jnm/CASE REPORT

TECHNETIUM-99m-DIPHOSPHONATE ACCUMULATION IN AMYLOID

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A well-documented case of multiple myeloma complicated by histologically demonstrable amyloidosis is presented. Technetium-99m-diphosphonate in the areas of amyloid deposition about the shoulders and hips is shown. This adds another dimension to the extraosseous sites without demonstrable calcification where accumulation of bone-seeking radiopharmaceutical can be observed. In patients where symmetrical uptake of such agents is noted in the periarticular soft tissue, particularly of the hips and shoulders, amyloidosis must become a diagnostic consideration. This is particularly true in patients presenting with undiagnosed arthralgia.

Soft-tissue uptake of bone-scanning agents has been described in a wide variety of diseases (*1*). Extraosseous tumor uptake of ^{87m}Sr and ^{18}F has been described in tissue without calcification by Chaudhuri (*2*) and Papvasiliou (*3*) and in neoplasm where calcification is frequent by O'Mara (*4*). Concentration of ^{99m}Tc-polyphosphate, ^{99m}Tc-diphosphonate, and ^{18}F in cerebral infarction has been reported by Grames (*5*) and Wenzel (*6*). We would like to present a case in which uptake of ^{99m}Tc-diphosphonate was observed in amyloid deposits. To our knowledge, this has not previously been reported.

CASE HISTORY

A 47-year-old white woman was admitted for the first time to Arizona Medical Center in August 1973. The patient had experienced chronic pain in her legs and back since childhood. In 1972, she experienced an increase in shoulder and hip pain with paresthesias of both hands. A diagnosis of carpal tunnel syndrome was made and surgery was performed elsewhere. There was no postoperative improvement. During the year prior to admission she had experienced progressive pain in all joints and neck. The symptoms were worse at night and in the early morning and were associated with progressive immobilization. During the 6 months prior to admission she was unable to walk without extreme discomfort. During this time she had been treated as a rheumatoid arthritic subject but showed no response to any of the usual modalities of therapy. Two months prior to admission she had noticed nodules in her tongue and dark spots on her eyelids.

Physical examination on admission revealed several small, purple, papular nodules on both upper eyelids. Similar firm nodules were found in the tongue. Symmetrical soft-tissue fullness was noted over the hips and shoulders, the latter consistent with a "shoulder-pad" sign (*7*). Swelling, with limitation of motion, was present in both wrists and several of the proximal interphalangeal joints. Marked pain with movement and severe limitation of movement was present in both shoulders and hips. Subcutaneous nodularity was noted about the elbows.

Radiographs demonstrated bilateral, symmetrical, soft-tissue fullness in the shoulders, hips, (Fig. 1A and B), and wrists without obliteration of the subcutaneous fat, and general preservation of the fascial fat planes. A slight degree of inferior subluxation was present at both glenohumeral joints. No soft-tissue calcification was identified. Deossification was present in the spine, pelvis, humeri, and femurs. Lack of generalized osteopenia was indicated by normal cortical thickness in the second metacarpals. Multiple lucencies associated with endosteal scalloping were present in both humeri indicating an abnormal process located in the marrow. Additional less prominent lytic areas were present in the proximal radii, ulnas, scapulas, and carpal bones.

A bone scan was performed in the anterior and posterior projections 3 hr after intravenous injection of 10 mCi of ^{99m}Tc-diphosphonate (Diagnostic Isotopes). The scan demonstrated symmetrically in-

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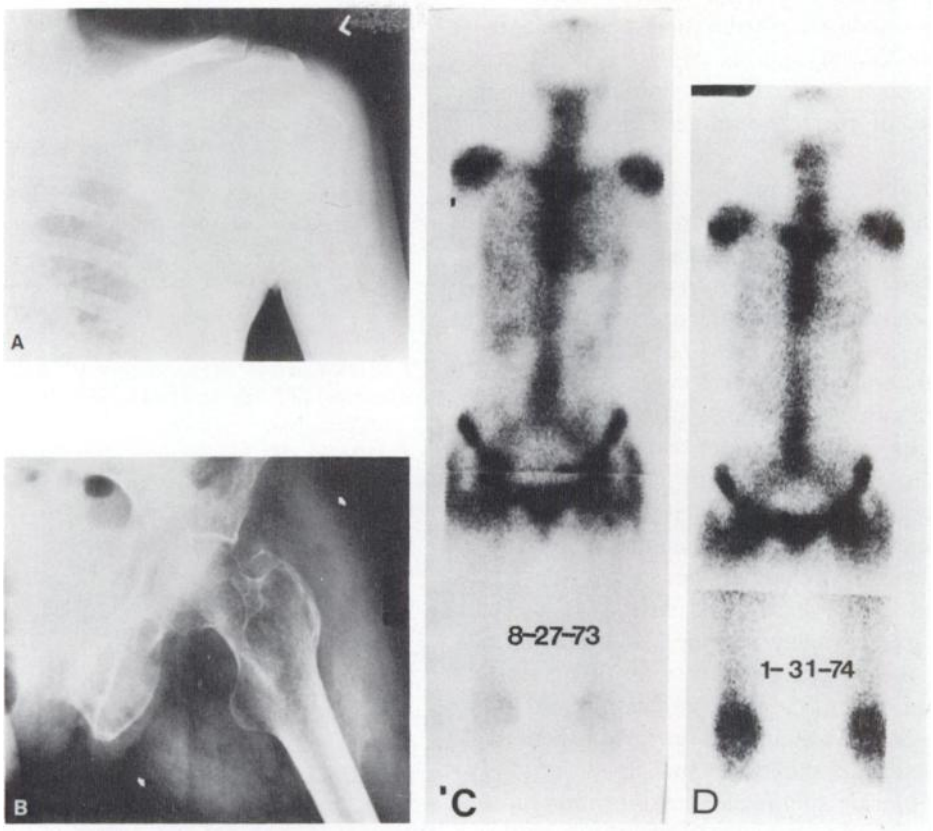

FIG. 1. (A) Radiograph of left shoulder utilizing soft-tissue technique showing soft-tissue fullness without obliteration of subcutaneous tissue planes. Mild subluxation is noted. (B) Radiograph of left hip demonstrating soft-tissue fullness as delineated by arrows. (C) Bone scan in anterior projection with 10 mCi ^{99m}Tc-diphosphonate 3 hr after injection showing extraosseous accumulation in symmetrical pattern in periarticular soft tissue about hips with increased shoulder joint uptake bilaterally. (D) Repeat bone scan 5 months later with same technique. Although patient had shown clinical improvement, there is minimal change seen on bone scan. It should be noted repeat study was performed during exacerbation of patient's illness.

creased uptake in the shoulder joints bilaterally and striking extraosseous activity in a symmetrical pattern in the periarticular soft tissue about the hips (Fig. 1C).

Laboratory studies were consistent with mild renal failure; the urine was positive for Bence Jones protein. Hypercalcemia was also present. A bone marrow biopsy was consistent with plasma cell myeloma. Tests for rheumatoid factor and antinuclear antibody were negative. Serum protein electrophoresis demonstrated hypogammaglobulinemia. Urinary protein electrophoresis showed a monoclonic peak typical of Bence Jones protein with free kappa chains.

Biopsies of the nodules of the eye, tongue, and the soft tissue of the right shoulder were obtained. Histological examination was strongly positive for staining for congo red and cresyl violet. Birefringence was also demonstrated. Electron microscopy of the shoulder tissue showed a matrix of randomly orientated fibriles consisting of two parallel filaments in the 50–120 Å range, consistent with the ultrastructure morphology of amyloid.

A diagnosis of multiple myeloma with secondary amyloidosis was made and the patient was placed on a treatment regime of melphalan, prednisone, occupational therapy, analgesics, and muscle relaxants. A repeat bone scan 5 months later showed minimal change with continued soft-tissue uptake in the same symmetrical pattern (Fig. 1D). Although the patient had clinically improved in the interim, it must be noted that the second bone scan was obtained during an exacerbation of her illness.

Following a move to another part of the country, she fractured her left hip necessitating surgical repair. At surgery, biopsy of the periarticular soft tissue confirmed the presence of amyloid in the area of the extraosseous uptake about the hips.

DISCUSSION

Amyloidosis is a complex entity that may present as a primary disease with or without heredofamilial characteristics or as a complication of various disease states. These states include chronic infectious diseases, chronic inflammatory diseases, neoplasms, and metabolic diseases. It may simulate or be associated with rheumatoid arthritis and the early differential

diagnosis is frequently difficult. Multiple myeloma and rheumatoid arthritis are the most common predisposing causes of amyloidosis (*8,9*). Bilateral carpal tunnel syndrome may be the initial complaint and the history of corrective surgery is not uncommon.

The radiographic findings in amyloidosis are a reflection of the diffuse multisystem involvement that may occur in this disorder (*10*). Osseous deposition can produce lytic lesions that may be indistinguishable from the changes of multiple myeloma when the latter disease is also present (*11*). Pathologic fracture of the humeral and femoral necks is not infrequent. Joint abnormalities most often result from amyloid deposits in the synovium, capsule, and periarticular soft tissues (*12*). Both large and small joints are characteristically affected frequently in a bilateral symmetrical fashion. Rheumatoid arthritis is frequently suspected clinically because of the type of involvement of the hands and wrists (*13*). The characteristic radiographic findings of rheumatoid arthritis such as periarticular erosions, joint space narrowing, and periarticular deossification are not demonstrated. Soft-tissue fullness may be particularly prominent about the shoulders and the hips (Fig. 1A and B). Inferior subluxation of the humerus is frequently seen (*1,5*). It must be emphasized that amyloidosis is a pathological diagnosis based on the proper histological examination of the tissue sections from an involved area. Criteria for the pathological diagnosis have been well described (*14,15*).

The exact mechanism for uptake of ^{99m}Tc-diphosphonate in amyloid is unknown. Although calcification in areas of amyloid deposition has been described (*9*), no such activity was evident radiographically in the soft-tissue areas of concern in this patient. It is presumed that the demonstration by scanning techniques of this soft-tissue activity is the result of the more sensitive nature of the bone scan when compared with detection of early calcification or ossification radiographically.

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