Clinical Research Paper

Correlation of MRI features to histopathologic grade of soft tissue sarcoma

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Background and Objective: Peripheral tumor growth pattern plays an important role in the local recurrence and metastases of soft tissue sarcoma. This study was to determine the peripheral growth pattern of soft tissue sarcoma by magnetic resonance imaging (MRI), explore its correlation to histological grade, and assess biological features of soft tissue sarcoma before operation.

Methods: MRI was performed in 59 patients with soft tissue sarcoma. T1- and T2-weighted images were obtained using a spin-echo pulse sequence. Tumor margin, peritumoral high signal intensity sign and peritumoral low signal intensity capsule-like sign were evaluated on MR images. All patients were confirmed and graded by histopathology. Results: The histological grade of soft tissue sarcoma was closely related to the margin appearance (p < 0.05): the margin was well-defined in 60.0% grade I tumors, and poorly-defined in 60.0% grade III tumors. No significant difference in the occurrence rates of peritumoral high signal intensity sign and peritumoral low signal intensity capsule-like sign was found between grade II and grade III tumors (p > 0.05). The occurrence rate of peritumoral high signal intensity sign was significant lower and that of peritumoral low signal intensity capsule-like sign was significant higher in grade I tumors than in grade II-III tumors (10.0 vs. 74.4%, 80.0 vs. 15.4%, p < 0.05). Conclusion: The peripheral tumor growth pattern is related with histological grade, and may reflect the biological behaviors of soft tissue sarcoma.

Soft tissue sarcoma is a rare malignant tumor, consisting about 1% of all malignant tumors, and its pathologic types are diverse and complex. The most common prognosis factors of soft tissue sarcoma in the extremities include histopathologic grade, tumor size, location and depth, extra-compartmental extension and presence of metastasis. Among these factors, histopathological grade is one of the most important factors. Peripheral tumor growth pattern is the essential factor which affects the local recurrence and metastasis of soft tissue sarcoma, but its correlation to histologic grade of tumors has not been reported in detail. In this study, we used magnetic resonance imaging (MRI) to determine the correlation of peripheral growth pattern of soft tissue sarcoma to its histologic grade, and assess its biological behavior before operation.

Materials and Methods

General clinical data. Clinical data of 59 patients with pathologically confirmed soft tissue sarcoma in the extremities were selected. Of the 59 patients, 39 were men and 20 were women, aged from seven months to 78 years with a median of 38 years; 12 had liposarcoma, nine had synovial sarcoma, nine had malignant fibrous histiocytoma, seven had leiomyosarcoma, seven had fibrosarcoma, five had rhabdomyosarcoma, four had malignant schwannoma, two had neuroblastoma, two had neurofibrosarcoma, and two had acinar sarcoma.

MRI examination. Thirty-five patients received MRI examination using Gyroscan 0.5T-superconductive magnetic resonance imager (Philips Medical Systems), with a scanning matrix of 256 × 256, a section thickness of 4.0–15.0 mm in viewing of tumor size, and a intersection gap of 0.4-1.5 mm. Spin-echo (SE) sequence was adopted, with repetition time (TR) of 413-695 ms, echo time (TE) of 15–30 ms, and excitation of 2–4 times for T1-weighted imaging (T1WI), and TR of 1 800-3 877 ms, TE of 80–150 ms, and excitation of 0.4–1.5 mm. Spin-echo (SE) sequence was adopted, with repetition time (TR) of 413-695 ms, echo time (TE) of 15–30 ms, and excitation of 2–4 times for T2WI. Routine axial plane with coronal or sagittal plane were obtained.

MRI analysis. The MRI findings of soft tissue sarcoma were analyzed regarding: 1) tumor margin which was classified as well...
defined margin (>90% of tumor margin was clear), poorly defined margin (>75% of tumor margin was unclear) and mixed margin (an interventious status); 2) the presence of peritumoral high signal intensity sign on T2WI which appeared as enhanced signals at peritumoral areas, unclear margin, and no mass effect or soft tissue deformation; and 3) the presence of peritumoral low signal intensity capsule-like sign.

Pathologic grading of soft tissue sarcomas. Tumors were graded I–III according to the French Federation of Cancer Centre grading system. This tumor grading system is mainly based on tumor differentiation, nuclear mitosis and tumor necrosis.

Statistical analysis. The data were analyzed by R x C Crosstabs Chi-square test using SPSS13.0 software, and a p value of less than 0.05 was considered significant.

Results

The correlation of MRI appearances to pathologic grade of soft tissue sarcoma in the 59 patients is referred in Table 1. The pathologic grade of soft tissue sarcomas was related with the definition of their margins ($\chi^2 = 21.38$, $p < 0.05$). The relevance ($r_p$) between the pathologic grade of soft tissue sarcomas and tumor margins was 0.516, indicating relevance between them: the higher the tumor grade, the higher the proportion of poorly defined tumor margin. Twelve (60.0%) of the 20 grade I tumors had well defined margins, while 12 (60.0%) of the 20 grade III tumors had poorly defined margins (Figs. 1–3).

The difference in the occurrence rates of peritumoral low signal intensity capsule-like sign between grade II and grade III tumors was not significant ($p > 0.05$), while this rate was significantly higher in grade I tumors than in grade II–III tumors (80.0% vs. 15.4%, $p < 0.05$). Sixteen grade I tumors had peritumoral low signal intensity capsule-like sign (Fig. 1).

Discussion

The growth of soft tissue sarcomas presents as an acentric, spherical enlargement, which mainly pushes its surrounding tissues, rather than invades. Under the stimulation of tumor growth, fibroblast reactive hyperplasia may be seen in its surrounding tissues, forming layers of fibrous capsules (true capsule). With gradual tumor enlargement, its surrounding normal tissues are oppressed, forming a relatively compact compression zone, and the oppressed cells become atrophied, forming a layer of fibrous capsule (pseudo-capsule). A relatively thick capsule or pseudo-capsule may present peritumoral capsule-like low signal intensity band on MRI, which is prominent on T2WI.3-5 In our study, this phenomenon was noted in 22 (37.3%) of the 59 sarcomas, and it is associated with the malignancy of tumors ($p < 0.05$). Most of the cases with peritumoral low signal intensity capsule-like sign were grade I tumors, while most of the cases without this sign were grade II–III tumors.

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Table 1  The correlation of MRI features to pathologic grade of soft tissue sarcoma

<table>
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<tr>
<th>Pathologic grade</th>
<th>Cases</th>
<th>Well-defined</th>
<th>Mixed</th>
<th>Poorly defined</th>
<th>Peritumoral high signal intensity sign</th>
<th>Peritumoral low signal intensity capsule-like sign</th>
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Figure 1. Grade I myxofibrosarcoma in the left thigh. (A) Fibrosarcoma cells are sparsely arranged, cell atypia is not obvious and few nuclear mitosis are noted (HE ×200). (B) On T2-weighted axial MR image, tumor margin is well defined with peritumoral low signal intensity capsule-like sign (arrow).
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Figure 2. Grade II liposarcoma in the right leg. (A) Many liposarcoma cells are spindle; obvious cell atypia and scanty nuclear mitosis are noted (HE ×200). (B) On T2-weighed axial MR image, tumor margin is poorly defined with peritumoral high signal intensity sign (arrow).

Figure 3. Grade III malignant fibrous histiocytoma in the right thigh. (A) Obvious cell atypia and giant cells are showed in malignant fibrous histiocytoma tissue (HE ×200). (B) On T2-weighed axial MR image, tumor margin is poorly defined with peritumoral high signal intensity sign (arrow).

to the cases with peritumoral low signal intensity capsule-like sign in our study, no postoperative recurrence was developed, suggesting that peripheral growth pattern of soft tissue sarcoma is an important factor which influences postoperative recurrence and metastasis. Our results indicated that the capsule/pseudo-capsule of low-grade malignant soft tissue tumors has a barrier effect against tumor growth infiltration, and the barrier can not be disrupted easily; however, high-grade malignant tumors can totally disrupt the capsule/pseudo-capsule, and infiltrate its surrounding tissues, resulting in diminishment of peritumoral low signal intensity capsule-like sign.

Tissue reaction may be observed between capsules and surrounding normal tissues in high-grade, fast growing sarcomas, that is, mesenchymal cell proliferation, inflammatory cells, tissue edema, vascular neogenesis and other granulomatous changes, known as reactive zone. The surrounding capsule and reactive zone are the body's defensive reaction against the non-specific stimulation of tumors, which cannot suppress tumor growth. Some sarcoma cells can disrupt the capsule, enter the reactive zone, and form small isolated nodules, known as satellite nodules. The peritumoral reactive zone appears as a peritumoral high signal region on T2WI, either weak or strong, may be caused by peritumoral edema or tumor cell infiltration, showing rapid and prominent enhancement in tumor-infiltrated muscles with high initial slope, and slow enhancement in edematous muscles with low initial slope. Moulton et al. had reported peritumoral high signal intensity sign in 30 out of 46 cases of malignant soft tissue tumors. In our study, 52.5% (31/59) of soft tissue sarcomas had this sign, which was associated with tumor malignancy. The presence of peritumoral high signal intensity sign suggests peritumoral tumor cell infiltration, which prompts high tumor malignancy degree (mainly grade II–III tumors).

Even though differentiation of benign and malignant soft tissue tumors cannot just depend on MRI findings, peripheral growth pattern is an important reference for diagnosing a malignant soft tissue tumor, which reflects the invasiveness of a tumor. The marginal appearances of malignant soft tissue tumors on MRI are various, which can be divided into three types: well defined, mixed and poorly defined. Pathologically, oppressed and atrophic peritumoral tissues can be seen in well defined type, which arrange in layers and form a fibrous capsule; the emergence of tumor and surrounding tissues can be seen in poorly defined type, with adjacent muscle fiber edema or peritumoral tumor cell infiltration, without capsule or pseudo-capsule; local edema or peritumoral tumor cell infiltration can be seen in the unclear part of mixed type. In our study, tumor margins of mixed and poorly defined types accounted up to 71.2% (42/59) of all cases; the marginal appearances is associated with tumor malignancy. The lower the clarity of a tumor's margin, the higher the degree of malignancy.

The poor prognosis of most soft tissue sarcoma patients is due to the tendency of peritumoral infiltration and blood metastasis, while local tumor infiltration presents as the absence of peritumoral low signal intensity capsule-like sign, the presence of peritumoral high signal intensity sign, and poorly defined tumor margin on MRI. The morphologic characteristics of tumor margin helps determine tumor extent and design treatment plans, such as determine radiation field or operation extent. Our results indicate that tumor marginal

basis remains controversial: some scholars had claimed that peritumoral high signal intensity sign is caused by peritumoral edema, while most scholars had proven pathologically that peritumoral high signal intensity sign on T2WI, either weak or strong, may be caused by peritumoral edema or tumor cell infiltration, or both, and these two cannot be easily identified according to their signal intensities or morphologic features on images. The differentiation of peritumoral tissue edema or tumor cell infiltration is essential for assessing tumor extent and providing guidance for local surgical or radiotherapy approach. If peritumoral tissue edema is mistaken as tumor infiltration, the tumor might be up-staged by error. Dynamic contrast-enhanced MRI may be useful for differentiating peritumoral edema and tumor cell infiltration, showing rapid and prominent enhancement in tumor-infiltrated muscles with high initial slope, and slow enhancement in edematous muscles with low initial slope. Moulton et al. had reported peritumoral high signal intensity sign in 30 out of 46 cases of malignant soft tissue tumors. In our study, 52.5% (31/59) of soft tissue sarcomas had this sign, which was associated with tumor malignancy. The presence of peritumoral high signal intensity sign suggests peritumoral tumor cell infiltration, which prompts high tumor malignancy degree (mainly grade II–III tumors).

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appearance is associated with tumor malignancy, which helps to understand the biological behavior of tumors before operation. However, as far as we known, the correlation of marginal growth pattern to the prognosis of soft tissue sarcoma has not been reported, which requires further studies.

References