Development of an inflammatory synovitis following total-dose infusion of iron-dextran

A case report

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Summary

Total-dose iron-dextran infusions have been reported to cause exacerbation of the disease in patients with rheumatoid arthritis and ankylosing spondylitis. A case of prolonged polyarthritis following a total-dose iron-dextran infusion in a patient with no evidence of rheumatoid arthritis or ankylosing spondylitis is reported.

Intravenous administration of an iron-dextran preparation for iron deficiency anaemia has been stated to cause an acute exacerbation of joint symptoms in patients with rheumatoid arthritis and ankylosing spondylitis, but other authors have not confirmed this. In all the cases described joints appear to have returned to their pre-infusion state within a few weeks. We report on a patient with no apparent rheumatoid arthritis or ankylosing spondylitis who developed prolonged inflammatory synovitis following iron-dextran infusion for anaemia.

Case report

A 40-year-old White woman was admitted to our unit at H. F. Verwoerd Hospital on 26 November 1980, complaining of very painful polyarthritis that had appeared 5 weeks earlier after an iron-dextran infusion. The patient had consulted her general practitioner for a pain in her foot, later diagnosed as interdigital neuroma. Anaemia had been noted and 40 ml iron-dextran preparation was administered by intravenous infusion. Eight hours after the infusion acute severe pain developed in the lower back, knees, ankles, right shoulder, sternoclavicular joint, left wrist and second metacarpophalangeal and joint of the left hand, as well as the proximal distal interphalangeal joints of both hands. She was given muscle relaxants and steroids but obtained only moderate relief from the pain and was transferred to our unit 5 weeks after onset of her symptoms.

Thorough history-taking could elicit no reason for the anaemia other than a history of moderate menorrhagia. The patient said she had recently lost 9 kg in weight. There was no history or evidence of rheumatoid arthritis or ankylosing spondylitis.
Examination

On admission to our unit she was pale, with a blood pressure of 110/70 mmHg, a pulse rate of 90/min and a temperature of 36.5°C. No abnormalities of the cardiovascular or respiratory systems, the abdomen or the central nervous system were found. Both knee joints were swollen and painful with synovitis and were held in 15° flexion. She could not extend her knees fully. Her ankles and the second metacarpophalangeal joint of the left hand were also swollen with synovitis. Despite 5 weeks of steroid therapy she could not walk because of severe pain in the knees and ankles.

The tenderness of the distal interphalangeal joints, as well as tenderness and mild synovial thickening of the proximal interphalangeal joints, was present. The patient also complained of morning stiffness.

Investigations

Laboratory investigations on admission showed: a red blood cell count of 4.72 x 10^12/L; a total white cell count of 7.5 x 10^9/L; haemoglobin concentration 10.3 g/dl; haematocrit 0.340 L/L; mean corpuscular volume 72 fl; mean corpuscular haemoglobin 22 pg; mean corpuscular haemoglobin concentration 31 g/dl; reticulocytes 1.7%; and platelet count 255 x 10^9/L. The differential count was normal. The red cells showed anisocytosis, microcytosis, hypochromia, poikilocytosis and diffuse basophilic stippling. The ESR (Westergren) was 74 mm/h on 26 November, 70 mm/h on 3 December, and 103 mm/h on 11 December.

Routine kidney and liver function tests were normal and the Rose Heller and antinuclear factor tests and tests for gonorrhoea, syphilis, Yersinia, Brucella, Salmonella, Shigella and tuberculosis were negative. There were no microscopic abnormalities of the urine. Serum vitamin B12 was marginally low at 360 pg/ml (normal 400 - 1020 pg/ml). The serum folate acid value was normal and the serum iron values were as follows: 5.4 mmol/l on 26 November, 5.5 mmol/l on 9 December, 7.8 mmol/l on 12 May 1981, and 10.0 mmol/l on 19 May 1981 (normal 10.0 - 30.0 mmol/l). The serum transferrin level was 39.0 mmol/l on 9 December 1980; 47.0 mmol/l on 19 May 1981; and 59.3 mmol/l on 10 June 1981 (normal 22 - 37 mmol/l).

Bone marrow aspiration on 1 December 1980 yielded mildly decreased cellular elements but contained normally cellular narrow fragments. There was no abnormality in granulopoiesis, and erythropoiesis was normoblastic and adequate. Megakaryocytes and exceptionally large numbers of platelets were present. There was an increase of iron in the fragments but no sideroblasts were present. The picture was that of chronic anaemia.

A synovial biopsy of the left ankle was carried out on 10 December. The histological picture was that of subacute inflammatory synovitis with fibrin deposits in an early stage of organization on the surface. Vascular proliferation was present, with a very mild lymphocyte and plasma cell infiltrate. There was no lymphoid follicle formation but small quantities of haemosiderin pigment were present. Mild superficial synovial cell hyperplasia was present but no definite follicle formation was noted. Immunofluorescence studies revealed fibrinogen in the synovial surface and in some blood vessel walls. No IgG, IgM or IgA complement deposits were found.

Radiographic examination of the chest, skeleton and joints was negative, except for soft-tissue swelling of the knees and ankles and to a lesser extent of the proximal interphalangeal joints. No bony erosions were seen. The ECG was normal. Uterine dilatation and curettage was performed because of the history of menorrhagia and revealed normal endometrium in the proliferative phase. An intradermal sensitivity test with dextran and iron-dextran was done without untoward reaction.

Discussion

Reddy and Lewis1 noted that two types of reaction occurred in patients with rheumatoid arthritis given iron-dextran intravenously: a febrile response and an exacerbation of the arthritis only in those joints already affected. The exacerbation occurred 3 - 24 hours after administration of the preparation; exacerbations lasted as long as 2 weeks and required an increase in maintenance dosage of steroids. It would appear that intramuscular injection of the preparation does not produce this joint reaction.

Lloyd and Williams2 reported on 10 patients with rheumatoid arthritis given iron-dextran. One had a severe anaphylactoid reaction and in 8 the ESR rose following the infusion. Three patients showed pronounced deterioration in grip strength. A significant number of medium-sized and large-sized joints were worse, but small joints of the hand were involved to a much lesser degree.

There appear to be no reports in the literature of patients with exacerbations of rheumatoid arthritis or ankylosing spondylitis developing a prolonged polyarthritis with synovial inflammatory changes following iron-dextran infusion.

The exacerbations previously described in the literature were more of the nature of a hypersensitivity reaction, occurring between 3 and 24 hours after the infusion. The administration of saccharated oxide of iron intravenously to patients with rheumatoid arthritis did not cause disease exacerbations.3 Sensitivity reactions to dextran have been well documented,4 which suggests that the dextran (and not the iron) in the complex causes the reactions described. Intradermal tests with dextran and iron-dextran in our patient yielded no untoward reaction, confirming similar findings of others.5,6,7

Our patient differed from those described in the literature in that she had no clinical features of disease and in particular no evidence of rheumatoid arthritis or ankylosing spondylitis. An apparent incidental finding of anaemia was made during a visit for an unrelated complaint; this anaemia has still not been satisfactorily explained, although it has improved spontaneously during the ensuing follow-up period of 6 months. Our patient went on to develop a fairly severe polyarthritis, mainly of the large joints but of some small joints as well.

On admission to our unit the patient was still unable to walk owing to severe pain, particularly in the weight-bearing joints, despite nearly 5 weeks of steroid therapy. Prolonged therapy with steroids was needed to control the symptoms, although full clinical recovery had occurred by the end of 6 months.

We have since interviewed a second patient with no evidence of rheumatoid arthritis or ankylosing spondylitis who developed an acute polyarthritis following a total-dose iron-dextran infusion. She recovered over a period of a few weeks.

REFERENCES