¹¹¹Indium-labelled white blood cells in the diagnosis of Felty's syndrome

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SUMMARY The use of isotope scanning of the spleen in conjunction with ⁵¹Cr-labelled red blood cells has become an established technique in the evaluation of patients with hypersplenism.¹ As far as we are aware the similar technique using labelled white blood cells to demonstrate splenic sequestration in a neutropenic patient has not been described. We report a case where this technique proved valuable in confirming the diagnosis and in predicting a favourable response to splenectomy.

Case report

A 70-year-old man presented in September 1978 with a two-week history of dysphagia, hoarseness and anorexia. He also complained of an eight-month history of migratory polyarthralgia involving mainly his hands and feet. He had received various medications including: phenylbutazone one tablet tid; frusemide one tablet mane; indomethazine 25 mg qid; ferrous gluconate one tablet bd; distalgesic two tablets prn; tetracycline 250 mg qid. Physical examination revealed a nodule over his right elbow but no other evidence of a destructive arthropathy or splenomegaly.

Investigation revealed an increased erythrocyte sedimentation rate of 60 mm in the first hour, haemoglobin 12.3 g/dl, MCV 92 fl, MCH 30 pg. The white cell count was $3.9 \times 10^9/l$ with no neutrophils present. Bone marrow examination showed a marrow of normal cellularity, increased lymphocytes and plasma cells, with essentially normal red cell precursors and megakaryocytes but outstandingly there was a complete absence of granulocyte precursors beyond the promyelocyte stage. IgG concentrations were significantly raised at 28.2 g/l, IgA was 3.4 g/l and IgM 1.1 g/l. Rheumatoid factor was negative. Antinuclear factor was weakly positive, DNA-binding capacity 5.4% and the Paul Bunnell test negative. A barium swallow, meal, follow-through and enema were normal but upper gastrointestinal endoscopy revealed a severe monilial oesophagitis. An upper abdominal ultrasound demonstrated no abnormality.

Once malignancy was excluded the initial impression was that he had a drug-induced neutropenia complicated by monilial oesophagitis. All drug therapy was withdrawn and the oesophagitis was treated with nystatin. He then became pyrexial and despite several negative blood cultures, he was thought to be septicaemic and responded to ampicillin, gentamycin and barrier nursing. He appeared to have recovered fully and the neutropenia spontaneously improved with the white cell count rising to $5 \times 10^9/l$.

A few days later he developed a pyrexia, confusion and neutropenia and again responded to antibiotics. In an attempt to prevent further episodes of neutropenia, prednisolone 40 mg per day and azathioprine 200 mg per day were commenced. Despite this treatment, further recurrences of the neutropenia occurred, in December 1978 and March 1979, both episodes being associated with pyrexia which responded to antibiotics (Fig. 1).

A repeat bone marrow examination in February 1979 revealed that granulocyte precursors were plentiful, although the peripheral neutrophil count was only $0.5 \times 10^9/l$.

¹¹¹Indium leucocyte-imaging using the patient's white blood cells was carried out.² A 60 ml blood sample was taken from the patient, and the red cells were sedimented using dextran. The supernatant was transferred and the platelet-rich plasma was subsequently removed. The cells were suspended in saline and ¹¹¹Indium—chelated with 8-hydroxyquinoline (Oxine)—was added and incubated for 30 min. The cells were washed once and resuspended in saline. This was reinjected and imaging using a gamma camera was carried out 24 hours later (Fig. 2).

Fig. 1 Neutrophil count, September 1978 to March 1980

Fig. 2 ¹¹¹Indium granulocyte scan showing splenic sequestration

There was an abnormally high accumulation of radioactivity in the spleen. For the anterior view the spleen: liver ratio was 0.61 and the corresponding posterior view ratio was 1.9. This compares with an anterior view ratio of 0.21 ± 0.1 SD for patients with normal splenic function, in our experience. This information together with the repeat bone marrow led to a splenectomy being performed in May 1979. The spleen weighed 155 g, and microscopy showed congestion but was essentially normal. He made an uneventful recovery and this was followed by a rise in neutrophil count to normal levels which has now persisted for a year. The patient has had no further infections although his arthritis has progressed and he now has the classical clinical features of destructive seropositive rheumatoid arthritis.

Discussion

The triad of rheumatoid arthritis, splenomegaly and neutropenia was first described by Felty in 1924.³ The syndrome usually occurs in established rheumatoid arthritis, although cases have been described where the development of rheumatoid arthritis followed the neutropenia⁴ and also where neutropenia occurred without detectable splenic enlargement.⁵

However, in this case the diagnosis at presentation was not clear because the neutropenia preceded evidence of classical rheumatoid arthritis, the rheumatoid factor was initially negative, the marrow lacked granulocytes beyond the promyelocyte stage and the neutropenia followed a variable course. Cyclic neutropenia was considered but seems unlikely as there was no consistent pattern to the variations in neutrophil count, the transient increases in neutrophils occurring in the recovery phase of systemic infection and sustained response to splenectomy is not found in cyclical neutropenia.⁷ In this patient the subsequent development of seropositive rheumatoid arthritis and the response to splenectomy leaves little room for diagnostic doubt. However, while the diagnosis was still in doubt the

demonstration of excessive granulocyte sequestration in the spleen was valuable supporting evidence that splenectomy would be beneficial.

The cause of the neutropenia in Felty's syndrome is not clear and postulated causes include autoimmune neutrophil destruction,⁸ phagocytosis in the spleen⁹ and excessive migration.¹⁰ This case demonstrates that excessive splenic sequestration of granulocytes occurs in Felty's syndrome even in a normal size spleen.

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