Diffuse Pulmonary Uptake of Tc-99m Methylene Diphosphonate in a Patient with Non-tuberculosis Mycobacterial Infection

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Abstract Extra-osseous uptake of bone-seeking radiopharmaceuticals has been reported at various sites and it is known to be induced by various causes. Diffuse pulmonary infection, such as tuberculosis, can be a cause of lung uptake of bone-scan agent. Here we report on a patient with non-tuberculosis mycobacterial infection (NTM) who demonstrated diffuse pulmonary uptake on Tc-99m MDP bone scan. After medical treatment for NTM, the patient's lung lesions improved. Extraskelatal lung Tc-99m MDP uptake on bone scan may suggest lung parenchymal damage associated with disease activity.

Keywords Diffuse pulmonary uptake · Tc-99m MDP · Non-tuberculous mycobacterium

Introduction

Extra-osseous uptake of bone-seeking radiopharmaceuticals has been reported at various sites. Extra-osseous uptake can occur within a tumor, or in muscle, soft tissue, pleura, or

lung. Abnormal calcium deposition in soft tissue, followed by chemisorption of Tc-99m MDP, is thought to be a pathogenesis [1–4]. Diffuse lung uptake on bone scintigraphy has been reported in patients with hyperparathyroidism, hematologic malignancy and solid organ tumor, metabolic abnormality such as renal failure, vasculitis and pulmonary infection [5, 6]. We report a first case of a patient with non-tuberculosis mycobacterial infection who demonstrated diffuse pulmonary uptake on Tc-99m MDP bone scan.

Case Report

A 38-year-old man, a chronic heavy smoker, was hospitalized for increasing dyspnea of 2 months duration. He also complained of dry cough, fever, night sweats, and significant (6 kg) weight loss over the preceding 6 months. He was heterosexual and denied any past history of intravenous drug abuse or blood transfusion.

Initial blood investigation was essentially normal, except for a slightly elevated lymphocytic component (47.4%; normal range 20–44%) within the total white blood cell count of 6,300/mm³. The patient had normal renal function with a blood urea nitrogen (BUN) level of 12 mg/dl and creatinine of 0.9 mg/dl. The serum levels of calcium (9.1 mg/dl; normal range 8.8–10.5 mg/dl) and phosphate (3.9 mg/dl; normal range 2.5–4.5 mg/dl) were also normal.

However, he was found to be positive for HIV infection (viral load 158,000 copies) and was severely immunocompromised, with a CD4 count of 3/μl (0%).

A chest PA radiograph revealed disseminated nodular infiltration, predominantly within the right middle and whole left lung fields (Fig. 1a). A computed tomography (CT) scan of the chest showed tiny disseminated nodules with patchy, multifocal ground-glass opacities (GGO),

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Fig. 1 **a** The patient's initial chest PA showed disseminated nodular infiltration, especially in the right middle lung field and the whole left lung field. **b** Initial chest CT showed tiny disseminated nodules with patchy, multifocal GGOs

suggestive of miliary tuberculosis (Fig. 1b). The sputum was stain-negative for acid-fast bacilli (AFB) (repeated three times), but the sputum polymerase chain reaction (PCR) study for bacterial 16S rRNA revealed non-tuberculosis mycobacterial infection. Microbiological study of the blood culture was negative.

Fig. 2 The patient's bone scan showed diffuse radiotracer uptake in both lungs

The patient subsequently underwent a bone scintigraphy due to lower-back pain. The bone scan was performed 4 h after intravenous injection of 740 MBq Tc-99m MDP. There was no remarkable tracer uptake in the spine. Instead, there was diffuse bilateral pulmonary uptake and focal uptake in the proximal left tibia (Fig. 2). No abnormalities were seen in the corresponding radiograph of the left tibia.

The patient was started on anti-retroviral chemotherapy, anti-tuberculosis medication, and prophylaxis for *Pneumocystis carinii* and non-tuberculosis mycobacterium. Three weeks later, follow-up X-rays and CT scans of the chest demonstrated the improved extent of the multifocal GGOs (Fig. 3a, b). Nevertheless, the patient continued to deteriorate clinically, and he developed respiratory failure, secondary to chronic inflammatory demyelinating polyneuropathy involving the diaphragmatic muscles. He was transferred to a hospice facility for supportive care. A follow-up bone scan was not obtained.

Discussion

Occasionally, extraskelatal uptake in soft tissues can be seen on delayed bone-scan images [7, 8]. Uptake of bone-seeking radiopharmaceuticals in extraskelatal tissues can be categorized according to the underlying mechanisms: dystrophic calcification, metastatic calcification, increased ectopic osteoblastic activity, metastases from osteoid-forming primary tumors, and increase of calcium-binding tissue cations [1]. The lung is a common site of bone-specific radiopharmaceutical accumulation, which is thought that the relative alkaline environment surrounding the alveoli conduct calcium precipitation [5].

In the case of diffuse pulmonary uptake of Tc-99m MDP, the presence of biochemical abnormality and/or radiologic abnormality should be initially evaluated. One previous report found that 30 of 32 patients had biochemical abnormalities:

Fig. 3 After medical treatment for tuberculosis, the diffuse lung infiltrations improved on (a) chest X-ray and (b) CT

24 had hypercalcemia of varying etiologies and another six were chronic dialysis patients. Except for one patient in the latter group, none of them had radiological evidence of pulmonary calcification. Even then, the calcifications seen radiographically did not correspond to the scintigraphic patterns. In contrast, only two patients with no biochemical abnormalities had extensive radiologic calcifications and were diagnosed with diffuse alveolar microlithiasis [9].

In the current patient, the blood calcium level was not elevated, and renal function was within the normal range. There was also no evidence of underlying malignancy. The patient's clinical course, immunocompromised status, and PCR results suggested an opportunistic infection of nontuberculous mycobacterium, in spite of negative sputum AFB [10–14]. In pulmonary tuberculosis patients, it has been reported that the mitochondria of some necrotic tissues contain hydroxyapatite crystals [15, 16]. In this patient, the lung parenchymal damage induced by miliary mycobacteria increased calcium-binding capacity and was followed by chemisorption of Tc-99m MDP. This could account for the scintigraphic pattern we observed.

Pneumocystis carinii pneumonia also frequently occurs in severely immunocompromised patients. Thus, the patient underwent concurrent prophylaxis for *Pneumocystis carinii* without confirmative histopathologic diagnosis. This possible opportunistic infection might also contribute to the abnormal scintigraphic pattern [6].

Diffuse pulmonary calcifications can be improved or revert to normal when the underlying cause is treated or normalized. And bone scintigraphy may be useful for differential diagnosis through providing information about disease activity [17–20]. The extent of the miliary infiltration improved in the subsequent chest CT in our patient. We would also expect an improvement in the scintigraphic appearance. Future investigation should be directed at evaluating the possible additional role of bone scans in the follow-up of such patients.

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