Thallium-201 Accumulation in Myositis Ossificans and in Juxta-Articular Ossification

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We present the findings on ^{201}Tl and ^{99m}Tc-MDP scintigraphy in three patients suffering from heterotopic ossification (two patients presenting with myositis ossificans and one patient presenting with juxta-articular ossification in combination with myositis ossificans). Since resection of the lesions has to be delayed until stabilization, ^{99m}Tc-MDP is often used as a parameter of lesional activity, although it is not optimal. For this clinical problem, we evaluated ^{201}Tl scintigraphy as a marker of metabolic activity. In addition to the well-documented uptake of ^{99m}Tc-MDP, marked accumulation of ^{201}Tl was observed in all heterotopic ossification sites. Hence, our results support the use of ^{201}Tl scintigraphy in the therapeutic management and monitoring of conditions associated with ectopic ossification. On the other hand, although myositis ossificans is sometimes clinically, radiographically and even histologically confused with extraosseous osteogenic sarcoma, ^{201}Tl accumulation may not be a helpful factor in the differential diagnosis due to the presence of tracer accumulation in both disorders.

Key Words: myositis ossificans; juxta-articular ossification; osteogenic sarcoma

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Heterotopic ossification consists of myositis ossificans and juxta-articular ossification. Myositis ossificans usually develops in one or more muscle groups after trauma. Less frequently, it appears in a generalized form, as a progressive, widespread ossifying process. Other patients develop juxta-articular ossification after a major trauma or surgical procedure for joint disease (*1*). In practice, imaging with ^{99m}Tc-MDP is used to plan an optimum date for surgical intervention for heterotopic ossifications (*2*), because extirpation of the lesions has to be delayed until the ossification has stabilized (*3*). In some cases, however, patients can undergo surgery and successful results can be obtained despite markedly positive bone scans (*2,4*). A second clinical problem in heterotopic ossification is that myositis ossificans may mimic masses suggestive of malignant tumors, such as osteosarcoma.

Thallium-201-chloride, a monovalent cationic radiotracer, is successfully used for myocardial perfusion imaging. Shortly after its introduction in nuclear cardiology, ^{201}Tl was also reported to show considerable accumulation in viable tumor tissue (*5–7*). Following these preliminary studies, several articles have been published concerning ^{201}Tl uptake in thyroid, breast, lung and brain malignancies, lymphomas, Karposi's sarcoma, bone and soft-tissue sarcomas. Three reviews of extracardiac applications of ^{201}Tl are available (*8–10*). Recently, thallium has been suggested for the diagnosis and therapeutic follow-up of bone tumors (*11,12*). The uptake mechanism of thallium in tissues is not completely known, but possible influencing factors include: regional blood flow, cell viability, cell type, the Na^+/K^+-ATPase system, the calcium ion channel system, the co-transport system, vascular immaturity with leakage and increased cell membrane permeability (*9*). Although its role in the detection of viable bone tumor is recognized, few data are available on ^{201}Tl accumulation in other bone pathologies.

We present three patients with heterotopic ossification whose scintigraphic studies showed lesional ^{201}Tl accumulation. The potential role of ^{201}Tl accumulation as a marker of lesional activity and its implications for the differential diagnosis are highlighted.

CASE REPORTS

Scintigraphic studies were obtained in one patient with histologically proven myositis ossificans (Patient 1) and in two patients who were clinically and radiographically diagnosed as suffering from myositis ossificans (Patient 2) and combined juxta-articular ossification and myositis ossificans (Patient 3).

Bone scans were obtained 5 hr after intravenous injection of 740 MBq ^{99m}Tc-MDP, using a LFOV gamma camera, equipped with a high-resolution, parallel-hole collimator and with the spectrometer peaked at 140 keV. Thallium scans were obtained 3-to-7 days after the bone scans. A dose of 150 MBq ^{201}Tl as thallous chloride was administered intravenously. Approximately 30 min later, planar images were acquired using the same system configuration and with the spectrometer peaked at the 69–80 keV x-rays of ^{201}Tl.

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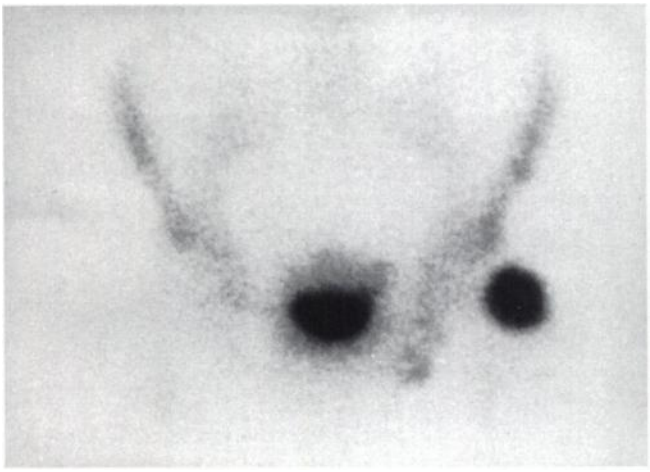

FIGURE 1. Technetium-99m-MDP bone scan shows a solitary concentric focus with increased peripheral tracer uptake and central rarefaction in the underexposed image at the left femoral neck.

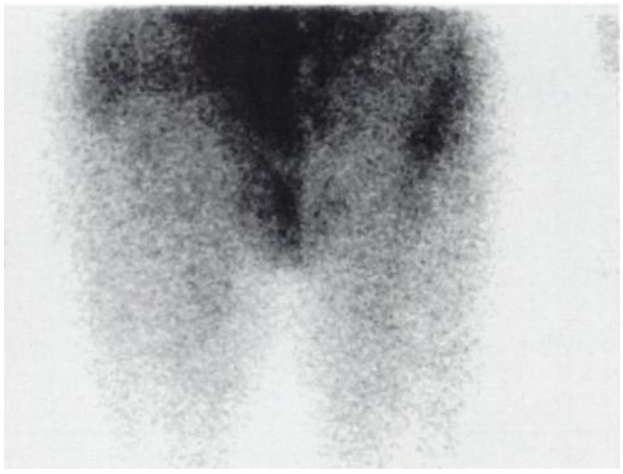

FIGURE 3. More diffuse and decreased ^{201}Tl uptake after the therapy in the same site.

Patient 1

A 28-yr-old man presented with pain of 3 mo duration in the left hip region after an episode of grand mal seizures. The clinical examination was unremarkable. Plain radiograph and x-ray CT revealed a radiodense, spherical lesion adjacent to the left femoral neck. At the same location, the ^{99m}Tc-MDP bone scan showed a solitary concentric focus with markedly increased peripheral tracer uptake and a relative decrease in the center of the lesion (Fig. 1). The diagnosis of myositis ossificans was confirmed by biopsy. Thallium-201 scintigraphy showed a matching focus of increased uptake (Fig. 2).

Two months after nonsteroidal anti-inflammatory therapy and rest, the hyperactivity had significantly diminished on the ^{99m}Tc-MDP scan. Concordantly, ^{201}Tl accumulation, as a reflection of lesional metabolic activity, was also decreased and had become more diffuse (Fig. 3).

Patient 2

A 60-yr-old woman with persistent pain in the right buttock for 2 mo was referred because of a hard, subcutaneous mass 10 cm in diameter in the right gluteal region. The ^{99m}Tc-MDP scan showed diffusely increased uptake in the lesion, suggestive of myositis ossificans. Increased ^{201}Tl uptake was found at the lesion site.

Patient 3

A 22-yr-old man, paraplegic for 6 mo, was referred for evaluation of radiographically confirmed juxta-articular heterotopic ossification in the right hip region and at both knees. The ^{99m}Tc-MDP scan revealed focally increased uptake in the right hip and the medial sides of both knees. In addition, myositis ossificans was suggested by the finding of diffuse increased ^{99m}Tc-MDP uptake in the distal thigh muscles. A thallium scintigram demonstrated increased activity at the juxta-articular heterotopic ossification sites and, to a lesser degree, at the myositis ossificans lesions (Figs. 4,5).

DISCUSSION

By reflecting blood flow, blood volume and bone turnover in involved tissues, ^{99m}Tc-MDP scintigraphy theoretically provides an indirect approach of the evolution of the

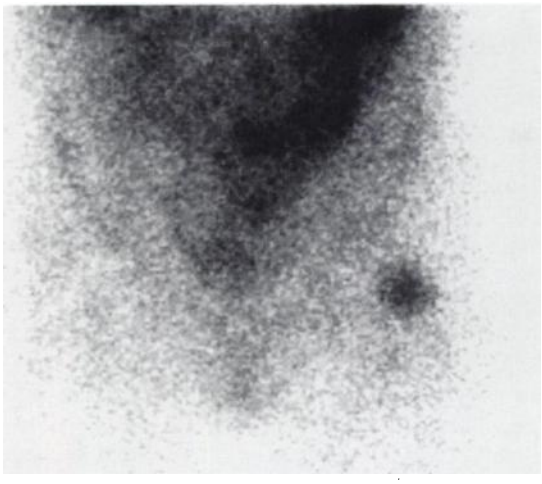

FIGURE 2. Matching focus of increased ^{201}Tl uptake at the same location.

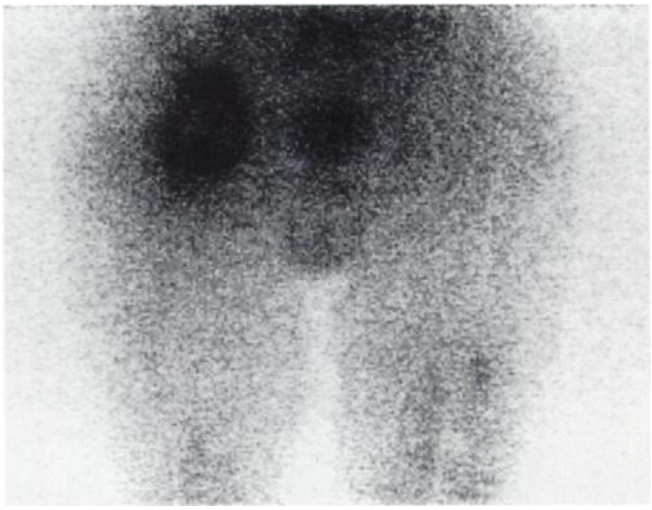

FIGURE 4. Increased ^{201}Tl activity at the juxta-articular ossification sites and to a lesser degree at the myositis ossificans lesions.

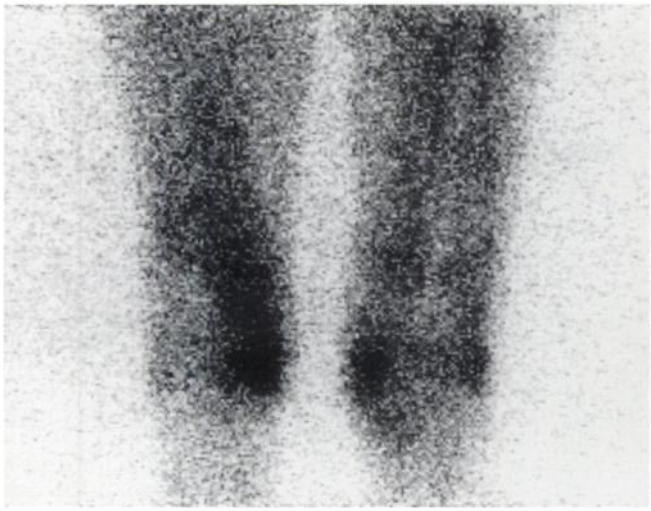

FIGURE 5. Increased ^{201}Tl activity at the juxta-articular ossification sites and to a lesser degree at the myositis ossificans lesions.

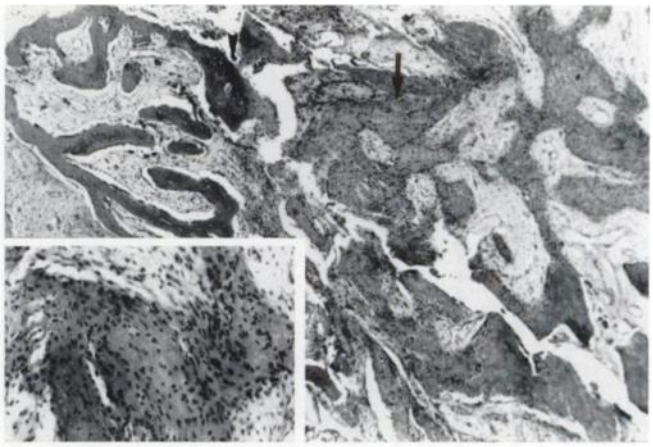

FIGURE 6. Myositis ossificans featuring the zoning phenomenon: centrally proliferating immature osteoid areas (arrow) lead to peripheral mature osseous trabeculae (arrow head) (H&E 64×). Inset: central cellular area where osteoid is formed (H&E ×160).

lesions. Therefore, the technique is used to plan the optimum time for surgical intervention for heterotopic ossifications (*2*), as previously discussed. Peters et al. and Rosenthall et al., however, reported successful surgical results in the presence of markedly positive bone scans (*2,4*). In contrast, ^{201}Tl uptake is likely to yield metabolic information on the cellular activity of heterotopic ossifications. Based on these theoretical considerations and clinical demand, we performed ^{201}Tl and ^{99m}Tc-MDP scintigraphy in three patients to assess lesional activity as a possible contraindication to surgical intervention.

In Patient 1, initial ^{201}Tl accumulation in myositis ossificans decreased and became more diffuse. This evolution suggests that ^{201}Tl uptake in heterotopic ossification depends on the disease stage. Patients 2 and 3 showed slightly to markedly increased ^{201}Tl accumulation at the heterotopic ossification sites, which was probably related to lesional stage. For Patient 3, however, although juxta-articular ossification may have a clinical history different from myositis ossificans, the histological structures are identical. Therefore, ^{201}Tl uptake in the heterotopic ossifications is not surprising.

These results extend the spectrum of ^{201}Tl localization to the evaluation of activity in heterotopic ossification sites. It would be interesting to study patients with heterotopic ossifications prospectively to examine whether ^{201}Tl uptake measurements are superior to three-phase ^{99m}Tc-MDP scans as a parameter of lesion maturation.

Myositis ossificans is one consideration in the clinical, radiological (*1*) and pathologic differential diagnosis of osteosarcoma, which may also include pathologies such as fracture callus, fibrous dysplasia, osteoblastoma, fibrosarcoma, chondrosarcoma, giant-cell tumor, malignant lymphoma and metastatic carcinoma (*13*). Because of ^{201}Tl accumulation in myositis ossificans, of ^{201}Tl scintigraphy in the differential diagnosis merits consideration.

It has been reported that preferential accumulation of ^{201}Tl is to be expected in malignant lesions of bone (*10,11,14–17*). Van der Wall et al. (*14*) noted an 88% sensitivity and 94% specificity for ^{201}Tl scanning in the identification of malignancy in solitary bone lesions, while Ramanna et al. (*16*) reported a sensitivity of 100% in bone and soft-tissue sarcomas. In a study by Elgazzar et al. (*18*) of 20 benign lesions, only one patient with tuberculosis had positive results.

Similar to myositis ossificans, osteosarcoma affects patients in the second decade, although an additional peak around 40 yr may be seen (*13*). Both disorders are well-vascularized and have cellular stroma with pleomorphic cells and clear mitotic activity. Especially in the early stage of myositis ossificans, cellular portions of the biopsy may often be confused with osteosarcoma (*19*). Histologically, myositis ossificans can be distinguished from osteosarcoma by a characteristic zoning phenomenon: centrally localized immature cellular areas and peripherally localized, more mature ossifying areas (Fig. 6). In contrast, osteosarcoma displays a reverse zoning effect: bone formation in the center of the lesion and spindle-cell formation at its margin (Fig. 7) (*19*). Although ^{99m}Tc-MDP images may reflect the architectural pattern as shown in Patient 1 (Fig. 1), central necrosis in osteoarcoma may interfere with the expected behavior.

As we have previously discussed, ^{99m}Tc-MDP scans may reveal central rarefaction in heterotopic ossification and in some osteosarcomas. Ramanna et al. described a donut sign (highly intense peripheral zone surrounding a relatively low level of activity on thallium scans of high-grade sarcomas of the bone and soft tissue) in 41 of 44 patients (93%), while low-grade sarcomas exhibited no donut sign on ^{201}Tl scans (*16*). The same authors demonstrated a rim sign in the knee of an osteogenic sarcoma patient on the ^{201}Tl scan, while the ^{99m}Tc-MDP and ^{67}Ga studies showed the entire area to be active (*12*). The use of ^{201}Tl in this context shows that osteosarcomas with central necrosis may have a donut sign, whereas heterotopic ossifications are not expected to because the more immature cellular areas (metabolically most

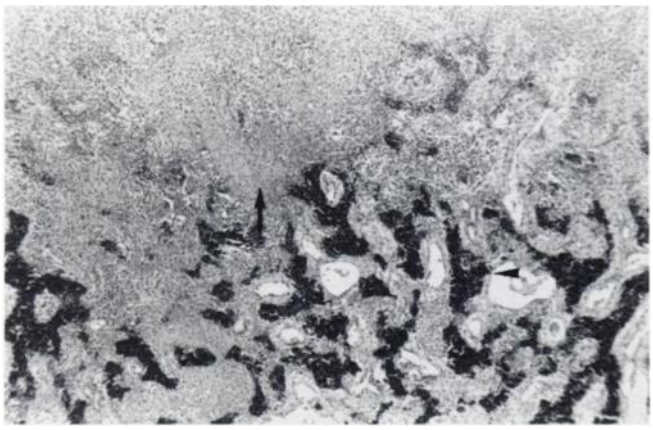

FIGURE 7. Osteosarcoma featuring reverse zoning phenomenon: centrally located osteoid trabeculae (arrow head) are surrounded by highly cellular peripheral proliferating spindle cells (arrow) (H&E 64×).

active areas) are found in the center of the lesion. In some patients, this discrepancy might hint at the right diagnosis.

CONCLUSION

Our results support the role for ^{201}Tl in the therapeutic regimen and monitoring of conditions associated with ectopic ossification. Although myositis ossificans may be confused with an extraosseous osteogenic sarcoma, early ^{201}Tl static planary imaging may not be helpful in the differential diagnosis.

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