Bone Scanning in Waldenstrom’s Macroglobulinemia

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We present a case report of a remarkably positive bone scan in a patient known to be suffering from Waldenstrom’s macroglobulinemia. Although bone involvement in this disease was originally thought not to be present, reports of bone involvement are becoming more frequent. Documenting the presence and extent of bone involvement is important because local palliative radiotherapy and/or orthopedic measures, similar to those recommended for patients suffering from multiple myeloma, may be required to prevent pathologic fractures and patient discomfort.


Waldenstrom’s macroglobulinemia (WM), as originally described in 1944, was thought not to involve the skeletal system. The bone marrow, lymph nodes, and spleen are the organs most often involved in this plasma cell dyscrasia. Although it has features in common with multiple myeloma, lymphoma and chronic lymphocytic leukemia, it can be differentiated from these other diseases by finding a monoclonal IgM immunoglobulin, in abnormally elevated amounts, by serum protein electrophoresis. This case concerns a patient with documented Waldenstrom’s macroglobulinemia with extensive bone involvement who had an exquisitely positive radionuclide bone scan. The role of bone scanning in this disease is discussed and compared to the role of bone scanning in a similar disease, multiple myeloma.

CASE REPORT

A 65-yr-old male presented to the hospital on October 5, 1983 complaining of ataxia, vertigo, and left-sided headache. Admission skull x-ray showed a single, small, left-sided lytic defect. The hematocrit was decreased to 34.3%, and a total serum protein was elevated at 8.6 mg/dl, of which 5.5 mg/dl was found to be globulin. Serum calcium was 9.5 mg/dl (nml 8.5-10.5) and alkaline phosphatase 45 mU/ml (nml 30-110). The sedimentation rate was found to be elevated at 126. A skeletal survey failed to reveal any additional lytic abnormalities. The baseline bone scan was negative. Bone marrow biopsy revealed plasma cytoplasmic cells consistent with Waldenstrom’s macroglobulinemia. Definitive diagnosis was made by serum protein electrophoresis which showed a spike in the gamma region. Quantitative serum gammaglobulins were 198 for IgG (nml 600-1,500), 19.1 for IgA (nml 60-290), and 5,610 for IgM (nml 150-200), which rose to 14,400 mg/dl 1 mo later. The patient was discharged home on chlorambucil therapy.

Over the following 2 mo he continued to be symptomatic, and on February 1984 chemotherapy was switched to cytoxan, vincristine, and prednisone. On March 7, 1984 he was readmitted with a serum calcium of 9.4, an alkaline phosphatase of 211, and a chest x-ray that showed compression of a thoracic vertebral body and collapse of the superior rib cage (Fig. 1). Repeat bone scan (Fig. 2) showed manifold osseous lesions involving almost the entire axial skeleton. He is currently receiving palliative BCNU and dexamethasone therapy.

DISCUSSION

WM is a lymphoproliferative disorder resulting in a monoclonal gammopathy. IgM, in pathological amounts, synthesized by the proliferating cells, accounts for most of the disease’s symptoms, at which we aim our medical management. As the IgM level of the plasma increases, plasma volume expands reflexive, causing the hematocrit to fall. Abnormal amounts of IgM also increase the viscosity of the blood, impairing circulation, and resulting in first peripheral and then central neurological problems. The excess protein in the serum also interferes with normal immune status and function.

In a somewhat related disease, multiple myeloma, in addition to a monoclonal immunoglobulin, a calcium mobilizing substance, “osteoclast activating factor” (OAF),
FIGURE 1

FIGURE 2
Remarkably positive bone scan done 11/16/84, showing manifold osseous lesions.
is known to be excreted by the pathological cells (1,2). OAF has been shown to stimulate local bone resorption by osteoclasts in the vicinity of the foci of myeloma in the marrow while simultaneously inhibiting local osteoblastic activity. This results in a locally aggressive tumor that causes a rise in serum calcium proportional to the mass of bone involvement, and also is believed to inhibit radionuclide uptake into these lesions. This is also the presumed explanation of the usually normal serum alkaline phosphatase levels despite often severe bone involvement.

Our patient with Waldenstrom's macroglobulinemia and a positive radionuclide bone scan had a continuously normal serum calcium, and a rising serum alkaline phosphatase level in proportion to his bone involvement. This suggests that even with lytic bone involvement resembling multiple myeloma, OAF is not present. Other possible causes of "hot areas" in the bone scan include diffuse metastases, diffuse metabolic diseases (including osteomalacia, active osteoporosis, and Paget's disease), hematologic diseases and fibrous dysplasia. Although patients suffering from multiple myeloma classically have purely lytic disease which usually results in a negative bone scan, in some of their lesions, microfractures may occur which can cause "hot areas."

Horner is credited with reporting the first case of WM with overt osteolytic lesions. Several subsequent reports (3–5) indicate that skeletal involvement is not as unusual as previously believed. In patients presenting with primary macroglobulinemia it is important to exclude or confirm the presence of osteolytic lesions. Their presence may require local palliative radiotherapy and/or orthopedic measures, similar to those recommended for patients suffering from multiple myeloma, to prevent pathologic fractures and patient discomfort. Not only can bone imaging signify the presence or absence of bone lesions, but it can also direct the more efficient use of skeletal x-rays for documentation of the extent, location, and response of bone abnormalities to interventional chemo- and radiation therapy.

REFERENCES