

Drug Induced Chronic Acquired Pure Red cell Aplasia in Adolescent boy

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Abstracts: Acquired Pure red cell Aplasia (PRCA) is a disorder seen rarely in children and adolescents. Drugs like sodium valproate and carbamazepine have emerged as an important cause of acquired PRCA, when used for a long duration. Apart from the neurological side-effects, haematological side-effects in form of aplastic anemia and agranulocytosis are well-documented in carbamazepine therapy. The haematologic side-effects of carbamazepine, although not common, should nevertheless be borne in mind due to the serious, prolonged and sometimes even fatal consequences. Carbamazepine is a commonly prescribed drug in today's scenario and it is important to be aware about its common and uncommon side-effects. We report a case of Carbamazepine induced pure red cell aplasia in an adolescent boy. Since, this drug induced PRCA is reversible if recognised early, it is worthwhile to be aware of this complication to prevent permanent morbidity due to generalised bone marrow hypoplasia. [Malipatil R A et al. NJIRM 2011; 2(3) :98-100]

Key Words: Pure red cell aplasia, carbamazepine, Adolescent boy

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Introduction: Pure Red Cell Aplasia (PRCA) is a rare condition of profound anemia characterized by the absence of reticulocytes and virtual Erythroblastopenia in the bone marrow¹. It may be congenital or acquired.

Acquired Pure red cell Aplasia (PRCA) is a disorder seen rarely in children and adolescents.^{1,2} Drugs like sodium valproate and carbamazepine have emerged as an important cause of acquired PRCA, when used for a long duration. Carbamazepine is a commonly used drug. Apart from the neurological side-effects, haematological side-effects in form of aplastic anemia and agranulocytosis are well-documented.³ We report a case of Carbamazepine induced pure red cell aplasia in an adolescent boy. Since, this drug induced PRCA is reversible if recognized early, it is worthwhile to be aware of this complication to prevent permanent morbidity due to generalized bone marrow hypoplasia.

Case Report : A 16 year old boy presented with history of weakness, breathlessness since three months and increased since two weeks. He was a known case of epilepsy on anticonvulsant therapy with carbamazepine since last 8 years. There was no history of bleeding tendencies, echymoses, bone pains, joint swellings or rashes. There were similar complaints about 3 years ago, but the boy was not evaluated thoroughly. He was given 3-4

points of blood and haemetenics. Family history was non-contributory.

On Examination, apart from pallor, general physical examination revealed no abnormality. On systemic examination, all the systems were within normal limits, except a functional systolic murmur.

Investigations: Hb- 3.1Gm%, PCV= 9.3%; RBC count = 0.90 million / cumm Retic = 0%. However, red cell indices were within normal limits. Peripheral smear revealed anisocytosis, poikilocytosis, normocytic normochromic red cells with occasional macrocytes and tear drop cells. The total count was mildly increased with Neutrophilia. Platelets were adequate. Bone marrow aspiration (Fig 1) and trephine biopsy revealed red cell hypoplasia with absence of giant pronormoblasts. The myeloid and megakaryocytic series were normal. M:E ratio was 10 : 1.

Renal and liver function tests were within normal limits, Stool for occult blood and ova – negative and HbF was 0.38% [to rule out thalassemia]. Direct and Indirect antiglobulin tests were negative. CT scan of chest ruled out thymomas. Mantoux test and chest x-ray ruled out Tuberculosis. RA factor, ANAs and Anti-dsDNA-Negative. HIV and HBSAg were also negative

These investigations ruled out the majority of secondary causes of acquired PRCA.

Considering the present history, past history, long term carbamazepine therapy and investigation findings, the diagnosis of Carbamazepine induced chronic PRCA made. After the cessation of the offending drug, patient was treated with supportive care for anaemia. There was steady improvement in Hemoglobin over the period of six weeks.

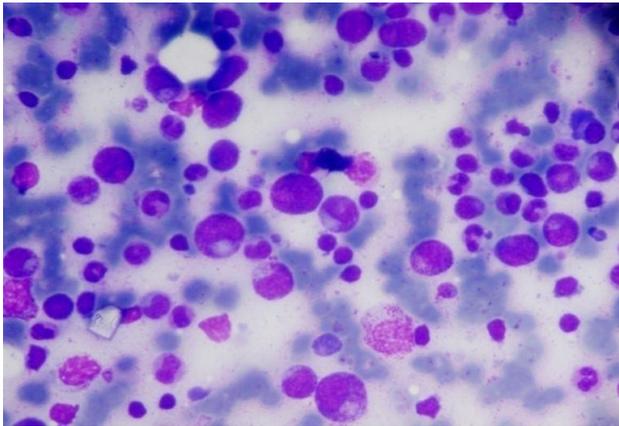


Fig 1: Bone Marrow Aspirate showing markedly decreased Erythroid series with normal Myeloid and megakaryocytes (Leishman stain - X400)

Discussion: Acquired pure red cell aplasia is a disease characterised by normocytic, normochromic anaemia, low haematocrit, reticulocytopenia and selective erythroid hypoplasia.² The first description of this entity was given in 1922 by Kaznelson H was: a progressive normochromic anemia with no signs of regeneration in the peripheral blood, no polychromasia, no reticulocytes, no erythroblasts; erythropoietic aplasia in the bone marrow with disappearance of all types of erythroblasts; normal leukopoiesis and thrombopoiesis and no enlargement of the spleen or lymph nodes.⁴ It may be congenital or acquired. Congenital PRCA is also known as Diamond-Blackfan syndrome. In the Congenital PRCA there is injury to the stem cells in utero.²

Acquired PRCA which is rare in children and adolescents, may be primary or Secondary. It has been postulated that primary PRCA has an

immunological basis which has been confirmed by in-vivo and in-vitro studies.⁵ The secondary causes for Acquired PRCA are Malnutrition, Thymoma, Autoimmune diseases (Rheumatoid arthritis, Systemic lupus Erythematosus, Malignancies (leukemia, Lymphoma, Multiple Myeloma, and Carcinomas of several organs), drugs (including alpha Interferons, Lamivudine, INH, Diphenylhydantoin, Sodium valproate, Carbamazepine etc.) and infections like infectious mononucleosis, viral hepatitis Parvovirus B19 and tuberculosis.² PRCA may represent the prodrome to a Myelodysplastic syndrome (MDS).^{1,2,3,5} Acquired primary PRCA commonly occurs at a mean age of 60 years. Rare familial cases have been reported. The male to female ratio is 2:1.

Although, haematological complications like aplastic anemia due to carbamazepine therapy are well known but pure red cell aplasia is exceedingly rare. A slow progressive normocytic-normochromic anemia and reticulocytopenia, without leukopenia and thrombocytopenia in a patient who, except pallor, does not generally show abnormal findings on physical examination, should arouse the suspicion of PRCA.³

Pathogenesis involves immune dysfunction with antibodies directed against erythroid precursor cells or erythropoietin, or due to T-cell mediated suppression of erythropoiesis.² in our case, carbamazepine was considered as the probable causal association for isolated red cell production failure.

The exact mechanism of drug induced PRCA in most cases is unknown. The possible mechanisms suggested include (i) toxic interference by drugs with the metabolism of nucleated red cells, (ii) immunologically mediated reaction with antibody formation against red cell precursors and (iii) specific inhibitory effect on DNA synthesis probably at the step of deoxyribonucleotide formation. Drug-induced PRCA is usually reversible after discontinuation of the offending drug.³

It may be pertinent to explain the neurologic, haematologic, hypersensitivity or dermatologic side-effects of carbamazepine; at the time of initiation of therapy; and advice patients for

regular monitoring of blood counts.³ Haematological dyscrasias are important because they can be rapidly fatal if progressive. It is recommended that a full blood count be performed before beginning therapy with carbamazepine and thereafter during the follow-up. Carbamazepine is a commonly prescribed drug in today's scenario and it is important to be aware about its common and uncommon side-effects.³

Conclusion: Acquired PRCA is rare in children and adolescents. Carbamazepine is known to cause neurological, hematological, dermatologic and hypersensitivity reactions as side-effects. It is important to educate patients about the need to identify early toxic symptoms of a potential drug-related side-effect and advise for regular monitoring. Carbamazepine is known to cause aplastic anemia and agranulocytosis. Pure red cell aplasia is a rare complication which has been noticed with carbamazepine, and is reversible with cessation of therapy.

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