used are cyclosporine, cyclophosphamide, azathioprine, rituximab.

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