Clinical note

Unusual extraosseous tumoral accumulation of $^{99m}$Tc-MDP in non-Hodgkin's lymphoma in two cases

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A B S T R A C T

The authors describe a rare pattern of soft tissue uptake observed in a $^{99m}$Tc-MDP bone scintigraphy of two patients with the diagnosis of non-Hodgkin's lymphoma. Both patients had abdominal masses and bone scintigraphy revealed unusual $^{99m}$Tc-MDP uptake in the abdominal region. The possible mechanisms of soft tissue uptake of bone seeking agents are discussed.

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Introduction

$^{99m}$Tc methylene diphosphonate (MDP) bone scintigraphy is a valuable method used to evaluate skeletal abnormalities, but important nonosseous findings may also be present on the images.

Extraskeletal uptake in soft tissue structures on bone scan has been reported occasionally in literature. Such an abnormal $^{99m}$Tc-MDP uptake can be neoplastic, hormonal, inflammatory, ischemic, traumatic, excretory or artifactual. Pathogenesis of soft tissue uptake of bone seeking agents is usually multifactorial and in some instances the exact mechanism is not apparent. Any process that evokes soft tissue calcification (dystrophic, metastatic or heterotopic calcification) or binding of radiopharmaceuticals to macromolecules in the tissue might cause soft tissue uptake.

Recognition of abnormal soft tissue uptake on bone scintigraphy provides accurate interpretation and enhances the diagnostic value of the study.

In this report, a rare pattern of soft tissue $^{99m}$Tc-MDP accumulation in two patients with non-Hodgkin's lymphoma is presented.

Clinical cases

Patient no. 1

A 40 years old man was admitted to the hospital for abdominal swelling and aglutition. Weakness, sweating and weight loss were also present. His physical examination revealed hepatosplenomegaly, enlarged lymph nodes in the neck and hyper trophy tonsilae.

In laboratory tests hypercalcemia was present, liver function tests were increased and anti-HCV was positive, but tumor markers were normal.

On $^{99m}$Tc-MDP bone scintigraphy multiple ovoid and heterogeneous soft tissue uptake were seen in the toracoabdominal region (Fig. 1a). Additional static images in lateral and oblique projections were taken in order to rule out bone metastasis since the activity in the toracoabdominal region superposed bony structures. Bone metastases were not present.

Abdominal ultrasonography and computed tomography revealed hepatosplenomegaly, multiple solid masses in the liver and spleen, the largest having a diameter of 14 cm (Fig. 1b) and enlarged lymph nodes in the retroperitoneal and bilateral iliac regions. Enlarged lymph nodes in the neck and soft tissue masses in tonsillar regions were also detected.

The wedge biopsy specimen of nasopharyx was consistent with large B-cell lymphoma.
Fig. 1. Whole body $^{99m}$Tc-MDP bone scintigraphy and additional static images of patient no. 1 showing multiple heterogenous soft tissue uptake in the toracoabdominal region (a) and CT demonstrated multiple giant solid masses in liver and spleen (b).

Patient no. 2

A 66 years old man was admitted to the hospital for abdomинаl pain. His physical examination was normal, but he mentioned about his weight loss during the last 2 months. No other complaints were present.

An abdominal ultrasonography revealed a large tumoral mass filling the epigastric region. The mass was adjacent to porta hepatitis and right kidney. $^{99m}$Tc-MDP bone scintigraphy showed heterogenous soft tissue uptake in abdomen (Fig. 2a). There was intense bone tracer uptake on the right aspect of the lumbar region, which superposed and caused suboptimal evaluation of the right 11th costal arc. On the other bones metastasis was not detected.

Following computed tomography (Fig. 2b) confirmed the giant mass, which was adjacent to porta hepatitis and kidney in the right, stomach and spleen in the left and was extending to the right pelvic region retroperitoneally. Mediastinal and pelvic enlarged lymph nodes and splenomegaly were the other findings.

A wedge biopsy was performed to the retroperitoneal mass. Histopathological diagnosis was B-cell non-Hodgkin’s lymphoma.

Discussion

Visualization of activity in the soft tissue structures on a bone scan may be secondary to excess calcium in the soft tissue or binding of radiopharmaceuticals to macromolecules, denatured proteins or enzyme receptors in the tissue. This situation can occur in several diseases and cannot be explained by a single mechanism.

Calcium deposition in the soft tissue can be due to dystrophic or metastatic calcification, increased ectopic osteoblastic activity, metastases from osteoid-forming primary tumors (e.g., osteogenic sarcoma) and increase of calcium binding tissue cations (e.g., iron, magnesium). Mechanisms leading to increased extraosseous uptake of bone seeking agents not only include elevated tissue calcium deposition but also, extracellular fluid expansion, enhanced regional vascularity and altered capillary permeability in the tissues.

The initial phase of $^{99m}$Tc-MDP concentration in normal tissues is directly related to blood flow and vascularity. Increased regional perfusion is associated with enhanced tracer concentration in the tissues due to passive diffusion. Neovascularization has been suggested as an additional factor leading to significantly higher tissue concentrations of $^{99m}$Tc-MDP. Therefore tumor vascularity should also play a role in the tumoral accumulation of $^{99m}$Tc-MDP. In spite of this, histologic evidence of calcium has been reported to correlate most strongly with avid tracer uptake. But calcification is very rare in untreated Hodgkin’s or non-Hodgkin’s lymphoma and mostly seen after either radiation or chemotherapy, causing cell membrane disruption or altered cellular calcium transport. The bone scan of our patients were taken prior to treatment. CT did not show any visible calcification in the lesions of both cases, however microcalcification could not be definitely ruled out.

Fig. 2. $^{99m}$Tc-MDP bone scintigraphy of patient no. 2 showed heterogenous soft tissue uptake in abdomen, which was more evident in the right aspect of the lumbar region (a); CT confirmed giant mass localized retroperitoneally mostly in prevertebral region (b).
Serum calcium level was normal in patient 2, but slightly increased in patient 1, in the course of bone scan. When hypercalcemia is severe or when serum protein concentration is low, solubility product of calcium and phosphate is exceeded and precipitation of calcium salts in extracellular space occurs. However, unlike our cases, diffuse uptake of tracer is seen in visceral organs, first in the lungs and, in more severe cases, may also be noted in heart, liver, stomach and kidney in metastatic calcification, due to deposition of calcium salts in nonosseous, viable tissue in the presence of hypercalcemia.6

In literature, $^{99m}$Tc-labelled phosphonate binding has been reported in a number of extraosseous neoplasms and metastatic lesions. To our knowledge there are a few cases showing bone tracer uptake in lymphoma such as primary breast and testicular lymphoma, lymph node and splenic uptake.5,7–9 An in vitro study performed by Stone and Sisson10 showed significantly more uptake of $^{99m}$Tc-MDP by the dispersed lymphoma cells from the patient than by cultured lymphoblasts suggesting that the in vivo sequestration may have been, at least in part, an active intracellular process. Goyal and Bang7 reported bone tracer uptake in primary breast lymphoma but no calcification within the breast was evident. Mehta et al. observed lymph node uptake of $^{99m}$Tc-MDP in a patient with Hodgkin’s disease, whose $^{67}$Ga scan performed 3 days later demonstrated an intense uptake in a much larger area. The reason for different distributions of these two tracers should be differences in their mechanisms of uptake. It has been concluded that the abnormality in the $^{67}$Ga scan reflects uptake at sites of tumor, whereas the abnormality on the bone scan reflects increased local calcium ion concentration.8

In both of our cases, the number of areas showing soft tissue uptake is less than the lesions observed by anatomical diagnostic methods. Especially in patient 2, a part of the giant mass had shown more intense $^{99m}$Tc-MDP uptake, which indicates heterogeneous composition inside the mass. In bone scan of patient 1, other sites of tumoral involvement such as lymphadenopathies on the neck did not show MDP uptake. In our cases we could not state the exact mechanism of $^{99m}$Tc-MDP uptake. Calcification could not be demonstrated by CT or histopathological evaluation.

Multiple factors clearly play a role in tumoral uptake of bone agents. Being aware of the pathophysiologic basis of soft-tissue $^{99m}$Tc-MDP uptake can significantly enhance the diagnostic value of bone scintigraphy. Interpretation of additional soft tissue lesions on bone scintigraphy would guide the clinicians for further evaluation.

References