

## Short reports

# Soft tissue malignant lymphoma at sites of previous surgery

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### Abstract

Three diffuse centroblastic lymphomas developed at the site of previous surgery. Two were preceded by atypical lymphoid infiltrates. Clinical data, microscopic features, and immunophenotypic studies were reviewed. All three patients presented with soft tissue masses at the site of previous surgery and metallic implants, with no evidence of lymphadenopathy, hepatosplenomegaly, or bone marrow involvement. There was no history of immunosuppression or risk factors. In two cases the initial diagnosis was of atypical lymphoid infiltrate progressing to lymphoma. Pathological examination showed a diffuse centroblastic lymphoma with an angiocentric pattern in one case. Phenotypic studies confirmed B cell origin. Soft tissue malignant lymphoma, though uncommon, can occur at the site of previous orthopaedic surgery, in particular joint

### replacement. Atypical lymphoid infiltrate may signal such an event.

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here are reported cases of malignant soft tissue tumour such as malignant fibrous histiocytoma, rhabdomyosarcomas, chondrosarcoma, and spindle cell sarcoma complicating joint replacement surgery.<sup>1,2</sup> There is now growing evidence that some soft tissue malignant lymphomas occur after long standing antigenic stimulation in patients with a defective immune system. Lymphoma developing at the site of a metallic implant may theoretically result from the carcinogenicity of the metallic alloy, in particular from prostheses made of cobalt–chromium.<sup>2</sup> Other cases reported have developed after chronic osteomyelitis.<sup>3</sup>

This report deals with three cases of diffuse centroblastic lymphoma that developed at sites

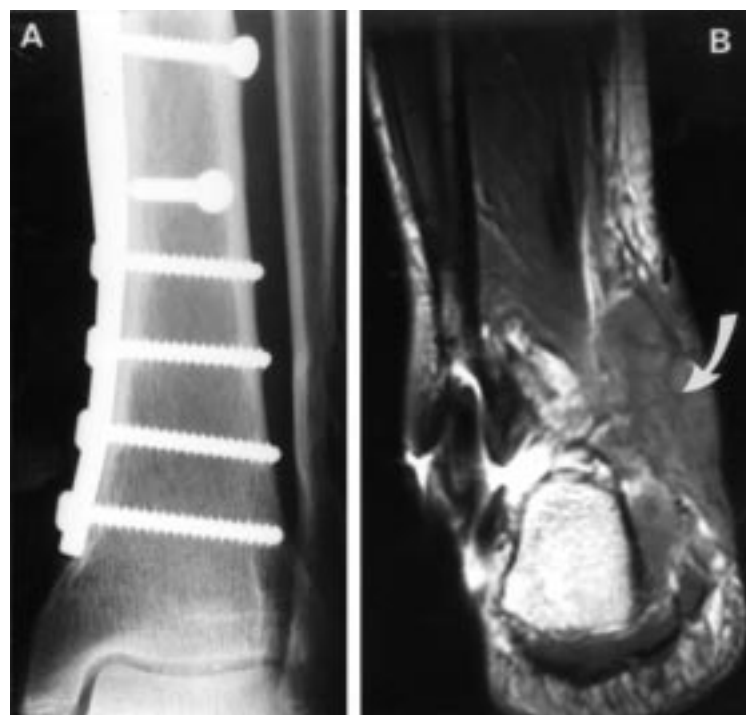


Figure 1 Radiograph of the tibia with internal fixation, anterior view (A); magnetic resonance imaging showed soft tissue mass (posterior view, arrow (B)).



Figure 2 Radiograph of total hip arthroplasty; computed tomography (inset) shows soft tissue mass (arrowed).

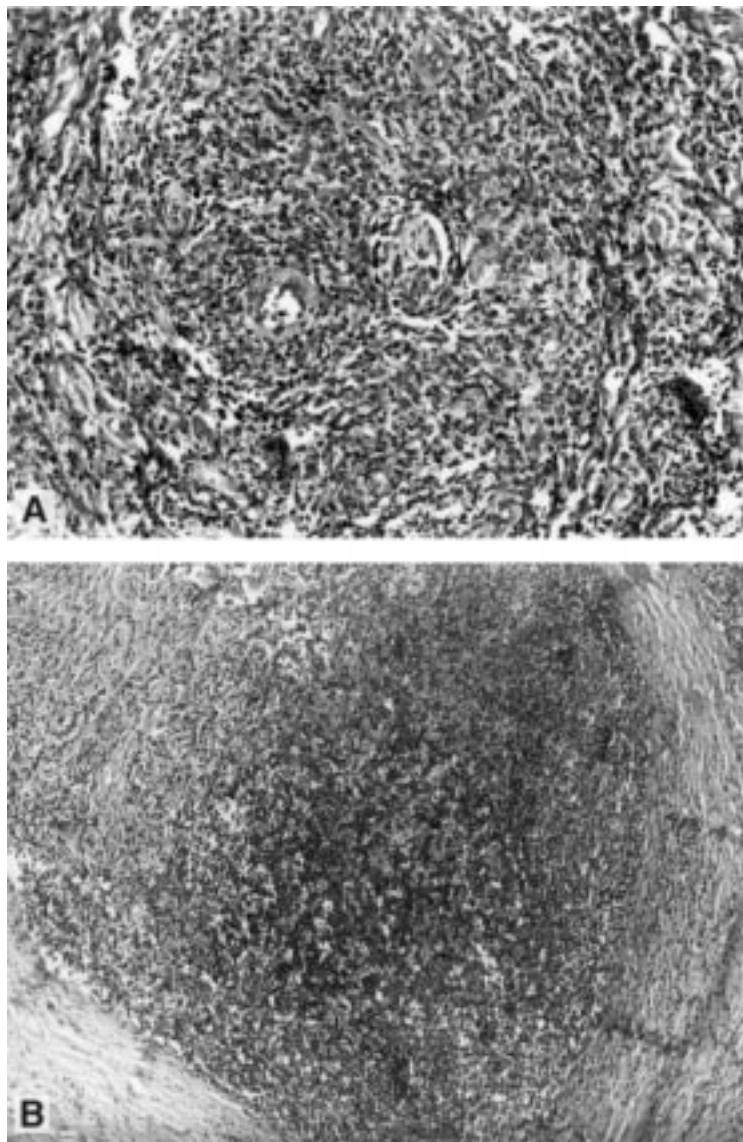


Figure 3 Biopsy showing atypical lymphoid infiltrate with prominent perivascular pattern in case 1 (A) and case 3 (B).

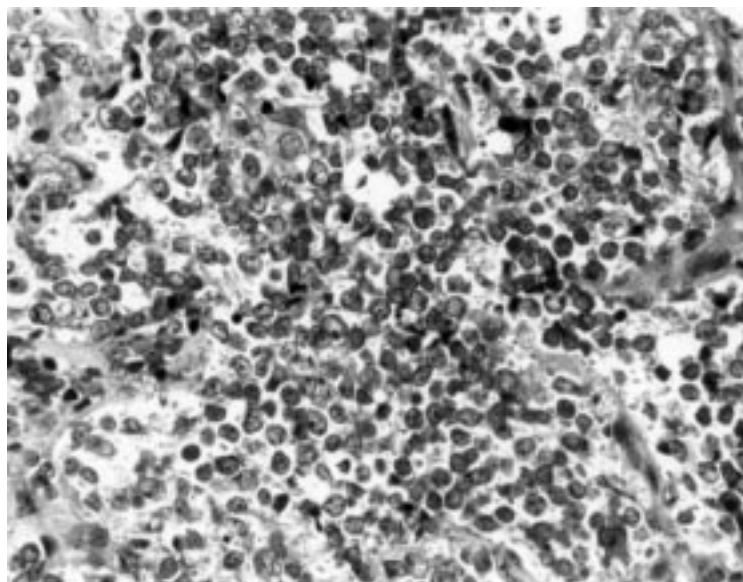


Figure 4 Histological section of a diffuse soft tissue centroblastic lymphoma.

of previous surgery in non-immunocompromised individuals. Two cases presented earlier as soft tissue masses with features of atypical lymphoid infiltrate. All these cases showed local aggressive behaviour with no constitutional symptoms, lymphadenopathy, or hepatosplenomegaly.

### Case reports

None of these cases was associated at presentation with lymphadenopathy, hepatosplenomegaly, or bone marrow involvement. No history of immunosuppression or risk factors was identified in any of the cases and HIV testing was negative.

#### CASE 1

A 25 year old male presented in 1996 with a slowly growing ankle mass following internal fixation for right distal tibial fracture in 1988 (fig 1A). Initial biopsies in 1995 showed atypical lymphoid infiltrate. Recent computed tomography (CT) and magnetic resonance imaging (MRI) demonstrated a large soft tissue mass involving the right medial malleolus and extending posteriorly between the tibia and the Achilles tendon (fig 1B). A biopsy was performed, followed by below knee amputation and chemotherapy. At six months after treatment the patient remained well with no signs of tumour recurrence.

#### CASE 2

A 63 year old female presented in 1995 with pain and swelling in the left thigh for the last six months. Past medical history revealed hip replacement in 1991 (fig 2). CT revealed a soft tissue mass measuring  $15 \times 7 \times 2.9$  cm involving the quadriceps muscle (fig 2, inset). Biopsy was submitted for pathological examination and this was followed by radiation and chemotherapy. Subsequent investigation revealed no spread of the disease.

#### CASE 3

A 45 year old female presented with a swelling over the left scapula for two years. Previous biopsy revealed atypical lymphoid infiltrate. The only significant finding in the past medical history was repeated surgery to the left scapular region for a benign recurrent lesion 12 years before (no pathology was available for review). The current biopsy showed a centroblastic lymphoma.

### Evaluation of pathology

All slides from these cases were reviewed. Immunophenotypic studies were performed using the following lymphoid markers: CLA, L26, and UCHL1 (Dako, Carpinteria, California, USA), CD15 and CD30 (Signet Laboratories, Dedham, Massachusetts, USA), and  $\lambda$  light chains (Dako). Flow cytometry was performed using standard techniques for various monoclonal antibodies including CD3, CD4, CD5, CD7, CD10, CD14, CD19, CD20, CD45, I3,  $\kappa$  and  $\lambda$  (Coulter Electronics of Canada, Burlington, Ontario).

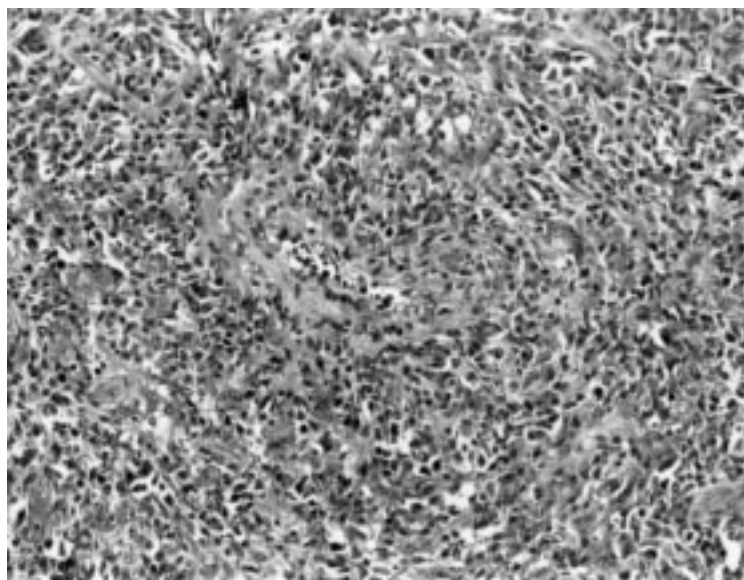


Figure 5 Photomicrograph showing vascular and perivascular lymphoma involvement.

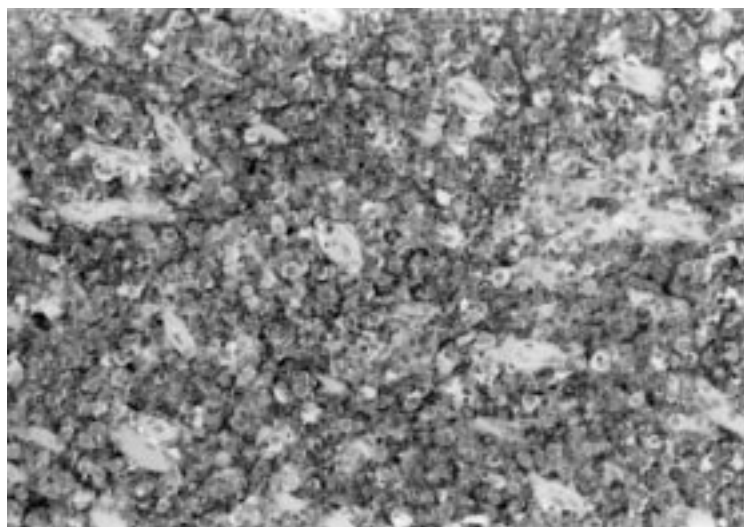


Figure 6 Immunoperoxidase study showing expression of L26 (CD20) marker.

### Results

Earlier biopsies in cases 1 and 3 revealed atypical lymphoid infiltrate (fig 3A and 3B). The infiltrate was composed of a mixture of lymphocytes, histiocytes, occasional large atypical cells, mature and immature lymphoid cells, with occasional lymphoid follicles. The infiltrates showed florid perivascular patterns in case 1, and immunohistochemistry studies revealed a mixture of T cell and B cell populations. Immunoglobulin and T cell receptor gene rearrangement was not identified in the atypical lymphoid infiltrate. Recent biopsies showed a diffuse centroblastic lymphoma. There was a diffuse lymphoid infiltrate which consisted of large cells with irregular nuclei and several prominent nucleoli, and abundant cytoplasm admixed with fewer lymphocytes and histiocytes (fig 4). In case 1, the infiltrate had an angiocentric and angiodestructive pattern (fig 5). Immunohistochemistry showed intense staining of the majority of the large cells with L26 (CD 20) (fig 6) and light chain. On flow cytometry analysis there was expression of

the B cell associated markers CD20+, CD19+, CD10+, and  $\kappa$ + light chain.

### Discussion

Soft tissue involvement by malignant lymphoma characteristically occurs in patients with previously diagnosed lymphoma involving lymph nodes or other sites. Lymphomas in soft tissue at presentation are considered to be primary only if the staging procedure excludes other sites of disease.<sup>4,5</sup>

Since the advent of internal fixation for fractures and particularly since the implantation of joint replacement prostheses, the possible carcinogenic effects of metals and their alloys have been a subject of concern.<sup>2</sup> Metal particles have been shown to accumulate in tissues adjacent to the implant and in the regional or distant lymph nodes, liver, and spleen. Wear debris is not biologically inert and its accumulation is associated with chronic inflammatory reaction of the synovium and necrosis of joint capsule and bone marrow. This is caused by activation of macrophages with an increase in eicosanoids, cytokines, and metallic proteinases.<sup>6</sup> Experimentally, certain compounds containing beryllium, cadmium, chromate, cobalt, iron, lead, nickel, zinc, and titanium have been shown to be carcinogenic on parenteral administration to animals.<sup>1,2</sup> A recent study on blood and bone marrow samples from patients with revision arthroplasty showed higher chromosomal aberration rate in cells adjacent to the prosthesis. Clonal expansion of lymphocytes without a serum paraprotein was also seen in a few patients.<sup>7</sup> The role of trauma in the causation of lymphoma is unproven and controversial. There are single case reports of possible relations between trauma and the development of malignant lymphoma.<sup>8-10</sup> In some cases trauma brought a malignant lymphoma to clinical attention.

Published reports include cases of malignant soft tissue tumours such as chondrosarcoma, malignant fibrous histiocytoma, rhabdomyosarcoma, osteosarcoma, and haemangioendothelioma associated with joint replacement surgery.<sup>1</sup> There is growing evidence that soft tissue malignant lymphomas occur after long standing antigenic stimulation at the site of metallic implant or after chronic osteomyelitis.<sup>3</sup> There are very few well documented cases of malignant lymphoma following orthopaedic surgery.

As joint replacement surgery is becoming one of the commonest surgical procedures, there is widespread epidemiological debate on the frequency of haematological malignancies in these patients. A cohort study from Sweden showed no significant increase in the incidence of leukaemia and lymphoma after total hip replacement,<sup>11</sup> and an association between joint replacement and local malignancy may be coincidental.<sup>12</sup> In this paper we report three additional cases of B cell lymphoma developing at sites of internal fixation and previous surgical procedures in non-immunocompromised patients. Two of these cases were initially diagnosed as atypical lymphoid infiltrates. In lymph

nodes atypical lymphoid hyperplasia comprises borderline cases in which the definitive diagnosis of benign or malignant disease cannot be made by microscopic examination or special studies. It is known that some of these cases may represent early lymphomas, while others represent abnormal reactions to various stimulants. Studies of this entity have shown the development of malignant lymphoma during the succeeding two to 13 years.<sup>13 14</sup> In our cases the lymphoma developed up to two years after the diagnosis of atypical lymphoid infiltrate. The disease process continued to be localised to the soft tissue, with no involvement of regional lymph nodes or systemic dissemination. The lymphomas had a diffuse pattern and were of B cell origin as demonstrated by phenotypic studies. The reason for the development of lymphoma is most likely to be multifactorial and may be related to the carcinogenicity of metal, x ray radiation, surgical trauma, chronic inflammation, and host factors.

In conclusion atypical lymphoid infiltrate at the site of surgery may represent the first manifestation of lymphoma and requires detailed clinical and pathological attention.

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