Hairy cell leukemia with interferon alpha and deoxycorticosterone acetate (DCA) has been described as a cause of diffuse osteosclerosis. Patients 1 and 2 presented with fatigue, splenomegaly, and pancytopenia. A bone marrow biopsy in patient 1 revealed a diffuse hairy cell infiltrate and a splenectomy in patient 2. Radiographs showed diffuse osteosclerosis of the ribs, vertebral bodies, pelvis, and proximal femora. Treatment with recombinant interferon-alfa 2a (rIFN-α2a) as described previously, followed by monthly cycles of deoxycoformycin (DCF) and recombinant interferon-alfa 2a (rIFN-α2a) was started. Patient 1 was treated for 14 months, while patient 2 was treated for 18 months. Both patients showed a reduction in bone marrow fibrosis and hematologic improvement. The authors conclude that diffuse osteosclerosis in hairy cell leukemia is a common finding and can be treated with interferon therapy.
Fig 1. Hematoxylin and eosin stain of bone biopsy of patient no. 1 showing osteosclerosis (A) and hairy cell infiltration (B) (original magnifications: A, × 32; B, × 128).

Fig 2. Plain radiographs of the pelvis (A) and chest (B) of patient no. 1, demonstrating diffuse osteosclerosis. Arrow indicates broken bone marrow biopsy needle, inside circle, from previous bone marrow biopsy attempt.
and open bone marrow biopsy. The liver and lymph nodes were infiltrated with TRAP positive lymphocytes. The open bone marrow biopsy revealed markedly thickened bony trabeculae, myelofibrosis, and an infiltrate of hairy cells. In November 1979, therapy began with clorambucil but the patient continued to require frequent RBC transfusions. Lithium carbonate was added in June 1981 without improvement in peripheral blood counts. Chlorambucil and lithium carbonate were both discontinued in December 1981 and oxymethalone was commenced in March 1982. In April 1982, the patient was hospitalized for bilateral pneumonia and an open lung biopsy revealed nonspecific pneumonitis and hairy cell infiltration into the lung parenchyma. He died in May 1982 of progressive pulmonary involvement with hairy cell leukemia.

**COMMENTS**

Bone involvement in hairy cell leukemia is a rare complication that usually manifests itself clinically by pain in involved skeletal areas. Pathologic fractures due to infiltration of the cortical bone by hairy cells have been reported. Radiographically these lesions have been predominately lytic in nature; however, bone scans are frequently positive suggesting that some osteoblastic activity is also present. This is the first report of diffuse osteosclerosis, without a lytic component, as a manifestation of bone disease associated with hairy cell leukemia. Both cases reported here had extensive bony sclerosis on radiographs, which in both cases was confirmed pathologically.

Both patients described here presented with hairy cell leukemia and diffuse bony osteosclerosis. Initially, it was possible to perform percutaneous bone marrow biopsies but as the hairy cell leukemia progressed this became impossible in both patients. This progressive “hardening” of the bone suggests that the sclerotic process was active and progressing in the early years of these patients’ disease. The sclerotic process in the second patient showed radiographic worsening that correlated with his progressive hairy cell leukemia and the first patient demonstrated radiographic stabilization after remission of hairy cell leukemia with effective therapy. Thus, in both patients the osteosclerotic process appears to have worsened as the patient’s hairy cell leukemia progressed and in one patient has stabilized after remission of the hairy cell leukemia. This suggests a causal relationship between hairy cell leukemia and the osteosclerosis.

Multiple myeloma, another B-cell neoplasm, classically results in osteolytic bone lesions with or without osteosclerosis. The neoplastic cells of multiple myeloma are arrested at a more stage of differentiation than hairy cells, which are malignant counterparts of pre-plasma cells. Bone involvement has not been reported in chronic lymphocytic leukemia, a B-cell neoplasm characterized by a proliferation of cells arrested at a stage of differentiation that is less mature than in hairy cell leukemia. Thus, the degree of cellular maturity may be an important variable in the development of bony complications in these B-cell disorders.

The development of bone disease in hairy cell leukemia may be related to the platelet dysfunction known to exist in this disease. The α-granules of platelets contain, among other things, platelet-derived growth factor (PDGF) and transforming growth factor-β (TGF-β). PDGF stimulates both DNA and protein synthesis in organ cultures of rat calvariae and has also been shown to stimulate bone resorption. TGF-β enhances bone DNA synthesis and the cells of the osteoblastic lineage appear to be the most sensitive to its mitogenic activity. Thus, both PDGF and TGF-β are growth factors that by themselves or in conjunction with other growth factors exert a major effect on bone remodeling. The α-granules of platelets in hairy cell leukemia have been shown to be decreased in number and to have lower concentrations of these growth factors. The platelets in hairy cell leukemia appear to be intrinsically normal in that the storage pool deficiency-like abnormality has been observed to resolve with effective hairy cell leukemia treatment. These data are consistent with the notion that in hairy cell leukemia an “exhausted-platelet” or storage pool deficiency-like state occurs, which leads to aberrant release of these growth factors. These locally released factors could result in the sclerotic or lytic bone lesions observed in our patients. The diffuse osteosclerosis seen in our patients included bony sites not usually thought to be active in hematopoiesis in adults and is certainly more extensive than the bone involvement previously reported in hairy cell leukemia. Therefore, it seems likely that the pathogenesis of osteosclerosis in hairy cell leukemia involves a humoral mechanism.

Treatment of the lytic bone complications in hairy cell leukemia can be accomplished by systemic therapy with α-interferon or dCF but local radiation therapy is also often required. The first patient reported here responded to combination therapy with both dCF and α-INF with an improvement in peripheral blood counts and normalization of soluble IL-2 receptor levels and her bone disease radiographically has remained stable. If the bone complications are indeed due to abnormal platelet release of growth factors, it would be anticipated that the bone disease might improve or stabilize with correction of the functional platelet abnormality. Further studies of growth factor release and bone cell activation by platelets in hairy cell leukemia and other B-cell neoplasms are needed.

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Diffuse osteosclerosis in hairy cell leukemia
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