Aggressive transformation of a quiescent primary bone lymphoma simulating Paget’s disease

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ABSTRACT

Primary multifocal osseous lymphoma is a rare and poorly recognized entity. Here, we present an instructive case of a young man who, six years after a local contusion of the left ankle, developed a painful polylobulated large soft tissue mass. This mass turned out to have arisen from the transformation of a centro follicular non-Hodgkin’s lymphoma into a diffuse large B-cell lymphoma involving the calcaneus, talus, cuboid and navicular bones. The diagnostic difficulties as well as the implications of this aggressive transformation are highlighted here.

Introduction

Primary non-Hodgkin’s lymphoma of the bone (PBL) is a rare malignant entity that accounts for less than 5% of all primary bone tumours, predominantly affecting the long bones of the lower limbs (1, 2). The sex ratio of this neoplasia is around 1.5:1 male:female and it may develop at any age. The diagnosis is frequently delayed and due to the non-specific clinical signs and equivocal radiographic findings, it requires a high index of suspicion. The majority of cases are classified as diffuse large B-cell non-Hodgkin’s lymphomas in the World Health Organization classification of hematological malignancies (3-5).

The most frequent symptoms of PBL are insidious local pain and soft tissue swelling, and local trauma is often reported prior to the diagnosis (6). The radiological presentation of this condition is highly variable, but the most common finding is a lytic or mixed density area showing a permeative or moth-eaten pattern, with or without a periosteal reaction, a soft tissue mass or a pathologic fracture (1, 2, 7). These radiographic findings frequently force us to carry out an extensive differential diagnosis with other bone diseases, and exceptionally this condition may simulate Paget’s disease of bone or osteomyelitis.

Since the incidence of non-Hodgkin’s lymphomas (NHL) has nearly doubled in recent decades and PBL is a potentially curable malignancy, it is important to remain aware of this entity (3, 8).

Case report

A 26-year-old man was remitted to our Rheumatology Unit for evaluation of possible Paget’s disease of the bone, due to a 6-year history of chronic pain in the left ankle and a lytic-destructive pattern alternating with sclerotic areas on x-rays. He indicated that after local contusion six years previously, he started to suffer insidious chronic pain in the left hind foot with local tenderness and a slight restriction of joint movement. Two years prior to attending our Unit, the patient had been studied at another centre where successive computed tomography (CT) scans and magnetic resonance images (MRI) had been obtained, in which only bone marrow edema of the calcaneus was detected. At that time, an open-biopsy of the calcaneus had been performed, where marked fibroblastic proliferation with scattered lymphocytes was detected with no evidence of pyogenic, fungal or mycobacterial infection. The histological interpretation was very difficult at this moment and Paget’s disease of the bone was diagnosed. Treatment with bisphosphonates was employed for six months and produced an evident clinical improvement.

In the two months prior to our evaluation, the clinical situation had changed dramatically. The patient had developed a painful and large polylobulated soft tissue mass (9 x 8 x 5cm) associated with signs of inflammation and an important restriction of movement in the left ankle (Fig. 1). No constitutional symptoms were referred to and on physical examination, no evidence of lymphadenopathy or organomegaly was detected. No peripheral lymphocytosis was found and the results of biochemical tests showed:

Fig. 1. A large polylobulated mass with signs of inflammation is evident in the left hind foot.
an erythrocyte sedimentation rate of 26 mm/h (Westergren); C-reactive protein values of 2.4 mg/dl (reference range: 0-0.8); LDH 516 U/l (240-480); and beta-2-microglobulin of 1,360 μg/l (700-3,500). Immunological tests were unremarkable, no antibodies against hepatitis A, B, C and human immunodeficiency virus were detected, and the Mantoux reaction was also negative. The CT-scan and MRI of the left ankle at this moment revealed a non-calcified soft-tissue mass of 9 x 8 x 5 cm, with an evident permeative pattern, irregular lytic lesions in the calcaneus, and the involvement of the talus, cuboid and the posterior part of the navicular bone (Fig. 2). Fine needle aspiration (FNA) identified pleomorphic large cells with an eccentric rounded nuclei and unevenly distributed chromatin. Some of these cells had a distinct central nucleolus and scant cytoplasm, and they were mixed with small mature lymphocytes (Fig. 3A). An additional soft tissue percutaneous biopsy was performed that revealed atypical lymphoid cells of the same characteristics to those described in the FNA, which were associated with a diffuse growth pattern and with non-neoplastic small lymphocytes. Immunophenotypic analysis detected the expression of the CD20 (Fig. 3B) and CD79 markers (indicative of a B-cell phenotype), as well as bcl-6, and the mild expression of CD10 and bcl-2. There was no staining for p53 and myeloperoxidase. CT scanning of the chest, abdomen and pelvis did not identify any pathological findings, and no bone marrow involvement was detected. Positron emission tomography was negative and
the whole-body radionuclide bone scan (technetium polyphosphate) revealed a marked increase in radiotracer uptake in the calcaneus, talus and distal epiphyses of the tibia. At this time, the calcaneus biopsy performed two years ago was revised, and the presence of atypical lymphocytes was noted suggestive of a low grade lymphoma.

With all the aforementioned features, a diagnosis was reached of diffuse large B-cell lymphoma involving the calcaneus, talus, cuboid and navicular bone. The patient received a combined treatment consisting of four cycles of chemotheraphy with cyclophosphamide, adriamycin, vincristine and prednisone (CHOP regimen) and rituximab (anti-CD20 monoclonal antibody), followed by consolidation radiotherapy. This treatment produced a favourable response and, after six months, he suffered no pain and the soft tissue mass and movement restriction had disappeared, enabling him to lead a normal life.

Discussion

We present here a clinical case of primary lymphoma of the bone that initially simulated Paget’s disease of the bone. Some features of this case are particularly noteworthy, such as the multifocal involvement of foot bones, the diagnostic difficulties, and the aggressive transformation from a quiescent low grade lymphoma. PBL usually affects long bones of the limbs and it is rarely seen in the hands or feet (2). Thus, multifocal involvement of the foot bones in PBL is certainly exceptional (9). The fact that four contiguous bones were involved in our patient, with the preservation of articular facets, makes us wonder if we are actually dealing with a case of primary multifocal osseous lymphoma (PMOL). This is a poorly recognized entity initially described by Oberling in 1928 and then later by other authors (9-10). However, the contiguous invasion of neighbouring bones due to the local spread of tumour cells through small vascular channels, could account for the multifocal nature of the disease in this patient (11).

The previous misdiagnosis of Paget’s disease of bone highlights the difficulties in diagnosing PBL. Although the majority of bone tumours have a characteristic histological pattern, the presence of dense fibrosis as observed here and the paucity of pathologic alterations in low grade lymphomas can lead to an erroneous diagnosis such as Paget’s disease of bone. Accordingly, a high degree of suspicion should be maintained in similar situations. A further feature of interest associated with this patient is the local transformation of a low grade bone lymphoma into a high grade one. Although this is a well-recognized feature of lymphomas, its occurrence in bone has been reported less often than in other locations.

In recent decades, the incidence of NHL has undergone one of the largest increases among all cancers worldwide (3). The reasons for this increase remain unclear, yet considering the wide spectrum of clinical and radiological features, it is important to correctly identify these cases, avoiding mistaken diagnosis, and to establish the appropriate therapy as early as possible. This is further stressed by the fact that PBL has a better prognosis than other primary bone tumours or disseminated NHL with secondary bone involvement (12, 13).

References