Case report

Arthritis associated with hairy cell leukaemia

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SUMMARY We report the case of a 65-year-old patient with a 15-year history of intermittent asymmetrical oligoarthritis, who subsequently developed splenomegaly, lymphadenopathy, and episodic leucopenia and thrombocytopaenia. Investigations revealed hairy cell leukaemia, and 'hairy cells' were detected in the synovial fluid. No other cause for this arthritis was found, and we consider the blood dyscrasia to be the likely cause. This case demonstrates a hitherto unreported association between arthritis and hairy cell leukaemia.

Leukaemic reticuloendotheliosis (LRE) or hairy cell leukaemia is a distinct clinicopathological entity which appears to belong to the lymphoproliferative group of disorders¹ and accounts for approximately 2% of all the leukaemias.² It was first recognised in 1958 by Bouroncle *et al.*³ Schrek and Donnelly⁴ noted the presence of numerous short villi around the lymphocyte cell membrane and imaginatively described them as hairy cells, giving the disease its short name. However, the diagnosis may be difficult to confirm, and the condition is often confused with lymphocytic lymphoma or even myelosclerosis. The present case not only illustrates the haematological diagnostic problem but is also unique in its apparent mode of presentation with arthritis, not a previously reported feature of the disease.

Case report

The patient was a man aged 65 years when first seen in May 1977. He gave a 15-year history of intermittent peripheral joint symptoms, including episodes of pain, swelling, and stiffness of both knees, the left ankle, and the right shoulder, accompanied by generalised stiffness, severe sweating, malaise, and general constitutional upset. The only other noteworthy medical history was of recurrent attacks of malaria while serving in the armed forces in the Far East during the second world war. A clinical diagnosis of rheumatoid arthritis had been made on admission to another hospital in 1962-3 and a synovial biopsy was reported to have been in support of

this. Treatment had consisted of prednisolone at a dose varying between 5 and 10 mg a day, which he had continued ever since. Attempts to reduce the dose of prednisolone had resulted not only in exacerbation of the arthritic symptoms but also in painful swelling of the axillary and inguinal lymph nodes.

On laboratory investigation the most significant findings noted on numerous occasions had been of leukopenia varying between 1.5 and $4 \times 10^9/l$, with a predominance of lymphocytes; and a thrombocytopaenia with a platelet count between 80 and $100 \times 10^9/l$. On clinical deterioration following a reduction in prednisolone dose in May 1978 he was admitted to the Royal South Hants Hospital for further investigations. He was then in fair general health and was afebrile. The left knee and ankle were inflamed with effusion, warmth, and tenderness, but synovial thickening was not detected clinically. The liver and spleen were enlarged some 2 fingers breadth below the costal margin, firm, and tender. Enlarged, soft, tender lymph nodes were palpable in both axillae and both groins. Other clinical findings were unremarkable.

Further investigations showed haemoglobin 11.3 g/dl; white cell count $2.1 \times 10^9/l$ (neutrophils 38%, lymphocytes 62%); platelets $85 \times 10^9/l$; ESR 95 mm/1 h. A peripheral blood film showed atypical lymphocytes, about one-third of which were hairy cells. Bone marrow examination, both sternal aspirate and trephine biopsy, confirmed hairy cell leukaemia. Cytochemistry showed cells positive for acid phosphatase (tartrate resistant). Serum lysozymes 10mg/l (normal 3.5-8 mg). Abdominal lymphogram revealed no abnormality. Electron

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microscopic studies on peripheral cells confirmed hairy cell leukaemia (Fig. 1). Hepatic and splenic radioisotope scan showed patchy filling defects suggestive of lymphomatous infiltration (biopsy not performed). A lymph node biopsy (axillary) showed a reactive hyperplasia only. Autoantibody screening: the sheep cell agglutination test for rheumatoid factor, and immunofluorescent staining for antinuclear factor, remained negative on 3 separate occasions.

Serum inorganic chemistry was normal. Plasma proteins: total proteins 84 g/l; albumin 41 g/l; globulin 43 g/l; electrophoresis normal. Immunoglobulins: IgG 10.8 g/l; IgA 15.0 g/l; IgM 1.4 g/l. Immunoelectrophoresis revealed IgA kappa paraprotein present in serum in contrast to the surface Ig phenotype of the neoplastic cells, which was classed as IgAM. Complement: C3, 1.54 g/l; C4, 0.27 g/l. HLA B27 negative.

Radiological joint survey showed minor degenerative changes in hands, feet, ankles, and knees, but no evidence of periarticular osteoporosis or erosions or other evidence of rheumatoid or erosive arthritis.

Synovial fluid microscopy showed some hairy cells, polymorphonuclear leucocytes, and a few monocytes. Total protein concentration was 50 g/l. No crystals were detected on polarised light microscopy and no organisms grown on culture.

Treatment with prednisolone 10 mg/day was continued, and his general condition improved, with regression of the lymph node enlargement and splenomegaly, and the arthritis subsided. On subse-

quent follow-up over a period of 12 months he continued in remission, apart from recurrent inflammation in the left knee and ankle.

Discussion

This case history demonstrates a hitherto undescribed association of arthritis with hairy cell leukaemia. The patient had an episodic nonerosive asymmetrical arthropathy over many years preceding the diagnosis of the hairy cell leukaemia, for which no other cause has been found. No positive evidence in favour of any other recognised inflammatory arthropathy has been detected over at least 15 years, and the presence of leukaemic 'hairy cells' in the synovial fluid appears to us to support a diagnosis of leukaemic arthropathy.

In particular, the arthritic lesions were inconsistent with rheumatoid arthritis (the previous diagnosis) for the following reasons: (i) Despite the long history of arthritis, the clinical picture does not resemble rheumatoid disease, and in particular there is no significant synovial thickening, the distribution of joint lesions has been mainly asymmetrical, inflammation of individual joints has completely remitted, and there has been no involvement of the small joints of the hands and the feet. (ii) Rheumatoid factor has not reached significant titres on repeated examinations. (iii) No radiological features of rheumatoid disease have appeared in spite of the long history, and in particular no erosions have been detected.

Arthralgia and joint swelling are recognised features of some cases of acute leukaemia,³⁻⁸ and migratory polyarthritis is the most commonly used descriptive term for the arthritis of leukaemia. The arthritis is usually asymmetrical, polyarticular, and often part of the initial manifestation of the disease. When arthritis occurs in the commoner forms of chronic leukaemia, it is often symmetrical and usually appears as a late manifestation. The arthritis is initially related to the activity of the disease and shows a predilection for involvement of knees, shoulders, and ankles. The cause of the arthritis in leukaemia has been variously ascribed to leukaemic infiltrates in the metaphyseal periosteum,⁸ haemorrhages in the joints and periarticular structures,⁹ or to leukaemic infiltrates in the synovial membrane.^{6,7,9}

Arthritis has not been reported in hairy cell leukaemia as either an early or late manifestation, although an association between polyarteritis nodosa and hairy cell leukaemia has been reported.¹⁰ However, we consider that hairy cell leukaemia is the likely cause of the arthritis in our patient, in view of the finding of hairy cells in the synovial aspirate and the failure to demonstrate any other cause, even after 15 years of arthritic lesions. Moreover, attempts to

Fig. 1 A typical 'hairy cell' with a highly irregular nucleus, with moderate peripheral chromatin condensation and abundant cytoplasm containing several ribosomal lamellar complexes. The cell outline is characteristically irregular, with many long surface processes, a mixture of undulating broad-based ruffles, and microvilli, in contrast to the short microvillous processes of normal peripheral lymphocytes. (Bar = 1 μ m).

reduce prednisolone dosage resulted not only in exacerbation of joint inflammation but also in lymphoreticular hyperplasia and lymph node enlargement accompanied by constitutional symptoms.

Hairy cell leukaemia is considered to be a low-grade malignancy of the lymphoreticular system and it is only slowly progressive. Treatment with corticosteroids has been tried in the great majority of cases, including our own, but it is not curative in the long term.^{1 2} With significant hypersplenism, splenectomy may be beneficial.¹¹

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