MRI Characteristics of Parosteal Lipomas Associated with the HMGA2-LPP Fusion Gene

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Abstract. Background: The magnetic resonance (MR) characteristics of parosteal lipomas with the HMGA2-LPP fusion transcripts are described. Patients and Methods: The expression of HMGA2-LPP fusion transcripts was determined using the reverse transcription-polymerase chain reaction method. Results: MR images of two cases with the fusion transcripts, a 56-year-old man and a 50-year-old woman, revealed heterogeneous high signal intensities on T1- and T2-weighted images, showing heterogeneous curvilinear enhancement on fat-suppressed T1-weighted images after Gd-DTPA injection, which resembled those of well-differentiated liposarcomas. Conclusion: Since the HMGA2-LPP fusion transcripts are exclusively detectable in benign mesenchymal tumors, testing HMGA2-LPP expression may be useful for differential diagnosis in cases of radiologically-suspected well-differentiated liposarcomas.

Parosteal lipomas are rare, benign fatty neoplasms composed of mature adipose tissue. They are deep-seated and firmly adherent to the periosteum of the underlying bone (1). A specific t(3;12)(q27-28;q14-15) chromosomal translocation, producing the high mobility group A2 (HMGA2)-LIM-containing lipoma-preferred partner (LPP) fusion gene, was detectable in some cases of lipomas, parosteal lipomas, pulmonary chondroid hamartomas and a case of a soft tissue chondroma (2-6). The HMGA2-LPP fusion gene encodes a protein that consists of the N-terminal DNA-binding domains of transcription factor HMGA2 (7) and the C-terminal LIM domains of trafficking factor LPP (8). Although the HMGA2-LPP fusion protein seems to be responsible for tumorigenesis (9), the radiological characteristics of the soft tissue tumors associated with HMGA2-LPP are not well documented. Recently, we reported a case of an unusual lipoma associated with the HMGA2-LPP fusion gene (10). This tumor in the patellar tendon showed curvilinear signal enhancement along the septa on fat-suppressed T1-weighted magnetic resonance (MR) images after gadolinium diethylenetriaminepentaacetic acid (Gd-DTPA) injection, which is one of the MR characteristics of a well-differentiated liposarcoma (11). Here, two additional cases of parosteal lipoma associated with the HMGA2-LPP fusion transcript are reported, with an emphasis on the MR findings.

Patients and Methods

Reverse transcription-polymerase chain reaction (RT-PCR) – detection of the HMGA2-LPP fusion transcripts. Parosteal lipomas were obtained at the time of surgery with written informed consent and were stored at ~80°C. Total RNA was extracted with the RNeasy Lipid Tissue Mini Kit (QIAGEN, Hilden, Germany). cDNA was synthesized with random primers (9 mer, TaKaRa, Tokyo, Japan) and was subjected to PCR amplification of the HMGA2-LPP fusion transcripts. A 680-bp fragment of the cDNA encoding the HMGA2-LPP fusion protein was amplified using the forward primer (HMGA2 exon 1) 5’-gatgagcgcacgcggtgagg-3’ and the reverse primer (LPP exon 11) 5’-ctaaaggtcagtgctcgccttg-3’. A 124-bp fragment of the cDNA encoding the glyceraldehyde-3-phosphate dehydrogenase (GAPDH) gene was amplified using the forward primer 5’-cagcgacacccactcctccacctt-3’ and the reverse primer 5’-catgaggtccaccaccctgttgct-3’ as a control.

For the PCR, 1 μl of single-stranded cDNA was used as a template. The 20-μl reaction contained 18 μl PCR SuperMix (Invitrogen, Carlsbad, CA, USA) and 10 pmol of each primer. Denaturation for 2 min at 95°C was followed by 35 cycles of 30 sec at 95°C, 30 sec at 60°C and 30 sec at 72°C. The PCR products were separated by 1% agarose gel electrophoresis and were visualized by ethidium bromide. The identity of the PCR products was confirmed by direct DNA sequencing.

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Results

Case reports

a) Case 1. A 56-year-old man noticed a painless elastic mass on the anterior aspect of the right thigh, and visited our clinic. Physical examination revealed an immovable firm mass at the right proximal thigh, measuring 8.5 cm in diameter. The mass did not show tenderness, redness or local warmth. Plain X-ray photographs and computed tomography images demonstrated a soft tissue shadow with an irregularly osseous protuberance (Figure 1). T1-weighted and T2-weighted MR images revealed a septable soft tissue mass with heterogeneous high signal intensity, measuring 6x7x10 cm (Figure 2), containing an irregular osseous protuberance which was continuous to the cortex of the femur. Fat-suppressed T1-weighted MR images showed curvilinear signal enhancement along the septa after Gd-DTPA injection (Figure 2). A $^{99m}$Tc HMDP bone scan showed signal accumulation to the proximal femur (Figure 3). The patient underwent marginal resection of the tumor including the bony protuberance of the femur, which proved to be well encapsulated. Macroscopically, the tumor was yellowish-white with a smooth surface and was lobulated with septa. Histologically, this tumor consisted of mature adipocytes, surrounding the osseous protuberance. Histopathological examination revealed the diagnosis of a parosteal lipoma. Total RNA was extracted from the tumor and RT-PCR analysis detected the HMGA2-LPP fusion gene transcript. The postoperative course was uneventful and the patient has no evidence of recurrence two years after the surgery.

b) Case 2. A 50-year-old woman noticed a painless soft mass at the medial side of the right ankle, and visited our clinic because the mass was enlarging. Physical examination revealed an immovable elastic soft mass at the medial side of
the right ankle, measuring over 10 cm longitudinally. The mass did not show tenderness, redness or local warmth. Plain X-ray photographs demonstrated a soft tissue shadow without mineralization (Figure 4). T1-weighted and T2-weighted MR images revealed a septable soft tissue mass with heterogeneous high signal intensity, measuring 15x3x2 cm (Figure 5), which was continuous to the tibia. Fat-suppressed T1-weighted MR images showed heterogeneous curvilinear signal enhancement along the septa after Gd-DTPA injection (Figure 5). Thallium scintigraphy did not show signal accumulation. The patient subsequently underwent marginal resection of the tumor. Macroscopically, the tumor was yellowish-white with smooth surface and was lobulated with septa. Histopathological examination revealed the diagnosis of a parosteal lipoma and the HMGA2-LPP fusion transcripts were detectable. The postoperative course was uneventful and the patient has no evidence of recurrence one year after the surgery.

Discussion

On fat-suppressed T1-weighted MR images, the two cases of parosteal lipoma expressing the HMGA2-LPP fusion transcripts showed heterogeneous curvilinear signal enhancement along the septa after Gd-DTPA injection. This MR finding is similar to that of well-differentiated liposarcomas (11). Since HMGA2-LPP fusion transcripts are exclusively found in benign mesenchymal tumors, testing HMGA2-LPP expression may be useful for differential diagnosis in cases of radiologically-suspected liposarcomas.

We have recently shown that the HMGA2-LPP fusion gene may promote chondrogenesis by up-regulating cartilage-specific collagen gene expression through the N-terminal DNA-binding domains of HMGA2 (12). The heterogeneous high signal intensity documented by T1- and T2-weighted MR images may reflect possible chondrogenesis arising from the resident adipogenic cells or multipotential progenitor cells. We also have reported a case with an unusual lipoma in the patellar tendon, which contained a chondro-osseous component, showing typical endochondral bone formation (10). The heterogeneous curvilinear enhancement along the septa, demonstrated by fat-suppressed T1-weighted MR images after Gd-DTPA
Figure 4. Case 2. Radiographs of the right ankle, anteroposterior view (left) and lateral view (right). A juxtacortical radiolucent mass without mineralization located at the posterior aspect of the distal tibia.

Figure 5. Case 2. MR images, sagittal view. The T2-weighted (left) image revealed a septable soft tissue mass with heterogeneous high signal intensities at the medial aspect of the right ankle. After Gd-DTPA injection, the fat-suppressed T1-weighted image showed heterogeneous curvilinear signal enhancement along the capsule and the septa (center and right).
injection, was detectable in both cases presented here. The MR finding may be related to the neovascularization associated with the potential endochondral bone formation. Well-differentiated liposarcomas, which show similar Gd-DTPA enhancement on MR images, have not been linked to endochondral bone formation and, therefore, the mechanisms behind the radiological similarity are important for understanding the subsets of adipogenic tumors.

The radiological characteristics of parosteal lipomas have been well documented, including the signal intensity of the adipogenic component being identical to that of subcutaneous fat on T1-weighted MR images and lower on T2-weighted images, as well as the occasional presence of low-signal-intensity septa (13, 14). However, to the best of our knowledge, curvilinear Gd-DTPA enhancement along the septa on fat-suppressed T1-weighted images has not been associated with parosteal lipomas. In conclusion, together with our previous report (10), the two cases presented here establish a subset of adipogenic tumors hallmarked by the **HMGA2-LPP** fusion gene, showing the characteristic MR features.

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