FDG PET/CT and MR Imaging of CD34-Negative Soft-tissue Solitary Fibrous Tumor with NAB2-STAT6 Fusion Gene

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Abstract. Extrapleural solitary fibrous tumor (SFT) is an uncommon mesenchymal neoplasm of intermediate biological potential. Herein, we describe the radiological, histological, immunohistochemical and molecular genetic features of an SFT arising in the left thigh of a 55-year-old woman. Magnetic resonance imaging exhibited a well-defined mass with intermediate signal intensity on T1-weighted sequences and heterogeneous high signal intensity on T2-weighted sequences. Contrast-enhanced T1-weighted sequences showed strong homogeneous enhancement of the mass. A prominent vascular pedicle was visible. Integrated positron-emission tomography (PET)/computed tomographic (CT) scan demonstrated a moderate 18F-fluorodeoxyglucose (FDG) uptake (maximum standardized uptake value, 4.45) in the mass. Following an open biopsy, wide excision of the tumor was performed. Histologically, the tumor was composed of a proliferation of spindle cells in a fibrous stroma with focal hyalinization. Thin-walled branching hemangiopericytoma-like vessels were observed. Immunohistochemically, the tumor cells were diffusely positive for signal transducer and activator of transcription 6 (STAT6) but negative for CD34. The MIB-1 labeling index was less than 5%. Subsequent reverse transcriptase-polymerase chain reaction analysis identified a nerve growth factor inducible-A binding protein 2-STAT6 gene fusion. Our case supports the utility of STAT6 immunohistochemistry as an adjunct in the diagnosis of soft-tissue SFT with loss of CD34 positivity. To the best of our knowledge, this is the first report of the findings of 18F-fluorodeoxyglucose (FDG) positron-emission tomography (PET)/computed tomography (CT) in soft-tissue SFT.

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Case Report

A 55-year-old woman was referred to our Hospital with a 4-month history of a slowly growing, painless mass in the medial aspect of the left distal thigh. Physical examination revealed a 4-cm, elastic-hard, poorly-mobile, non-tender mass. Magnetic resonance imaging (MRI) exhibited a well-defined soft-tissue mass with no involvement of the underlying bone. The mass had intermediate signal intensity on T1-weighted sequences (Figure 1A) and heterogeneous high signal intensity on T2-weighted sequences (Figure 1B). Contrast-enhanced T1-weighted sequences showed strong homogeneous enhancement of the mass (Figure 1C). A prominent vascular pedicle was also observed. FDG-PET images demonstrated a moderate uptake in the left distal thigh (Figure 2A). CT showed a slightly hypodense mass,
with corresponding tracer uptake (Figure 2B). The maximal standardized uptake value was 4.45 (Figure 2C).

Following an open biopsy, wide excision of the tumor was carried out. Microscopically, the tumor exhibited a patternless

Figure 1. Axial magnetic resonance images of solitary fibrous tumor involving the left thigh. The mass has intermediate signal intensity on T1-weighted sequence (A) and heterogeneous high signal intensity on T2-weighted sequence (B). Contrast-enhanced T1-weighted sequence (C) demonstrates strong homogenous enhancement throughout the mass.

Figure 2. $^{18}$F-fluorodeoxyglucose (FDG) positron-emission tomography (PET)/computed tomographic (CT) images of solitary fibrous tumor. PET image (A) demonstrates an increased uptake of FDG in the left distal thigh (arrow). Axial CT (B) reveals a slightly hypodense mass. Integrated PET/CT image (C) shows a moderate FDG uptake in the deep soft-tissue mass. The maximum standardized uptake value was 4.45.

Figure 3. Histological findings of solitary fibrous tumor. A: The tumor was found to consist of bland spindle cells with stromal collagen and thin-walled branching hemangiopericytoma-like vessels (hematoxylin and eosin staining, original magnification $\times 40$). B: Tumor cells are ovoid to spindle-shaped with indistinct cytoplasm and rather vesicular nuclei (hematoxylin and eosin staining, original magnification $\times 200$).
pattern characterized by a combination of hypercellular, hypocellular and myxoid areas, accompanied by a storiform pattern, arborizing small blood vessels, and perivascular arrangement of tumor cells (Figure 3A). Tumor cells were ovoid to spindle-shaped with indistinct cytoplasm and vesicular nuclei (Figure 3B). Mitotic activity was low (fewer than three mitotic figures per 10 high-power fields). No necrosis was found. Immunohistochemically, the tumor cells were strongly and diffusely positive for STAT6 (Figure 4A) and focally for desmin (Figure 4B). Staining for CD34 (Figure 4C), CD99, B-cell leukemia/lymphoma-2 protein, S-100 protein, cytokeratin, epithelial membrane antigen, smooth muscle actin, murine double-minute 2, and cyclin-dependent kinase 4 was negative. The MIB-1 labeling index was less than 5% (Figure 4D). Subsequent reverse transcriptase-polymerase chain reaction (RT-PCR) analysis confirmed the presence of a NAB2-STAT6 fusion gene (Figure 5). Based on these features, the tumor was diagnosed as SFT.
The postoperative course was uneventful. At three months' follow-up, the patient is doing well with no evidence of local recurrence or distant metastasis.

Discussion

SFT is a rare fibroblastic neoplasm with variable clinical behavior. Although the majority of SFTs pursue a benign clinical course, approximately 10% of SFTs behave aggressively (1). The risk of local recurrence and metastasis correlates to the presence of atypical or malignant histological component, tumor size greater than 10 cm and positive surgical margins (1). We believe that it is important to manage and follow-up soft tissue SFTs in the same manner as other soft-tissue sarcomas.

There are only a few reports describing the imaging features of soft-tissue SFT (8-10). CT generally demonstrates a well-circumscribed mass. Lesions may be isodense or mildly hypodense relative to muscle and usually exhibit marked heterogeneous contrast uptake (10). Calcification is rare, occurring in approximately 9% of cases (8). On MRI, soft-tissue SFT typically appears as a well-defined mass with intermediate signal intensity on T1-weighted images and variable signal intensity on T2-weighted images. Foci of low signal intensity corresponding to the collagen content and hypocellularity may be seen on both T1- and T2-weighted images. Soft-tissue SFT usually demonstrates strong focal or diffuse enhancement after intravenous gadolinium administration. The presence of a prominent vascular pedicle, although not specific, is a useful distinguishing feature of soft-tissue SFT (9). The imaging findings in our case were consistent with these findings.

FDG-PET is being increasingly used for the evaluation and management of soft tissue tumors. However, the FDG-PET/CT findings of soft-tissue SFT have not been documented so far. In the present case, moderate FDG uptake was seen in the homogeneously enhancing soft-tissue mass. There are few descriptions regarding the FDG-PET/CT manifestations of benign and malignant pleural SFTs in the literature (11-16). These limited data indicate that benign SFTs exhibit no or mild FDG uptake and malignant SFTs tend to have higher FDG uptake than benign SFTs, likely due to their hypercellularity and less collagenous composition. Further prospective investigations are needed to detect the role of FDG-PET/CT in the differential diagnosis and grading of soft-tissue SFT.

The present case was a morphologically typical case of SFT, but immunohistochemical expression of CD34 was absent. Positive immunoreactivity for CD34 has been used as a diagnostic marker for SFT. However, approximately 5-10% of SFTs can be CD34-negative (1) and CD34 expression tends to diminish during the process of dedifferentiation (17-19). In contrast, a strong and diffuse nuclear expression of STAT6 was observed in our case. Recent immunohistochemical studies have demonstrated that STAT6 is a highly sensitive and specific marker for the diagnosis of SFT (4-7). Moreover, NAB2-STAT6 fusion gene has been described as a novel molecular hallmark in SFT (2, 3). This gene is derived from inverted intra-chromosomal fusion of the NAB2 and STAT6 genes on 12q13 and can be detected by RT-PCR, as in our case. Taken together, these findings indicate that STAT6 immunoreactivity and demonstration of NAB2-STAT6 fusion gene are especially useful in establishing the diagnosis of CD34-negative SFT.

In summary, we described the clinicopathological, radiological and molecular genetic findings of SFT occurring in the deep soft-tissue of the thigh in a middle-aged woman. Our case illustrates the utility of STAT6 immunohistochemistry as an adjunct in the diagnosis of soft-tissue SFT with loss of CD34 positivity. Although rare, soft-tissue SFT should be considered in the differential diagnosis of a deep, vascular soft-tissue mass with an increased FDG uptake.

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