INTRODUCTION

Pure red cell aplasia (PRCA) is the name given to a group of conditions in which there is a deficiency or virtual absence of nucleated red cell precursors from the bone marrow (erythropoietic hypoplasia), in the absence of abnormalities in the leucopoietic or thrombocytopoietic system. The marrow is normally cellular but is devoid of erythroblasts. This condition may appear as an acquired defect of either acute or chronic type, and a congenital form (Josephs-Diamond-Blackfan syndrome).1 Acquired form of PRCA is associated with hemolytic disorders, infections, malnutrition, hepatitis, thymoma, various other neoplasms, immunological disorders, drugs and chemical agents etc.1,2 There are only few reports of development of PRCA during antituberculous chemotherapy.3-6 The present report is an additional one and also emphasize the need for clinicians to be aware of this rare haematological complication that may arise during antituberculous chemotherapy.

CASE REPORT

A case of pure red cell aplasia following antituberculous chemotherapy for sputum positive pulmonary tuberculosis is being described in a 46-year old male patient. Bone marrow aspirate revealed hypocellular marrow with a profound erythroid hypoplasia and a high myeloid/erythroid ratio. Patient responded to isoniazid withdrawl and corticosteroid therapy.

Keywords: Pure red cell aplasia, Isoniazid, sputum positive pulmonary tuberculosis
consistent with pure red cell aplasia. Other investigations revealed no evidence of haemolysis, Bence Jones proteinuria and LE cell phenomenon. Schilling test, direct and indirect Coombs test were also negative. Ultrasonography and other radiological examination ruled out mediastinal mass or thymoma. Patient was managed with three units of fresh blood transfusion. Than we suspected isoniazid as a cause of red cell aplasia after referring literature. Isoniazid was withdrawn and rest antituberculosis drugs were continued with oral prednisolone 40 mg/day which was gradually tapered and finally stopped after four weeks. Steptomycin was added instead of isoniazid. His hemoglobin rose to 9 gm% and reticulocyte count 2.2%. Withdrawal of isoniazid, instituting steroid therapy and three units of blood transfusion resulted in hematological recovery. Patient is still on treatment.

DISCUSSION
PRCA is characterised by an isolated anaemia and a bone marrow of normocellularity in which there is an almost complete absence of erythroblasts with normal myeloid cells and megakaryocytes.\(^4,7\) The reticulocyte count is low while the platelet count and leukocyte count are normal. The pathogenesis of PRCA is heterogeneous. A congenital form of PRCA is the Diamond-Blackfan anaemia. Approximately 50% of the patients have genetic mutations that predominantly affect the erythropoietic lineage.\(^4\) The acquired form of PRCA is much more common. Most cases of acquired PRCA are autoimmune-mediated. Various autoimmune mechanisms are postulated such as autoantibodies against erythroblasts or erythropoietin, natural killer (NK) cell mediated or T lymphocyte mediated lysis of erythroblasts.\(^4,8\) The autoimmune mediated PRCA is associated with infections (parvo-B19 virus), autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus) or neoplasias (thymoma, lymphoma and carcinoma).\(^7\) Specific situations in which autoimmune-mediated PRCA can occur are during pregnancy and after allogeneic bone marrow or stem cell transplantation due to ABO incompatibility.\(^7\) Drug as causative agent is in approximately 5% of the cases with acquired PRCA.\(^8,9\) More than 30 types of drugs have been reported in the literature.\(^8\) Most reports describe only limited number of patients.\(^7\) However, the causal relationship for isoniazid is well documented. Isoniazid-induced PRCA was first described by Goodman in 1964.\(^3,5\) Since then, a few more cases are reported in the literature.\(^4,9\) Isoniazid-induced PRCA appeared relatively late during therapy. The duration of exposure to isoniazid before presentation of anaemia ranged from two to six months. In all cases, full recovery occurred in a period of few days to weeks after drug discontinuation. The pathogenesis of isoniazid-induced PRCA is not known. Some authors suggested an idiosyncratic form of metabolic interference of the erythrocyte production.\(^3,4,10\) Others suggested mechanisms include a direct toxic effect of isoniazid or its metabolite on the erythroid precursor cells, formation of autoantibodies or an inhibitory effect on DNA synthesis.\(^7,9\) Furthermore, isoniazid binds to pyridoxine and depletes pyridoxine supplies which can cause an anemia.\(^10,12\) Isoniazid is often combined with other antituberculous drugs which also can induce haematologic abnormalities.\(^10,12\) In our case, however, a causal relationship between PRCA and isoniazid seems likely because of the prompt recovery after discontinuation of isoniazid only.

FIGURES & LEGANDS

REFERENCES