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Diaphyseal medullary stenosis with pleomorphic malignant fibrous histiocytoma of the bone: ^{99m}Tc hydroxymethylenediphosphonate and ^{201}Tl chloride scintigraphy findings

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Diaphyseal medullary stenosis (DMS) is an extremely rare hereditary bone dysplasia, which was first described by Arnold in 1973. DMS has a high incidence of pleomorphic malignant fibrous histiocytoma (MFH). In this paper, we report the imaging findings of DMS with pleomorphic MFH of the bone, mainly describing ^{99m}Tc hydroxymethylenediphosphonate (HMDP) and thallium-201 (^{201}Tl) chloride scintigraphy findings. On ^{99m}Tc HMDP scintigraphy, focal increased uptake area of the right femur corresponded to the area of bone marrow invasion of the tumor and bone infarction. The mechanism of the uptake of ^{99m}Tc HMDP to the extraosseous lesion was not clear. On ^{201}Tl chloride scintigraphy, the increased uptake of the periphery of the mass seemed to reflect the aggressiveness of invasion and the cellularity.

Key words: diaphyseal medullary stenosis, malignant fibrous histiocytoma, ^{99m}Tc HMDP, ^{201}Tl chloride

INTRODUCTION

DIAPHYSEAL MEDULLARY STENOSIS (DMS), first described by Arnold in 1973 as autosomal dominant bone dysplasia,[1] is an extremely rare clinicopathological entity manifested by medullary stenosis along the diaphyseal segments of the long tubular bone with overlying endosteal cortical bone thickening. To date only five families, including that of our case, have been reported.[1–8] The major features of dysplasia are DMS with overlying cortical thickening and a high incidence of malignant transformation to pleomorphic malignant fibrous histiocytoma (MFH) of affected bones, affecting about 40% of patients.[2]

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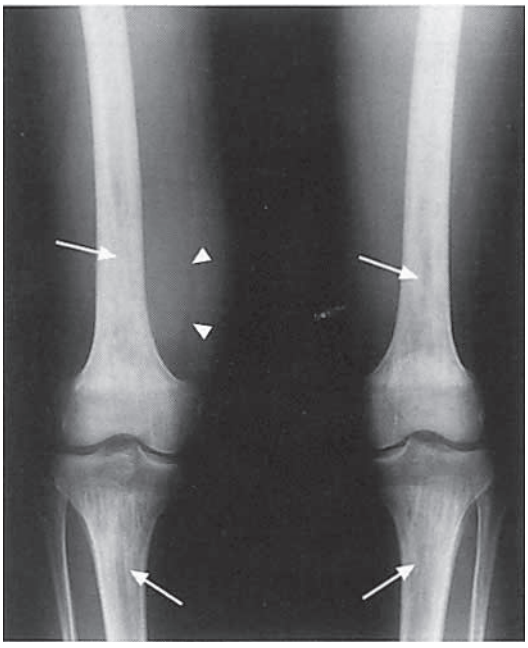
In this report we detail a case of DMS with pleomorphic MFH of the bone that was previously reported by Muroya et al. in 2001 and by Douya et al. in 2002.[7,8] The former mainly described the genetic abnormalities of this patient and the latter the radiographic features in all the members of this family. We provide further information of the same case about the findings of DMS with pleomorphic MFH of the bone, mainly describing ^{99m}Tc hydroxymethylenediphosphonate (HMDP) and thallium-201 (^{201}Tl) chloride scintigraphy findings.

CASE REPORT

A 42-year-old man presented with a 6-month history of progressive swelling and dull pain in the right lower posterior thigh. Laboratory data were normal. Physical examination revealed an elastic, firm mass measuring approximately 10 mm × 10 mm located in the right posterior thigh above the knee. The mass was slightly tender and tightly fixed to the femur.

Radiograph demonstrated a soft tissue mass posterior to the femoral diaphysis and the posterior cortical



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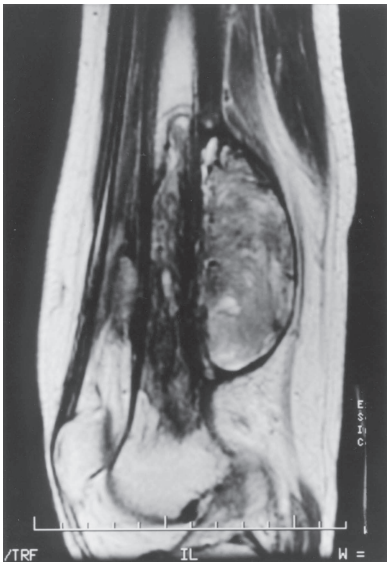

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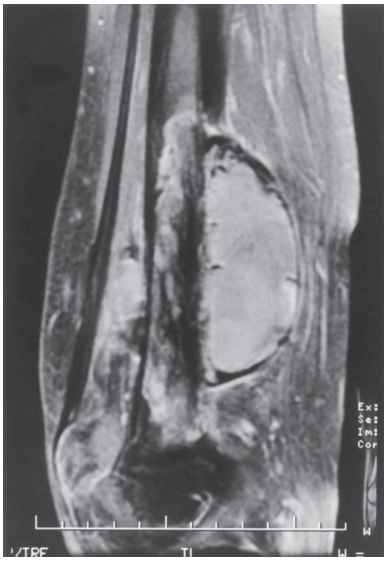

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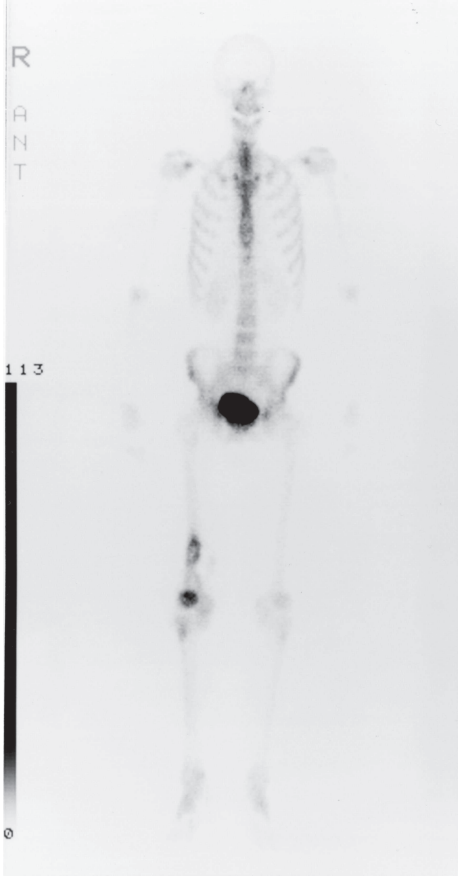
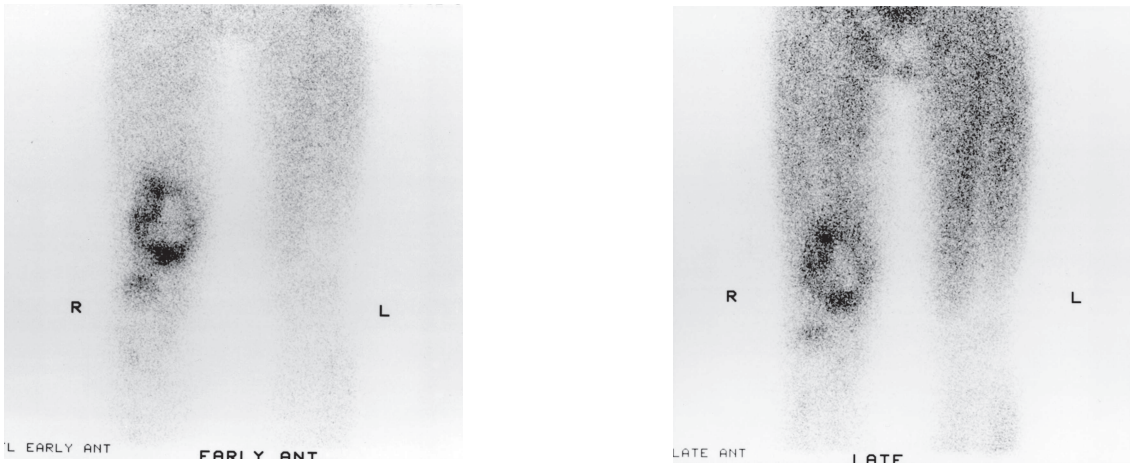


D

destruction of the right femur measuring 11 cm at the largest diameter, suggestive of direct invasion by the soft tissue mass. A front view of the bilateral femur and tibia showed longitudinal linear striations in the distal end of the femur and the proximal end of the tibia (Fig. 1A). A systemic skeletal survey showed the linear striations and diaphyseal stenosis of the long tubular bones (the femur, tibia, and humerus) and showed bilateral acetabular bone sclerosis.

Computed tomographic (CT) scan of the right thigh showed a large soft tissue mass with cortical destruction in the posterior aspect. Precontrast CT revealed neither calcification nor ossification. Contrast-enhanced CT scan demonstrated peripheral enhancement of the mass. Magnetic resonance (MR) images of the right femur showed a large mass extending from the bone marrow to the adjacent soft tissue with cortical destruction. The mass showed homogeneously low signal intensity on T1-weighted MR



E F

Fig. 1 A: Radiograph demonstrates longitudinal linear striations in the distal end of the femur and the proximal end of the tibia bilaterally (*arrows*). Also noted is tumor shadow in the distal end of right femur (*arrowheads*). B: Sagittal T2-weighted MR image shows a large mass with bone marrow and soft tissue invasion. C: Sagittal gadolinium-enhanced T1-weighted MR image shows heterogeneous enhancement. D: ^{99m}Tc HMDP shows abnormal accumulation in the distal diaphysis of the right femur and the right patella. E: ^{201}Tl chloride scintigraphy demonstrates increased uptake in the distal end of the right thigh in the early phase. F: ^{201}Tl chloride is insufficiently washed out in the late phase.

images and heterogeneously from iso to high signal intensity on T2-weighted MR images (Fig. 1B). On gadolinium-enhanced T1-weighted MR images the mass showed heterogeneous enhancement (Fig. 1C). The mass did not invade the right patella on MR images.

Whole body bone scintigraphy was performed four hours after an intravenous injection of 740 MBq ^{99m}Tc HMDP. ^{99m}Tc HMDP scintigraphy showed focal increased uptake in the distal diaphysis of the right femur and in the right patella and showed focal defect of ^{99m}Tc HMDP in the distal shaft of the right femur (Fig. 1D). Slight extraosseous uptake corresponding to the periphery of the soft tissue mass was seen. There was not abnormal uptake of ^{99m}Tc HMDP in the other bones including bilateral femur, tibia, and humerus which showed the linear striations.

^{201}Tl chloride scintigraphy was performed after an intravenous injection of 74 MBq. ^{201}Tl chloride scintigraphy showed increased uptake in the distal end of the right thigh in the early phase, consistent with the periphery of the mass (Fig. 1E) and ^{201}Tl chloride activity was insufficiently washed out in the late phase (Fig. 1F); these findings indicated the possibility of malignant tumor. The area showing increased activity of ^{201}Tl chloride and the enhanced area on contrast-enhanced CT and on gadolinium-enhanced T1-weighted MR images seemed to correspond. The right patella also had slightly increased activity of ^{201}Tl chloride both in early phase and in late phase.

The patient underwent open biopsy. Histologic examination showed proliferation of histiocytic cells with distinct cell borders, ample cytoplasm and pleomorphic nuclei frequently intermingled with large bizarre giant cells, together with increased atypical mitotic figures and tumor necrosis. The histological diagnosis of pleomorphic MFH was made.

Although the patient received preoperative chemotherapy, it was not effective. Therefore the patient underwent above-the-knee amputation after completion of the chemotherapy. Grossly, the tumor aggressively invaded the bone marrow and the surrounding muscles and partially had small necrotic or hemorrhagic areas without massive central necrosis. The cellularity and mitotic figures were dominant in the peripheral area of the tumor. The amputated distal femur and proximal tibia showed fragments of necrotic lamellar bone characterized by empty lacunae and fat necrosis with dystrophic calcification, which were consistent with those of bone infarction. At the end of proximal and distal ends of tumor, the tumor raised the layers of periosteum of the femur, indicating that the tumor arose from the bone. In the right patella, histologically there was no invasion or metastasis of the tumor and no degenerative change. The patients died of multiple pulmonary metastases one year after the operation.

DISCUSSION

DMS with pleomorphic MFH of the bone is rare bone dysplasia and cancer syndrome characterized by multiple longitudinal linear striations in the metaphysis and cortical thickening in the diaphysis of the long tubular bones

with a strong predisposition to sarcomatous transformation.[3,4] The first familial case was described to have fibrosarcoma of the bone by Arnold and the colleagues.[1] To date, five familial cases have been reported to have sarcomatous transformation of the proximal tibia, distal femur, and leg. We present scintigraphic findings of DMS with pleomorphic MFH of the bone. In five families, twelve cases were associated with sarcomatous transformation which included fibrosarcoma (n = 5), MFH (n = 3), bone sarcoma or tumor not otherwise specified (n = 4).

DMS has a high incidence of malignant transformation to MFH, affecting about 40% of patients between the second and fifth decade.[2,4] Although the etiology of DMS is not unknown well, it has been hypothesized that defective osteoclast resorption (that is, failure to remove the inner layers of the periosteal derived bone) results in cortical thickening of long tubular bones and abnormal osteoblastic function results in easy fracture as well as deformity.[2] Martignetti and colleagues have identified loss of heterozygosity (LOH) encompassing the critical region in tumor tissue. These results suggest the gene for DMS with pleomorphic MFH of the bone is at tumor suppressor gene on 9p21-22.[5,6] The haploinsufficiency of the gene results in DMS caused by multiple osteonecrosis. The nullisomy of the genes is causative of pleomorphic MFH of the bone.

Radiographic manifestations of DMS were multiple linear striations caused by medullary osteonecrosis and cortical thickening reactive to cortical osteonecrosis. Opened growth plate of the iliac crest with acetabular osteonecrosis was seen in adult patients with diaphyseal medullary stenosis.[4] Radiographic findings of DMS are very similar to those of osteopathia striata which often shows multiple linear striations of tubular and flat bones.[2] Malignant transformation of osteopathia striata has not been reported.[2] On ^{99m}Tc HMDP scintigraphy, both DMS and osteopathia striata can demonstrate abnormal increased uptake in the affected bones.[9] Kenan et al. reported that the young patient with DMS showed multifocal increased uptake of ^{99m}Tc HMDP in the affected long tubular bones, indicating the increased bone turnover state.[4] In contrast, in the current case, there was no abnormal uptake of ^{99m}Tc HMDP in the affected bones showing linear striations, indicating the inactive bone turnover state. Focal increased uptake area of the right femur on ^{99m}Tc HMDP scintigraphy corresponded to the area of bone marrow invasion of the tumor and bone infarction. The mechanism of the slight peripheral uptake of ^{99m}Tc HMDP to the extraosseous lesion is not clear although it is well known that the uptake of ^{99m}Tc HMDP by malignant tumors can be seen to some content, for example in lung cancer, regardless of the degree of necrosis and liver metastasis of colon cancer regardless of the presence of calcification.

The major factor determining the early phase ^{201}Tl chloride uptake is believed to be the regional blood flow. On the other hand, delayed phase uptake is thought to reflect the number of viable cells and cellular activity.[10] In this case, the increased uptake of the periphery of the mass shown on ^{201}Tl chloride scintigraphy seemed to reflect the aggressiveness of invasion and the cellularity.

^{99m}Tc HMDP and ^{201}Tl chloride scintigraphy could delineate the lesion in the current patient with DMS with MFH. The high incidence of sarcoma in this dysplasia is an important reason that it be recognized early so that monitoring of the dysplasia and surveillance of the other family members can be accomplished.

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