Technetium-99m(V)Dimercaptosuccinic Acid Uptake in Intra-abdominal Massive Deposit of Amyloid Protein

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Technetium-99m(V)dimercaptosuccinic acid (DMSA) scintigraphy was performed in two patients with pathologically confirmed primary amyloidosis. Both patients had tumor-like deposits of AL-type amyloid in the abdomen. Marked uptake of the tracer by the amyloid deposits was noted. Technetium-99m-(V)DMSA scintigraphy appears to be useful in detecting the distribution of amyloid deposits and in determining the appropriate site for biopsy.

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Amyloidosis is a group of diseases that are characterized by the deposition of one of several proteinaceous materials known as amyloid in one or more organs. Massive deposits of amyloid that resemble tumors are called amyloid tumors. Such lesions are rare and are found mainly in the respiratory, gastrointestinal and urinary tracts in patients without plasmacytoma (*1*). Diagnosis is established by demonstrating amyloid deposits in appropriate tissue specimens. Imaging diagnosis of such lesions has been attempted with ^{99m}Tc-tagged phosphate (*2–4*), ^{67}Ga-citrate (*5*) and ^{123}I-labeled human serum amyloid P component (SAP) (*6*). The usefulness of ^{99m}Tc(V)dimercaptosuccinic acid (DMSA) in the evaluation of amyloidosis associated with plasmacytoma in the head and neck region has been reported previously (*7*). In this article, we describe two patients with primary amyloidosis, in whom marked uptake of ^{99m}Tc(V)DMSA in amyloid tumors in the abdomen and other sites was noted.

PATIENTS AND METHODS

Studies were performed on two patients with histologically proven primary amyloidosis. Technetium-99m(V)DMSA was prepared as previously reported (*8*). DMSA purity was analyzed by thin-layer chromatography, and no free pertechnetate or other ^{99m}Tc derivatives were detected. Imaging was performed at 2 and 18 hr after an intravenous dose of 15 mCi ^{99m}Tc(V)DMSA. Other radiologic studies were performed within 20 days before these scans.

Case Reports

Case 1. A 52-yr-old woman presented with a right pleural tumor and chest wall mass in 1987. Biopsy specimens revealed massive deposition of eosinophilic and Congo red positive proteinaceous material. Electron microscopic examination and the Congo red staining pattern observed by polarizing microscopy confirmed that the material was amyloid of the AL-type. Serum M-protein and urinary Bence-Jones protein were negative, so primary amyloidosis was diagnosed. In 1991, she presented with masses in the diaphragm, chest wall, clavicle and spine. Computed tomography (CT) showed a homogeneous tumor of the diaphragm. Technetium-99m(V)DMSA scanning showed marked accumulation of the lesions to the chest wall, diaphragm, right clavicle and spine (Fig. 1).

Case 2. A 75-yr-old man was admitted to Kyoto National Hospital with ileus and recovered following conservative treatment. Multiple submucosal tumors were found in the duodenum and jejunum on a barium study, but the exact extent of the lesions could not be determined. CT scans demonstrated thickening of the duodenal and jejunal walls (Fig. 2), and marked accumulation of ^{99m}Tc(V)DMSA was seen in the duodenal and jejunal lesions (Fig. 3). Biopsy of the duodenal submucosal tumors showed massive deposition of eosinophilic and Congo red positive proteinaceous material. Histochemical studies demonstrated that this material was an amyloid deposit of the AL-type. There were no other abnormalities found with various investigations and the final diagnosis was primary amyloidosis.

DISCUSSION

The presence of amyloidosis can be suspected from various signs and symptoms, but the definitive diagnosis can only be made by histochemical analysis of biopsy specimens. Amyloidosis may involve multiple organs and evaluation of the extent of amyloid deposition is often difficult. The present study demonstrated the localization of ^{99m}Tc(V)DMSA in lesions produced by primary amyloidosis in the abdomen and other sites.

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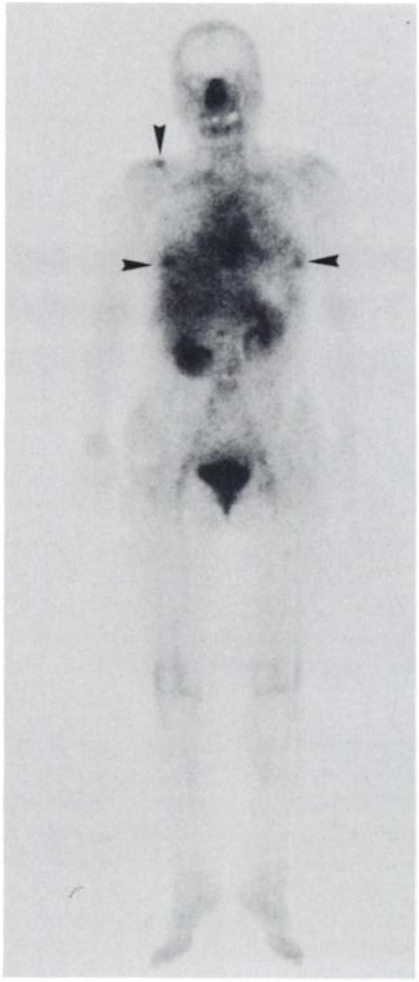

FIGURE 1. Technetium-99m(V)DMSA whole-body scan for Patient 1. High accumulation (arrows) is shown in lesions of the chest wall, diaphragm and right clavicle.

In radionuclide imaging of amyloidosis, ^{123}I-labeled SAP is reportedly specific, but the preparation of this tracer is technically intricate (*6*). In contrast, the accumulation of ^{99m}Tc-tagged phosphate or ^{67}Ga-citrate is nonspecific.

We previously reported the selective localization of ^{99m}Tc(V)DMSA in medullary thyroid carcinoma and not in other types of thyroid cancer (*9*). Amyloid seems to

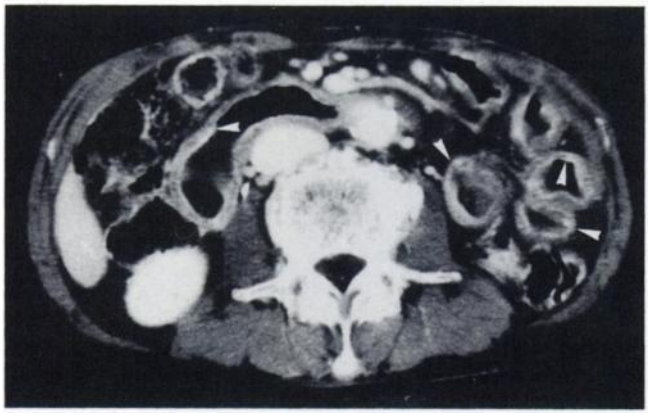

FIGURE 2. CT Scan of Patient 2 revealed thickening of the duodenal and jejunal walls (arrows).

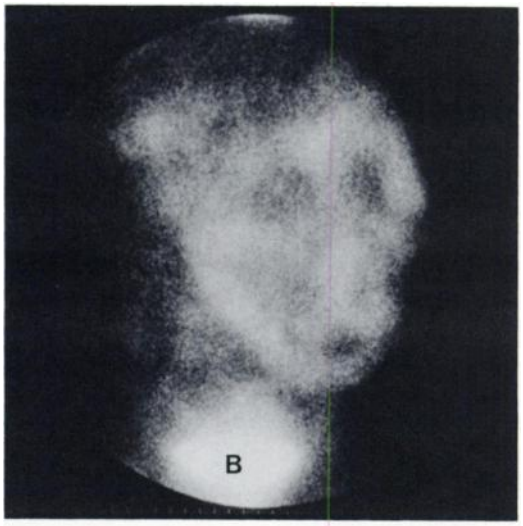

FIGURE 3. Technetium-99m(V)DMSA scan of Patient 2. Extremely high accumulation was found in the lesions of the duodenum and jejunum. "B" indicates the urinary bladder.

accumulate a large amount of ^{99m}Tc(V)DMSA and amyloid deposition is a conspicuous feature of medullary thyroid carcinoma. Furthermore, we have also reported the accumulation of ^{99m}Tc(V)DMSA in amyloid deposits associated with plasmacytoma in the head and neck region. Amyloid associated with multiple myeloma is of the AL-type and primary amyloidosis is also characterized by the deposition of AL-type amyloid. In contrast, secondary amyloidosis not associated with multiple myeloma involves the deposition of AA-type amyloid. We have found the accumulation of ^{99m}Tc(V)DMSA in AL-type amyloid deposits in both of these diseases.

Although background activity in the liver and kidneys was not negligible, ^{99m}Tc(V)DMSA scintigraphy demonstrated sufficient accumulation to detect intra-abdominal lesions in our two patients. In both patients, a whole body scan and abdominal planar ^{99m}Tc(V)DMSA scintigraphy helped to delineate the extent of the amyloid deposits more clearly than axial CT scans. For Patient 2, the exact localization and estimation of the degree of thickening of the intestine was difficult on CT scans because the small intestine was not easily distinguishable from the colon due to the postileus state. Since selection of the correct biopsy site is important in the histological diagnosis, scintigraphy was especially useful in this patient.

Clear and definite imaging of amyloid deposits, which has not been achieved with other radionuclide techniques, could be attained with ^{99m}Tc(V)DMSA scintigraphy. Further studies in more patients are necessary to determine the sensitivity and specificity of ^{99m}Tc(V)-DMSA scintigraphy for both amyloidosis associated with plasmacytoma and primary amyloidosis.

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SELF-STUDY TEST

Skeletal Nuclear Medicine

ANSWERS *(continued)*

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Item 2: Mechanisms of Radiopharmaceutical Uptake in Osseous Lesions

Answer: E

Bone-seeking radiopharmaceuticals are accumulated in greater degree at skeletal sites where there is increased blood flow (thus exposing that bone to more tracer for chemisorption over any given time), and also in sites of new bone formations where there is an increase in the surface area of hydroxyapatite crystals per unit volume of bone. Newly forming hydroxyapatite crystals are of smaller size than mature crystals and provide a relatively greater surface area for chemisorption of the tracer. Although both increased blood flow and new bone formation (with associated increase in crystal surface area) are important, several studies have shown that the magnitude of the change in blood flow is insufficient to account for the substantially increased tracer accumulation in epiphyseal plates, metastatic lesions and healing fractures.

A large mass of compact bone with normal blood flow and hydroxyapatite deposition will not necessarily have increased uptake; e.g., bone islands are not usually noticeably "hot" by scintigraphy.

The organic matrix has rather low affinity for the ^{99m}Tc diphosphonate agents when compared with hydroxyapatite crystals. There is little experimental evidence that alkaline phosphatase activity bears a relationship to the localization of bone-seeking radiopharmaceuticals.

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Item 3: Caudal Imaging of the Pelvis

Answer: E

Figure 1 shows bilateral focal uptake in the pubic area, which could be due to metastases or insufficiency fractures; however, retained urine in bladder diverticula is more likely. The true nature of the focal uptake is most easily demonstrated by performing a caudal scintigram of the pelvis, which can separate activity in the bladder from that in the pubis. In this patient, the pubic bones are normal and the activity is in the bladder diverticula. Additional delayed views the next day are also helpful to separate osseous lesions from activity in the urinary bladder, especially in patients who are unable to void fully at the time of initial imaging.

Imaging after furosemide is used to distinguish obstructive from nonobstructive pelvicalyceal dilatation, but not to evaluate lower urinary tract lesions. It is not indicated in this case, although a change in bladder configuration conceivably could result. Although SPECT of the pelvis would distinguish pubic from bladder activity, the question in this patient is more easily and less expensively resolved by a caudal scintigram. Plain radiography would be of value to distinguish metastases from insufficiency fractures, but it would not be appropriate until an osseous localization of the increased activity is confirmed. Gallium scintigraphy would involve additional expense, radiation exposure, and an unnecessary delay in diagnosis. Because ^{67}Ga uptake in metastatic lesions of prostatic cancer is often poor, the absence of definite abnormalities would not help greatly to distinguish metastases from fractures or true osseous lesions from bladder activity.

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Items 4-8: Scintigraphy of Fractures

Answers: 4, F; 5, F; 6, T; 7, F; 8, F

Tibial stress fractures are characterized by focal, fusiform accumulations of increased uptake of ^{99m}Tc MDP, whereas shin splints exhibit more diffuse uptake extending over a large length of bone, usually along the posterior cortical surface. The two usually are distinguishable scintigraphically.

Focally increased uptake of ^{99m}Tc MDP is usually apparent soon after an acute fracture, and nearly always by 72 hours after injury. However, Matin has shown that this response may be delayed in elderly patients, with some fractures not clearly apparent scintigraphically at one week.

Both sterile and infected hypertrophic pseudarthroses concentrate both ^{99m}Tc MDP and ^{67}Ga. Therefore, they are very difficult to distinguish by scintigraphy with these agents. The absence of ^{67}Ga uptake favors the absence of infection, but increased ^{67}Ga uptake is not necessarily due to infection. More recent studies indicate that ^{111}In white cell scintigraphy is more reliable for diagnosing infection in nonunited fractures.

The finding of normal or minimally increased ^{99m}Tc MDP uptake at a site of delayed union reflects a poor capacity to heal; in this situation piezoelectric stimulation does not promote effective healing. If there is a high concentration of the tracer about the fracture site, and if the gap between the fracture fragments is not large enough to be resolved by scintigraphy, the chances of stimulated healing are greater.

On average, ^{99m}Tc MDP images of vertebral compression fractures

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