CASE REPORTS

Pure red cell aplasia caused by D-penicillamine treatment of rheumatoid arthritis

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Abstract

A 40 year old woman with rheumatoid arthritis developed pure red cell aplasia after treatment with D-penicillamine 500 mg/day. D-Penicillamine was stopped and short term treatment with steroids resulted in complete recovery of bone marrow.

Although D-penicillamine has been found to be effective in the treatment of rheumatoid arthritis, the incidence of complications has been reported to be as high as 60%.¹ Blood dyscrasias and bone marrow aplasia have been reported previously, some of them with fatal outcome.² Pure red cell aplasia has been associated with rheumatoid arthritis, and many drugs, including non-steroidal anti-inflammatory drugs, have been incriminated in the development of such aplasia.³ To our knowledge, however, D-penicillamine has not been reported as the cause of pure red cell aplasia in patients with rheumatoid arthritis. We report the case of a patient who developed pure red cell aplasia while taking penicillamine. Cessation of treatment and institution of steroids resulted in complete recovery.

Case report

A 40 year old woman had a two year history of seropositive erosive rheumatoid arthritis. After treatment with a variety of non-steroidal anti-inflammatory drugs treatment with D-penicillamine 250 mg/day was started in August 1988 with gradual improvement in her clinical condition. Laboratory tests showed a haemoglobin of 128 g/l with normal white cell and platelet counts and a sedimentation rate of 25 mm/h. In June 1989 because of a flare of her disease the dosage was raised to 500 mg/day. Active synovitis subsided and since then the patient has taken only occasional paracetamol in addition. Routine blood tests performed a month later showed a haemoglobin of 73 g/l, packed cell volume 0.2 with 2.1×10^6 red cells and 0.2% reticulocytes. Her white cell count was 6.3×10^9 /l with a normal differential count, the platelet count was 474×10^9 /l, and the erythrocyte sedimentation rate was 89 mm/h. Bone marrow aspiration showed normal cellularity with increase in megakaryocytes, hyperplasia of myeloid series, and almost complete absence of erythroid precursors. Coombs' test was negative, serum iron and ferritin concen-

Laboratory results after stopping treatment with penicillamine

Date	Haemoglobin (g/l)	Reticulocytes (%)
2 Jun 1989	128	ND*
5 July 1989	73	0.2
16 July 1989	75	0.5
30 July 1989	85	6.0
13 Aug 1989	96	8.0
3 Sept 1989	112	3.0
8 Oct 1989	125	3.0

*ND=not done.

trations were high, while vitamin B-12 and folic acid were normal. Rheumatoid factor was positive at a titre of 1/5000, and the concentration of all serum immunoglobulins was slightly raised. A chest radiograph was normal except for mild interstitial changes. A presumptive diagnosis of penicillamine induced pure red cell aplasia was made, the drug was stopped, and treatment with prednisone 30 mg/day started. Her haemoglobin concentrations and reticulocyte counts increased gradually (table) and the prednisone dose was tapered. Three months later the patient had completely recovered and treatment was started with low dose methotrexate.

Discussion

Pure red cell aplasia is characterised by diminished or absent erythroblasts in the bone marrow with normal myeloid and megakaryocytic lineages. Laboratory examinations showed anaemia and reticulocytopenia with normal white cell and platelet counts. This selective damage of the erythroid lineage has been reported to occur with lymphoproliferative disorders, thymoma, neoplasms, autoimmune disorders, or to be drug related.⁴ An association between patients with untreated rheumatoid arthritis and pure red cell aplasia has been reported.⁵ Nevertheless, in most reports drugs have been incriminated in the cause of pure red cell aplasia: gold salts,⁶ azathioprine,⁷ and non-steroidal anti-inflammatory drugs.³ D-Penicillamine has been reported to cause transient bone marrow depression in up to 12% of patients,⁸ usually in a dose related mechanism. On the other hand, aplastic anaemia, which is serious and potentially life threatening, occurs as an idiosyncratic reaction only in some cases.^{8,9} Pure red cell aplasia attributed to D-penicillamine treatment has been reported in a patient

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taking the drug for more than 14 years for Wilson's disease.¹⁰ To our knowledge, however, this has not previously been reported as a cause for pure red cell aplasia in patients with rheumatoid arthritis. The concurrent use of paracetamol does not interfere with our conclusions as after withholding penicillamine treatment the bone marrow recovered despite the continuous use of the paracetamol. Pure red cell aplasia has commonly been shown to be an immunologically mediated syndrome¹¹; it should therefore be treated with the same rationale as immune haemolytic anaemia. Most authors recommended giving prednisone up to 60 mg/day for a period of four weeks and if no response occurs, cyclophosphamide can be added.⁴⁻⁵ Our patient responded quickly to drug discontinuation and short term corticosteroid treatment. Doctors should be aware of this rare side effect and we re-emphasise the importance of frequent blood counts in patients receiving penicillamine treatment.

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