Pure Red Cell Aplasia: A Rare Complication of Isoniazid Therapy

Ayush Shukla · Sanjay Mishra ·
Mili Jain · Anil Kumar Tripathi

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Introduction

Pure red cell aplasia (PRCA) is the term widely applied to isolated anemia secondary to failure of erythropoiesis. The cardinal findings are a low hemoglobin level, reticulocytopenia, and absent or extremely infrequent erythroid precursor cells in the marrow. Despite its infrequency, PRCA has been a subject of much laboratory research because of its link to an immune mechanism of erythropoietic failure and as a manifestation of parvovirus B19 infection and destruction of marrow red cell progenitors. However, because of its infrequency, PRCA has not been the subject of large or controlled clinical trials; as a result, therapeutic recommendations are based on single cases or small series. This condition may appear as an acquired defect of either acute or chronic etiology, or a congenital form (Diamond–Blackfan Anemia).

The acquired causes of PRCA include infections, malnutrition, thymoma, chronic lymphocytic leukemia, clonal myeloid disease, collagen vascular disease, post stem cell transplant, anti erythropoietin antibodies, pregnancy and drugs. The drugs are supposed to cause PRCA idiosyncratically and include diphenylhydantoin, sulfa and sulfonamide drugs, azathioprine, allopurinol, isoniazid, procainamide, ticlopidine, ribavirin, and penicillamine [1].

There are very few reports of development of PRCA during antituberculous treatment (ATT). In this article, we report an additional case and review the literature, thereby emphasizing the need for clinicians to be alert from this rare complication of ATT.

Case History

A 34-year-old lady with a history of pulmonary tuberculosis diagnosed in May 2012 and taken ATT for 6 months, presented to us with complaints of easy fatigue, malaise and weakness. On examination, pallor was present with no other significant finding. Chest X-ray compared from previous one had improvement in lung fields. She denied of any history of blood loss, however she told that she had developed jaundice after 2 months of ATT, and also that she grew pale and weak and her haemoglobin was found to be 6.2 g/dl with raised S. bilirubin. Isoniazid was stopped for 2 weeks, haemoglobin rose to 9.2 g/dl and bilirubin levels were normalized. Patient consulted private practitioner who restarted isoniazid following which her general condition again gradually worsened. Patient completed her course of ATT and was referred to us for hematological workup. Initial hematological evaluation revealed a haemoglobin of 4 g/dl, normocytic normochromic with mild anisocytosis, and a reticulocyte count of 0.3 %, white cells and platelet counts being both normal at 5,980/mm³ and 1.72 lac/mm³. Her blood sugar, liver function test, renal function test and urine examination were normal. All investigations for hemolysis were normal along with normal liver and spleen size. Bone marrow aspirate performed was suggestive of hypoproliferation of erythroid lineage. The morphology and maturation sequence of the myeloid cells and megakaryocytes was normal. The plasma cells

A. Shukla (✉) · S. Mishra · A. K. Tripathi
Department of Clinical Hematology and Medical Oncology,
King George's Medical University, Lucknow 226003, India
e-mail: ayushgeorgian@gmail.com

M. Jain
Department of Pathology, Hind Institute of Medical Sciences,
31/3, Patel Nagar, Sec-9, Indira Nagar, Barabanki,
Lucknow 226016, India

Fig. 1 Bone marrow aspirate showing hypoproliferation of erythroid lineage

and mononuclear lymphoid cells were also normal. No sideroblasts were seen on Prussian blue staining.

The marrow picture was consistent with pure red cell aplasia (Fig. 1). Ultrasonography and radiological examination ruled out any mediastinal mass. Infective causes like parvovirus were ruled out accordingly and there was no evidence of any malignancy. Other causes that may be responsible for PRCA were also ruled out.

We suspected Isoniazid to be the responsible agent here. Isoniazid was stopped, 3 units of packed red blood cells transfused and pyridoxine supplementation was given. Patient recovered successfully and became normal hematologically.

Discussion

Pure red cell aplasia (PRCA) in adults is a rare disorder characterized by acquired isolated erythroid hypoplasia and

is frequently associated with malignancy. The pathogenesis in most of the cases is immunological. Drug induced PRCA is very uncommon and accounts for less than 5 % cases. Till date about 70 cases have been reported, with around 30 drugs been implicated. Out of these, very few reports have been published relating PRCA to ATT, and Isoniazid has been implicated in all of them [2, 3].

The exact mechanism of drug induced PRCA is unknown in most of the cases. The possible mechanisms include toxic interference by drugs in the metabolism, immunologically mediated reaction with antibodies against red cell precursors and specific inhibitory effect on DNA synthesis. Isoniazid may also cause sideroblastic anemia, even rarer side effect [4–6].

Isoniazid induced PRCA is usually reversible after the discontinuation of the drug. It is mandatory for a clinician to be aware of this side effect as tuberculosis is highly prevalent in this part of world and isoniazid is an essential component of ATT. Proper knowledge about this fact may help in diagnosing the patient early and avoid morbidity and mortality.

References

1. Neal SY (2010) Pure red cell aplasia. In: William's Hematology, 8th edn. McGraw-Hill, New York, pp 485–493
2. Lewis CR, Manoharan A (1987) Pure red cell hypoplasia secondary to isoniazid. *Postgrad Med J* 63:309–310
3. Sen R, Singh U, Yadav MS et al (1989) Isoniazid induced pure red cell aplasia. *Indian J Tuberc* 36:41–43
4. Marseglia GL, Locatelli F (1998) Isoniazid-induced pure red cell aplasia in two siblings. *J Pediatr* 132:898
5. Gupta RC, Dixit R, Prasad N, Gupta N (2000) Pure red cell aplasia due to isoniazid: a case report and review of literature. *Curr Med Trends* 4:684–687
6. Dixit R, Dixit R, Dixit K (2003) Isoniazid induced pure red cell aplasia. *Indian J Allergy Asthma Immunol* 17(2):93–95