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Original Article

Imaging features of primary leiomyosarcoma of bone

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Abstract: Primary leiomyosarcoma of bone is a rare malignant bone tumor. The aim of this retrospective study was to characterize imaging features of the tumor. Imaging findings of ten patients (six men and four women; age range, 16-64 years) with histologically proven primary leiomyosarcoma of bone were retrospectively evaluated. None of the patients had preexisting disease or disease elsewhere at the time of diagnosis. Bone destruction including permeation (n = 8) and moth-eaten pattern (n = 2) can be found. Cortical change showed erosion (without expansion = 5, with expansion = 3), and penetration (n = 2). Aggressive periosteal response was present (Codman triangle = 2, speculated = 1). In long bones (distal femur = 5, proximal tibia = 1, distal radius = 1), all located in metaphysis extending to epiphysis in longitudinal plane. In sacrum (n = 3), all involved subchondral bone adjacent to sacroiliac joint. In seven cases with soft tissue mass, six were smaller than the greatest diameter of bone destruction. On T2-weighted images (n = 8), slightly hyper-intensity with remarkable hyper-intense area similar to water was demonstrated in seven cases. Extensive soft tissue edema was visible (6 out of 8 with MRI). To conclude, aggressive pattern, tending to elongated growing in long bones, not very hyper-intensity on T2-weighted imaging, and extensive soft tissue edema are characteristic imaging patterns of primary leiomyosarcoma of bone.

Keywords: Radiographs, X-ray computed tomography, magnetic resonance imaging, leiomyosarcoma, bone neoplasms

Introduction

Primary leiomyosarcoma (PLMS) of bone is an extremely rare malignant bone neoplasm showing distinct smooth-muscle differentiation [1]. Since first case was reported in 1965 [2], PLMS of bone have been described mostly in the form of case reports and focusing on histological diagnosis. It has been proved that surgical treatment with wide margins was the only effective treatment for PLMS of bone, whereas adjuvant chemotherapy in the present setting did not improve the overall survival [3]. Therefore, early and accurate diagnosis has a major impact on future therapeutic strategy. Although advances in immunohistochemistry, it is still difficult to make an accurate diagnosis by biopsy due to the limitations of the histological diagnosis of minute samples from highly heterogeneous primary malignant bone tumors [3]. Here, we present a series of cases involving the knee, as well as uncommon locations involving the forearm and sacrum.

Materials and methods

Study subjects

This retrospective study was approved by the institutional review board of our hospital, and written consent was obtained from all patients. The pathology database was searched for cases between January 2004 and December 2015. Ten patients, without a previous history of malignancy (six men and four women, 16-64 years old), underwent surgical excision with pathologically proven diagnosis of PLMS of the bone. All patients presented with progressive pain in the region of their affected bones.

Imaging techniques

Radiographs were performed using a digital radiography system (Philips Digital Diagnost, Philips Hamburg, Germany). CT scans were performed using a 16 Slice (Lightspeed, GE Healthcare, Milwaukee, Wisconsin) or 128 slice CT scanner (Discovery CT750 HD, GE Healthcare).

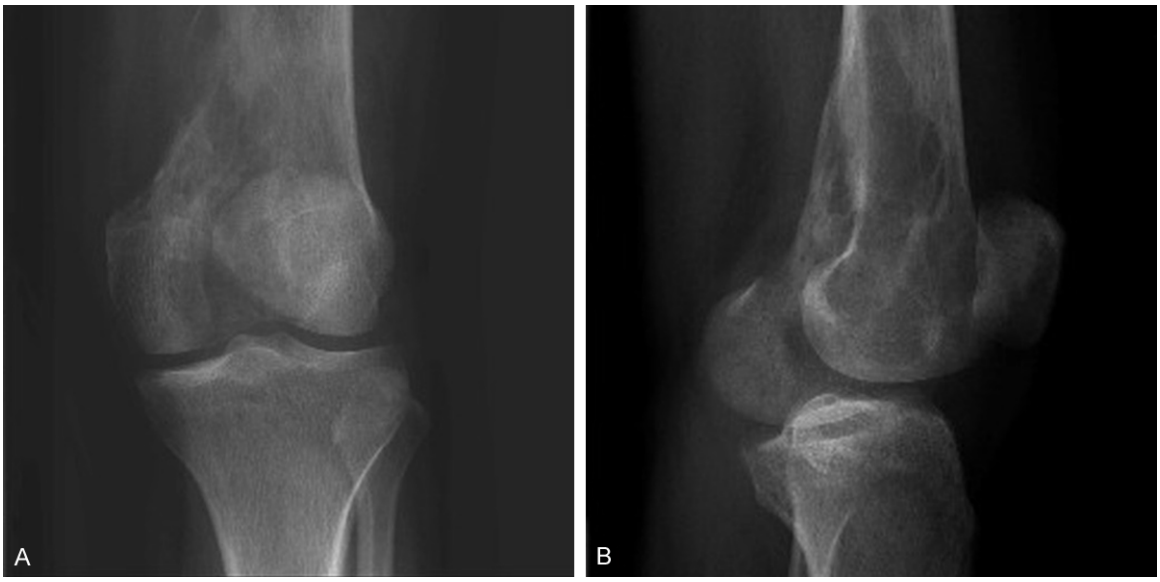

Figure 1. Primary leiomyosarcoma of the femur. A. The anteroposterior view radiograph shows a purely lytic lesion in the distal femur with extension to subchondral bone. The margin is indistinct and without sclerosis. Periosteal reaction was subtle. B. The lateral radiograph shows posterior cortical disruption of medial femoral condyle.

CT images were obtained with a 1.25-mm slice thickness, and reformatted with both bone and soft tissue algorithms. MR scans were performed using either a 1.5-T (Signa Advantage Horizon; GE Medical Systems) or 3.0-T MR scanner (SignaHDx; GE Medical Systems). Conventional MR protocols included T1-weighted spin-echo (TR/TE 560/12 ms) and T2-weighted fast spin-echo (TR/TE 3000/105 ms) with or without fat saturation. The contrast-enhanced MR protocol used a T1-weighted spin-echo sequence with fat saturation, after intravenous injection of 0.1 mmol/kg of gadolinium dimeglumine. Images were obtained with a 3-mm slice thickness and 1-mm interslice gap.

Imaging analysis

All available images were qualitatively reviewed by two experienced musculoskeletal radiologists in consensus. The following imaging features were recorded: Location in the skeleton; Distribution in a single bone (transverse and longitudinal plane in long bone); Pattern of bone destruction according to Lodwick classification system [4]; Cortical changes (erosion, penetration, and expansion); Periosteal response; Bone destruction extension compared with the size of soft tissue mass; CT density (hypo-dense, iso-dense, or hyper-dense compared with adjacent muscle); Mineralization in tumor; Signal intensity on T1- and T2-weighted images compared with skeletal muscle; homogeneity (homogeneous signal pattern consisted of predominantly uniform signal intensity throughout the lesion; a heterogeneous signal pattern consisted of a mixture of signal intensities); Enhancement degree and pattern on contrast-enhanced MR. Edema (intraosseous and soft tissue). Intraosseous and soft tissue edema was defined according to criteria derived from previous studies [5, 6]. Intraosseous edema was defined as a poorly-delineated area of homogeneous signal intensity adjacent to the tumor with intermediate signal intensity on T1-weighted images and high signal intensity in bone marrow on T2-weighted images with fat suppression. Soft tissue edema was defined as an area of poorly-defined but homogeneous high signal intensity, with a feather-like appearance in the soft tissues on T2-weighted images with fat suppression. When present, intraosseous and soft tissue edema were classified as minor (greatest diameter smaller than bone lesion), moderate (greatest diameter approximately similar to bone lesion), or extensive (greatest diameter larger than bone lesion).

Results

Radiographs were performed in eight of all the patients, CT scans in six patients, conventional MR scans in eight patients, and a contrast-

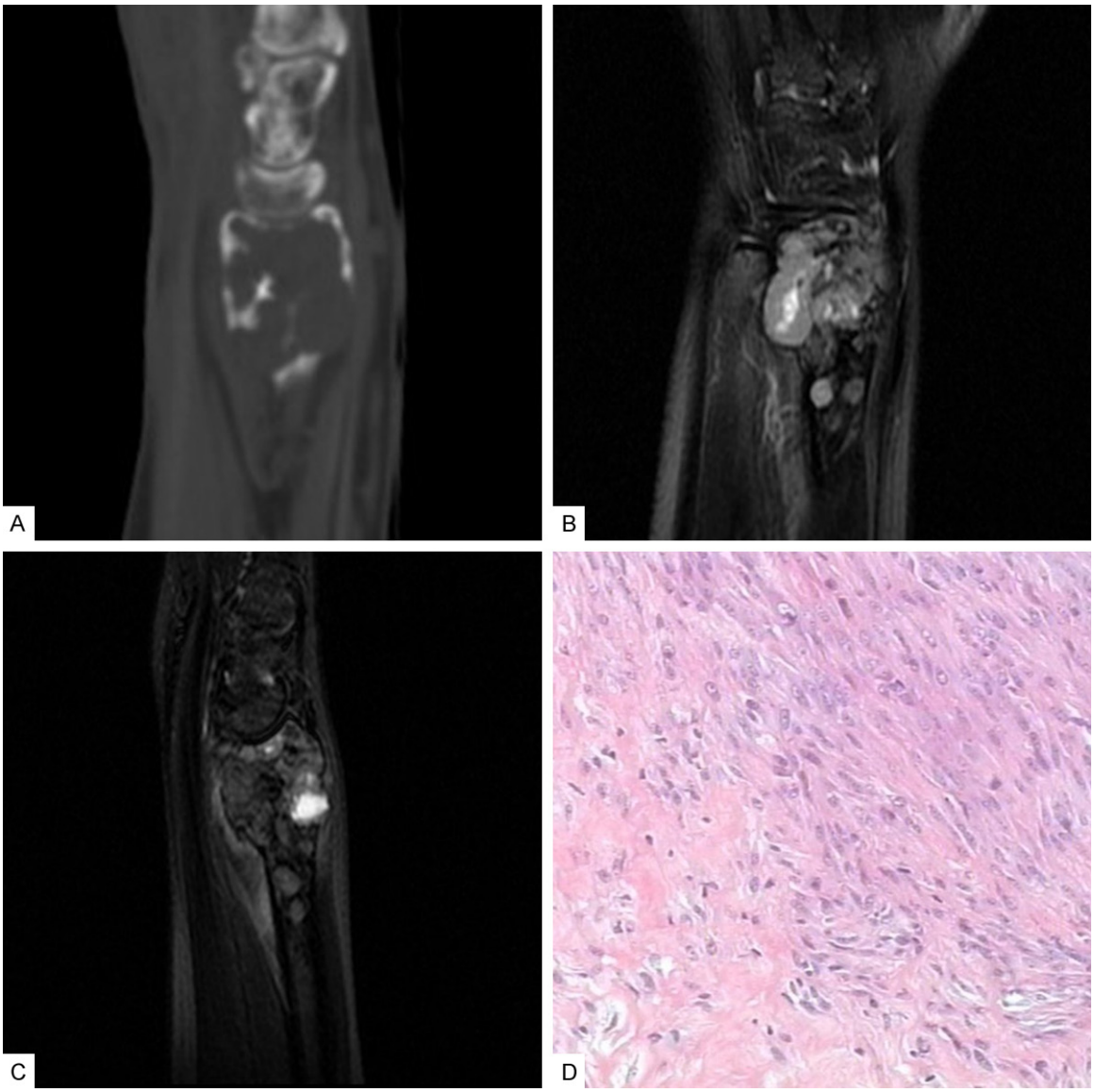

Figure 2. Primary leiomyosarcoma of the radius. A. CT scan with sagittal multi-planar reformation shows a lytic lesion in the distal radius with extension to the subchondral bone. Multiple cortical disruptions can be found on the anterior and posterior. B. The fat-suppressed T2-weighted image MR coronal demonstrates the tumor to be a little hyper-intense relative to muscle, with a central irregular area of high signal intensity. Cortical breakthrough and a small soft tissue mass are shown on the medial side of the radius. C. The Fat-suppressed T2-weighted image sagittal demonstrates extensive soft tissue edema surrounding the radius. D. Light-micrograph (HE, ×100) shows a proliferation of spindle cells arranged in interlaced bundles, having elongated nuclei with blunt ends. An area of necrosis is also noted.

enhanced MR scan in one patient. The anatomical locations of LMS of bone included distal femur (n = 5; **Figure 1**), proximal tibia (n = 1), distal radius (n = 1; **Figure 2**), and sacrum (n = 3). In long bones (n = 7), tumors located in eccentric (n = 4), centric (n = 3) in transverse plane of the long bones. All located in metaphysis extending to epiphysis (subchondral bone) in longitudinal plane (**Figures 1** and **2A**). In sacrum, two occupied unilateral sacral wing and one occupied the whole sacrum. All involved subchondral bone adjacent to sacroiliac joint. Permeation bone destruction was found in eight patients and moth-eaten bone destruction was showed in two patients. Soft tissue mass was demonstrated in seven patients, six of which were smaller than the greatest diameter of bone destruction. Five

patients revealed with cortical erosion, two with penetration, three with erosion and expansion. Periosteal response was present in three patients, Codman triangle (n = 2) and speculated (n = 1) respectively. On CT scans, all six cases demonstrated homogeneous hypo-density. Calcification was demonstrated in two cases, and thick bone trabecular or sequestrum was found in three cases (**Figure 2A**). On MR, five cases showed homogeneous iso-intensity and three showed heterogeneous iso- to hypo-intensity on T1-weighted imaging. Seven cases demonstrated slightly hyper-intensity with remarkable hyper-intense area similar to water on T2-weighted imaging (**Figure 2B** and **2C**), and one case showed heterogeneous hyper-intensity like water. Marked enhancement with low-intensity area at the center was revealed in the only one case with post-contrast MRI. Minor intraosseous edema was visible in four of the eight cases with MRI scans, while extensive soft tissue edema was found in six cases (**Figure 2B** and **2C**). Pathology of all cases demonstrated spindle cells arranged in intersecting fascicles, resembling leiomyosarcoma from other locations (**Figure 2D**).

Discussion

PLMS of bone is extremely rare, the prevalence of it is not known, and it is not addressed in the most recent WHO edition of Bone and Soft Tissue Tumors [1]. It is speculated that the tumor arises from pre-existing smooth muscle cells in the walls of intraosseous blood vessels [7], although an origin from a multi-potential mesenchymal stem cell capable of smooth muscle differentiation cannot be ruled out [7, 8]. The disease has a wide age distribution (9-87 years), with a peak incidence in the fifth decade of life. Males and females were almost equally affected [1]. Bone pain, a palpable mass, and pathologic fracture, are the major symptoms causing patients to seek medical attention [7, 9]. Pathologic fracture may be an associated finding in about 20% of cases [7, 10]. Many studies report that PLMS of bone has an aggressive osteolytic appearance accompanied by a moth-eaten appearance or permeation, lack of a sclerotic margin, endosteal erosion, cortical breakthrough, no or subtle periosteal reaction, and an occasional pathologic fracture [11]. These imaging features are consistent with most of our study. Exceptionally, aggressive periosteal reaction appeared in three of our ten cases. However, the features are nonspecific and can only indicate it is an aggressive tumor.

PLMS of bone occurs mostly in the lower extremity around the knee (distal femur or proximal tibia) [7, 9, 12, 13], followed by the ilium and humerus [10, 13]. The metaphyseal region is the typical site involved in the long bones [7, 14] and is often associated with epiphyseal, juxta-articular, or diaphyseal extension [10, 11]. In a series reported by Gordon et al., all four of their cases were located in the juxta-articular metaphysis [15]. The tumor is primarily intramedullary, and may extend to the soft tissues [10, 16]. Sundaram et al. reported soft-tissue extension in 66% of cases, with the soft tissue masses being small [11]. Imaging feature of the locations and small soft tissue masse may be associated with the elongated growing pattern of PLMS [11]. The current findings are compatible with these features previously reported. All cases in long bones involved epiphysis extending to subchondral bone. We confirm that this kind of growing pattern might be helpful to diagnose this tumor.

The signal intensity on T2-weighted MR images may be helpful in differentiating from other aggressive osteolytic lesions [11]. The signal intensity of the tumor has been described as isointense compared with that of muscle on T1-weighted images, and intermediate to hypointense on spin echo T2-weighted images with respect to normal bone marrow. When compared with skeletal muscle, signal intensity appeared hyper-intense, but less intense than water [15]. The most osteolytic lesions are hyper-intense on T2-weighted images [17]. In our series, signal intensity showed slightly hyper-intense compared with muscle, and revealed hyper-intense area similar to water (tumoral necrosis). The features of hypo-, iso- or slightly hyper-intensity on T2-weighted imaging might correspond to a fibrous or muscle component [10, 11].

Peritumoral edema in PLMS of bone has been previously mentioned [11, 15, 18]. It was thought to be inflammatory edema secondary to tumor infiltration through cortex to soft tissue [18]. Soft tissue edema is more frequently found in malignant tumors but is often not more extensive than in benign tumors [19]. However, extensive soft tissue edema was found in six of

eight cases with MRI. Although MR signs of intraosseous edema do not seem to be safe indicators of the biological potential, obviously extensive edema of this tumor may be some useful for differential diagnosis.

Mineralization in PLMS of bone has not been widely reported and been thought to be rare. In the present study, calcification and thick bone trabecular or sequestrum demonstrated in five of six cases with CT scans. Mineralization in PLMS of bone was concluded to be caused by either non-neoplastic ossification or dystrophic mineralization in the tumor [20]. Whatever, it can be recognized that mineralization can be present in PLMS of bone. Description of enhancing pattern of PLMS of bone is limited. Most cases showed peripheral enhancement [10, 11, 21] as our cases. Central area did not enhance due to necrosis. Rarely, spoke-wheel-like enhancement may occur due to central tumor necrosis and/or septa [10].

The imaging findings mentioned above are shared with other aggressive tumors, and have many differential diagnosis including fibrosarcoma of bone, solitary plasmacytoma of bone, primary lymphoma of bone, giant cell tumor of bone, undifferentiated high-grade pleomorphic sarcoma of bone, osteomyelitis, and metastatic tumor [9, 15, 22]. Solitary plasmacytoma of bone occurs more commonly in axial bone or the proximal femur, where red bone marrow is abundant. Specific features of primary lymphoma of bone are the relatively minimal cortical destruction in the presence of extensive soft tissue and marrow involvement [23]. Giant cell tumor of bone shows no or minor soft tissue edema (50%) [19], and does not have considerable length as PLMS of bone. Undifferentiated high-grade PLMS of bone does not often extend to the subchondral bone, with the epicenter remaining in the metadiaphysis [24]. The sequestrum and extensive soft tissue edema were reminiscent of osteomyelitis. It is worth noting that CRP has been found to be a relatively sensitive indicator in the distinction of osteomyelitis from primary bone tumors, as elevated CRP levels are seen in 60% of patients with osteomyelitis, but very rarely in other bone tumors [25]. Metastatic lesion prefers spine and proximal femur, whereas PLMS of bone tends to occur around knee [26]. Besides, metastatic lesion tends to be smaller at time of diagnosis than PLMS of bone [11, 27]. After reviewing all the features, it is also apparent that it is very difficult to differentiate PLMS of bone from fibrosarcoma of bone.

To summarize, we present an imaging series of PLMS of bone, highlighting features of the tumor, including aggressive pattern, tending to elongated growing in long bones, not very hyper-intensity on T2-weighted imaging, and extensive soft tissue edema. It could be helpful to make diagnosis of this tumor before surgery according to these features.

Disclosure of conflict of interest

None.

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