Hepatic Uptake of Tc-99m-Labeled Diphosphonate in Amyloidosis: Case Report

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Hepatic uptake of a "bone-seeking" radionuclide, in a patient with biopsy-proven amyloidosis of the liver, is described and discussed.

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CASE REPORT

A 47-year-old black male postal worker presented for evaluation of intermittent pruritis. Transient elevation of alkaline phosphatase and bilirubin had occurred with the onset of symptoms 1 yr before admission. Both values were again elevated 9 mo later when hepatomegaly was first discovered. Oral cholecystogram was negative. The history was otherwise unremarkable, without evidence of alcoholic excess.

On admission, the liver span was 16 cm by percussion, without palpable splenomegaly. The alkaline phosphatase was 320 mU/ml (normal, 30–85), and fractionation was inconclusive. The bilirubin measured 1.4 mg% (normal, < 1.0), and 0.65 mg% was "direct" upon fractionation. Proteinuria was present: 1.061 g in a 24-hr urine specimen. Serum protein electrophoresis revealed an "M" spike in the gamma III fraction of 1.86 g%, but urine protein electrophoresis was normal. Blood myeloma study was consistent with a monoclonal gammopathy of the IgG type K variety. The lupus erythematosus preparation, antinuclear factor, purified protein derivative, rapid plasma reagin, and fluorescent treponemal antibody were all normal. Liver–spleen scintiphotos with 4 mCi of Tc-99m sulfur colloid (Figs. 1A and 1B) showed early reversal in the hepatic-splenic ratio and mild hepatomegaly with heterogeneous uptake. A bone scan performed 7 days later (Fig. 2), using 15 mCi of Tc-99m-labeled diphosphonate, revealed no evidence of bony abnormality but did show significant hepatic uptake of the tracer. Conventional radiographs showed no hepatic calcification and no bony lesions. Bone-marrow aspiration revealed mild to moderate mature plasmacytosis and lymphocytosis without definite evidence of either multiple myeloma or amyloidosis. Rectal biopsy was also negative for amyloid. Subsequent liver biopsy, using Congo Red staining, demonstrated diffuse replacement of liver parenchyma by amyloid deposits. Prominent hepatic uptake of radionuclide was again apparent and unchanged on a repeat bone scan (not shown) performed 6 mo after the original.

DISCUSSION

Amyloidosis results from the extracellular deposition of an amorphous eosinophilic glycoprotein with characteristic staining and polarization properties. Electron microscopy reveals a unique fibrillar composition. The condition may be idiopathic, age-related or associated with a variety of pathologic states including chronic infection, chronic inflammation, connective-tissue diseases, neoplasm, and metabolic derangements. Multiple myeloma and rheumatoid arthritis are the two most common predisposing conditions. It may assume a localized or generalized form. Liver involvement is common histologically, although hepatic symptoms are rare. Bilirubin and liver enzyme values are usually not markedly elevated.

Hepatic amyloidosis may produce a variety of non-specific scintigraphic patterns on standard liver-spleen scans. The scan may appear normal, may demonstrate a diffuse infiltrative process within the liver, or on occasion may produce a localized area of decreased uptake indistinguishable from neoplasia (*1,2*).

The present case demonstrates uptake of a "bone-seeking" agent in the liver of a patient with biopsy-

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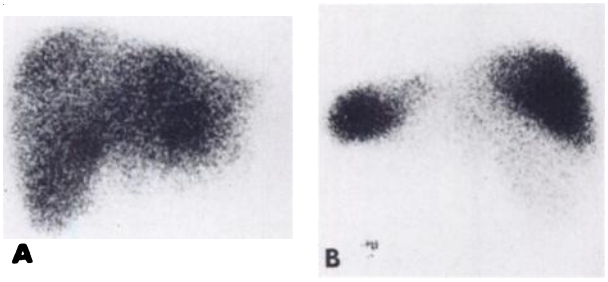

FIG. 1. (A) Liver-spleen scan (Tc-99m S colloid) demonstrating heterogeneous liver uptake compatible with diffuse infiltrative disease of liver. (B) Posterior liver-spleen scan demonstrating abnormal hepatic-splenic ratio.

proven hepatic amyloidosis, in association with a monoclonal gammopathy. Van Antwerp (*3*) has described a single case of Tc-99m diphosphonate uptake in biopsy-proven amyloid deposits of the hip and shoulder joints in a patient with multiple myeloma, also without plain-film radiographic evidence of soft-tissue calcification. Kula (*4*) reported diffuse soft-tissue localization of Tc-99m diphosphonate in amyloid deposits of the extremities in two patients. Sostre et al. (*1*), however, make no mention of hepatic uptake of F-18 in bone scans performed on two of seven patients with primary amyloidosis. Uptake of various bone-scanning agents in uncalcified, extraosseous soft tissue has been found in a variety of unrelated disease states such as infiltrating intraductal breast carcinoma (*5,6*), abscess (*6*), brain metastases from squamous cell carcinoma of the lung (*6*), lymphoma (*7*), myocardial infarction (*8*), uncalcified myositis ossificans (*9*), and hepatic tumors (*10*). These agents also localize in areas of dystrophic soft-tissue calcification visible on standard roentgenograms, such as calcified splenic infarcts (*11*).

The mechanism of uptake of Tc-99m-labeled diphosphonate in radiographically uncalcified hepatic amyloidosis is not known, but one hypothesis seems tenable. Since amyloid deposits may calcify radiographically (particularly amyloidosis involving the skin and lungs), hepatic uptake in our case may reflect the sensitivity of the nuclide to early alterations in calcium content locally, before radiographically demonstrable calcification. This hypothesis is supported by Silberstein's experimental work in laboratory animals (*12*) in which increasing tissue retention of Tc-99m Sn diphosphonate correlates with the calcium content of the tissues analyzed. The relationship is not a linear one, however, since actively growing tissues accumulate more radionuclide than do "mature" tissues with identical calcium content. Pepys (*13*) has isolated a plasma protein (protein AP) that is consistently found in all amyloid deposits and shows calcium-dependent binding. Furthermore, diphosphonate has been used clinically to treat patients with progressive dystrophic soft-tissue calcification (*14*). As an alternative explanation for radionuclide uptake in soft tissue, Chaudhuri (*6*) suggests the possibility of high concentrations of phosphatase enzyme systems in certain tumors. Further experimental and clinical observations will be necessary to elucidate the diagnostic significance and mechanisms of uptake of "bone-seeking" radionuclides in extraosseous locations.

FIG. 2. Initial bone scan (Tc-99m diphosphonate) demonstrating prominent uptake by liver.

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