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Synovial Sarcoma with Massive Myxoid Feature
- A Case Report -

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Focal myxoid change in synovial sarcoma is not uncommon, although the presence of predominantly myxoid stroma is very rare. Recognition of synovial sarcomas with massive myxoid feature is important because these can easily be mistaken for other myxoid soft tissue neoplasms. We report a case of a synovial sarcoma with massive myxoid feature in the left thigh of a 54-year-old woman. Wide excision of an 8.5×7.0×5.0 cm, well-circumscribed and lobulated tumor was performed. The cut surface was gray, soft, and myxoid. Histological examination showed proliferation of spindle cells in the predominantly myxoid stroma. There were small areas with features more typical of synovial sarcoma, including uniform, spindled cells with fascicular growth patterns, collagenous stroma, mast cell infiltration, and hemangiopericytoma-like vascular patterns. Immunohistochemical examination showed focal positivity of the tumor cells for epithelial membrane antigen (EMA). Tumor cells were all negative for cytokeratin (AE1/AE3), cytokeratin 7, S-100 protein, smooth muscle actin, and desmin. Ultrastructurally, tumor cells showed desmosomes and microvilli. Our case underscores that, in order to make a correct diagnosis, immunohistochemical and ultrastructural examination is essential.

Key Words : Synovial sarcoma; Soft tissue; Myxoid; Sarcoma

Synovial sarcoma is a mesenchymal spindle cell tumor which displays variable epithelial differentiation.[1] It accounts for 5 to 10% of soft tissue sarcomas.[2] Synovial sarcoma mainly occurs in young adults and occurs more commonly in males than in females. Histologically, synovial sarcoma is either biphasic or monophasic. Focal myxoid change in synovial sarcoma is not uncommon. The presence of predominantly myxoid stroma had rarely been reported.[3,4] Krane *et al*.[4] described synovial sarcoma with predominantly myxoid change as myxoid synovial sarcoma. Myxoid synovial sarcoma can be easily confused with other myxoid spindle cell neoplasms.[5,6] Therefore, the recognition of myxoid synovial sarcoma is important. Here, we describe a case of a synovial sarcoma with a massive myxoid feature of the left thigh of a 54-year-old woman, and review the relevant literature.

CASE REPORT

A 54-year-old woman presented with a mass in her left upper thigh which had been present for six months. The egg-sized mass was first noted six months before and the mass began to grow more rapidly from two months before admission. Her medical history was noncontributory. Physical examination revealed a hard, movable mass in the left upper thigh. No pain and tenderness were present. Magnetic resonance (MR) images showed a soft tissue mass in the left upper thigh. There was low signal on the T1-weighted image and high signal on the T2-weighted image (Fig. 1). A wide excision was performed.

Grossly, the tumor measured 8.5×7.0×5.0 cm, and was well-circumscribed and lobulated (Fig. 2). The cut surface was gray, soft, and myxoid. The tumor was located within the skeletal muscle. Histologically, the tumor showed a spindle cell proliferation in the predominantly myxoid stroma, which constituted more than 90% of the tumor mass (Fig. 3A). In the myxoid area, spindled tumor cells had tapered nuclei and poorly-defined cytoplasm, in a loosely fascicular or reticular pattern. In some areas, the tumor showed uniform spindle cells, typical of synovial sarcoma (Fig. 3B, C). The chromatin was finely dispersed. There were foci of collagenous stroma, mast cells infiltration, and hemangiopericytioma-like vascular pattern. Mitotic counts were 15-20 per 10 high-power fields. Focal necrosis was present. Glandular differentiation was not observed. The myxoid stroma stained

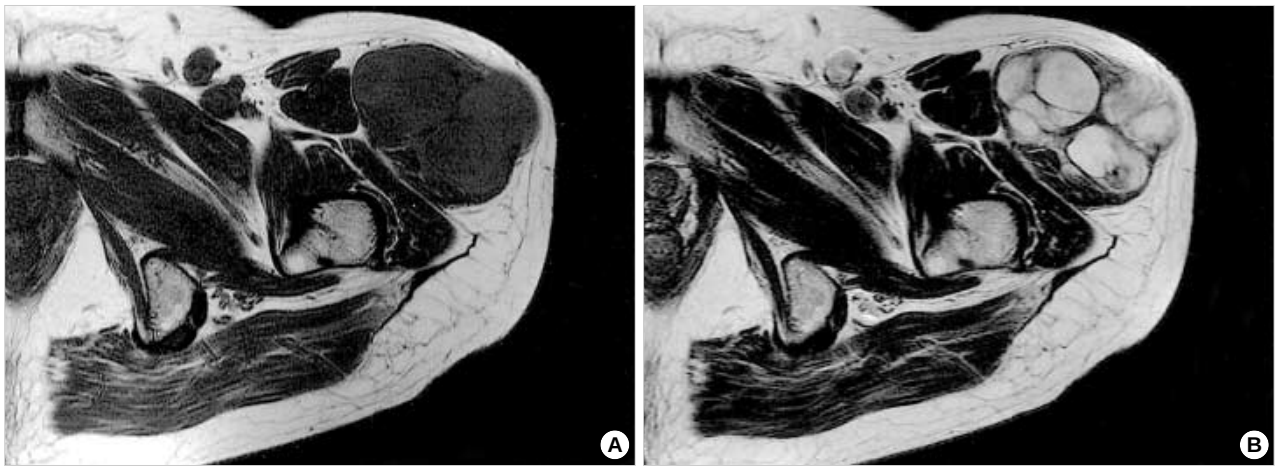

Fig. 1. MR images of the left thigh tumor. (A) Axial T1-weighted image shows low signal intensity. (B) Axial T2-weighted image shows high signal intensity.

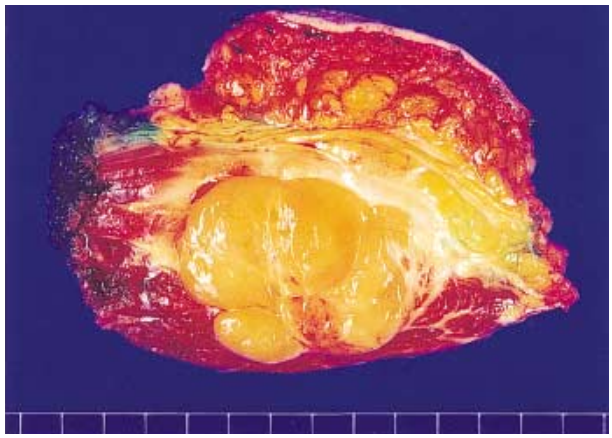

Fig. 2. Gross findings of the left thigh tumor. The left thigh tumor shows an 8.5×7.0×5.0 cm, well circumscribed, lobulated, and myxoid appearance.

positively with alcian blue and was inhibited by prior hyaluronidase treatment. On the immunohistochemical stain, tumor cells showed focal positivity for EMA, particularly in the fascicular spindle cell area (Fig. 3D). Tumor cells were all negative for cytokeratin (AE1/AE3), cytokeratin 7, S-100 protein, smooth muscle actin, and desmin. Ultrastructurally, tumor cells showed desmosomes and microvilli (Fig. 4). Our diagnosis was myxoid synovial sarcoma. Adjuvant chemotherapy was administered. Twelve months after the surgery, the patient remains in good health.

DISCUSSION

Synovial sarcoma is a soft tissue sarcoma which usually arises adjacent to joints or tendon sheaths, particularly in the lower extremities. Its histogenesis is unknown. Most of the patients present with a palpable, deep-seated mass that is often painful.[2] Some tumors have radiologically irregular calcification that is occasionally massive.[1]

Synovial sarcoma has a wide histologic spectrum that includes three variants: monophasic, biphasic, and poorly differentiated.[2] Common histologic features of synovial sarcoma include a variably collageous stroma with a hemangiopericytoma-like vascular pattern, intratumoral calcification, and mast cells.[4] Myxoid change is not uncommon, but it is generally so focal as to be diagnostically inconsequential.

The term myxoid synovial sarcoma was first described in 1999 by Krane *et al*.[4] who defined myxoid synovial sarcoma as a condition in which myxoid stroma constitutes greater than 50% of the studied surface area. Krane *et al*.[4] documented a series of myxoid synovial sarcoma in which marked myxoid change initially obscured the diagnosis and led to confusion. Moffatt *et al*.[7] reported the cytologic features of synovial sarcoma with predominantly myxoid stroma.

We reviewed our case, as well as seven previously reported cases of myxoid synovial sarcoma.[4] The age of the patients ranged from 12 to 54 years (median age 20 years). The male-to-female ratio was 1:1.25. Six tumors arose in the lower limbs (four in the thigh and one in the knee), two arose in the upper limbs (one in the elbow and one in the forearm), and one arose in the head and neck (arytenoid region).

According to a report by Krane *et al*.[4], myxoid synovial sarcoma constituted only 2% of all synovial sarcoma encountered in a consulting practice. The extent of myxoid change in synovial sarcoma was variable. The present case had myxoid stroma which constituted more than 90% of the tumor volume. In our case, the presence of uniform, spindle cells with a fascicular growth

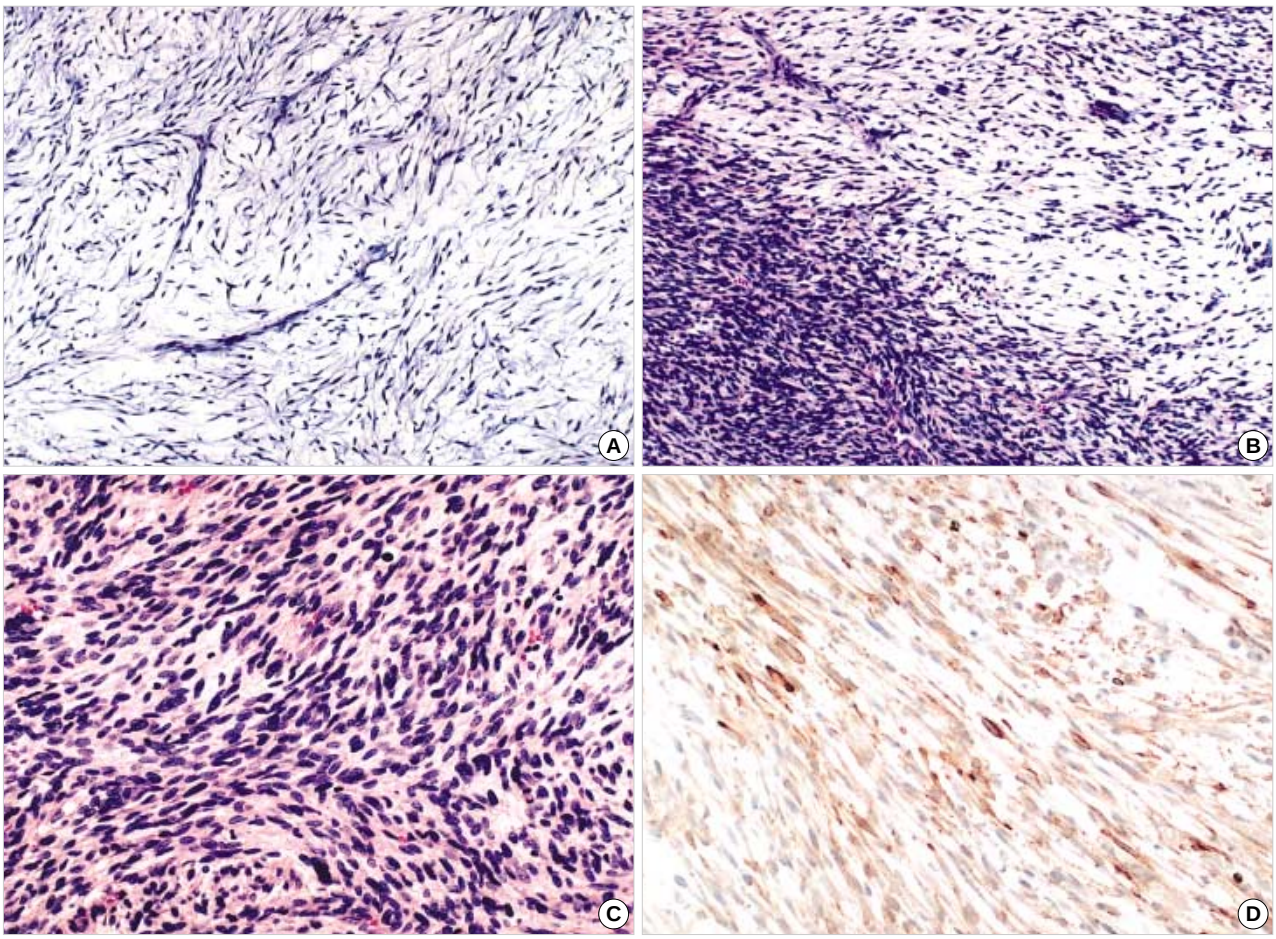

Fig. 3. Histologic findings of the left thigh tumor. (A) The tumor shows a spindle cell proliferation in the predominantly myxoid stroma. (B) The tumor shows transition from cellular area to myxoid area. (C) The tumor cells show uniform, spindle shaped nuclei. (D) The immunohistochemical stain shows focal positivity for EMA.

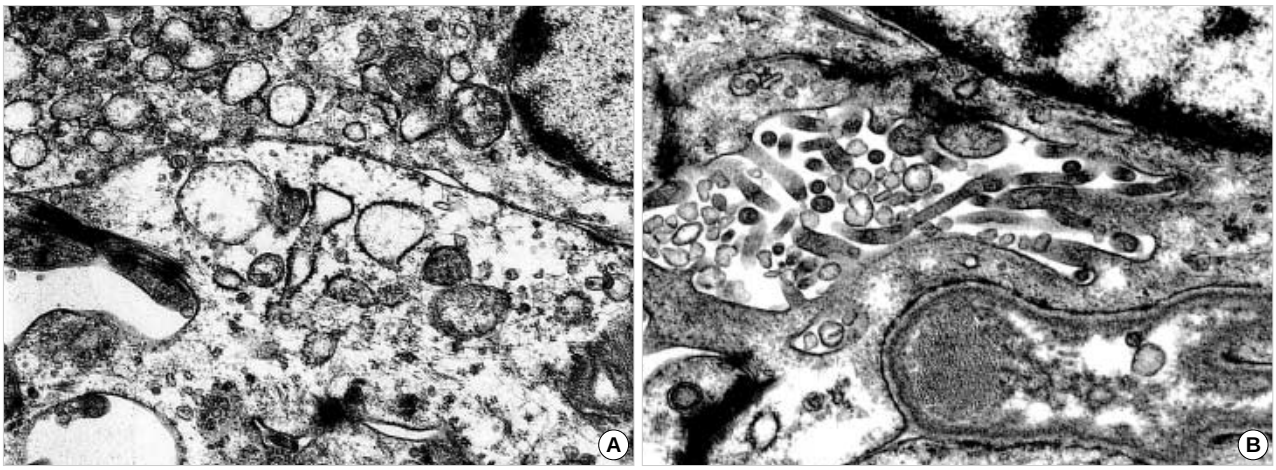

Fig. 4. Electron microscopy of the tumor cells. (A) Tumor cells show desmosomes (original magnification, ×15,000). (B) Tumor cells show projecting microvilli (original magnification, ×10,000).

pattern, with foci of collagenous stroma, mast cells, and focal hemangiopericytoma-like vascular pattern suggested features of synovial sarcoma. In Krane's series, two of seven cases showed small foci of glandular (biphasic) differentiation.[4] In the present

case, no glandular differentiation was observed.

The origin of myxoid material in synovial sarcoma is unknown. It has been suggested that myxoid material may be associated with a degenerative process or a product of stromal fibroblasts. Myxoid material has never been found in the cytoplasm of tumor cells, thus, it is unlikely to be produced by tumor cells.

The predominantly myxoid change is not uncommon in many soft tissue neoplasms. Because of the relative chemosensitivity of synovial sarcoma, it is important that they be distinguished from other myxoid spindle cell sarcomas.[8-10] The histologic differential diagnosis of synovial sarcoma with massive myxoid feature includes aggressive angiomyxoma, low grade fibromyxoid sarcoma, myxoid liposarcoma, myxoid leiomyosarcoma, myxofibrosarcoma, and myxoid malignant peripheral nerve sheath tumor (MPNST).[5,6] Aggressive angiomyxoma has prominent blood vessels and desmin positive tumor cells. Low-grade fibromyxoid sarcoma is distinguished by its whorled growth pattern and its more prominent fibrous stroma. Myxoid liposarcoma typically contains multivacuolated lipoblasts and anastomosing vessels embedded in myxoid background material. Myxofibrosarcoma may resemble synovial sarcoma, but the nuclear pleomorphism and hyperchromatism in myxofibrosarcoma are greater than those present in myxoid synovial sarcoma. Myxoid leiomyosarcoma contains intersecting fascicles with more abundant eosinophilic cytoplasm and cigar-shaped nuclei. Using immunohistochemical methods, myxoid leiomyosarcoma is immunoreactive with smooth muscle actin and desmin. In our case, tumor cells were negative for smooth muscle actin and desmin. The most problematic differential diagnosis of the present case is myxoid MPNST.[4] A perivascular accentuation (or whorling) of the tumor cells and the presence of heterologous elements favor a diagnosis of MPNST. Immunohistochemical analysis can be helpful in distinguishing synovial sarcoma and MPNST.[4,11] In the present case, tumor cells were positive for EMA and negative for S-100 protein, which favor synovial sarcoma over MPNST. Electron microscopy facilitates the diagnosis of synovial sarcoma when epithelial markers are not expressed and also aids in separating monophasic synovial sarcoma from other sarcomas.[12-14] In our case, tumor cells showed microvilli and desmosomes, which support the diagnosis of synovial sarcoma.

The specific chromosomal translocation t(X;18)(p11;q11) has been reported in more then >90% of synovial sarcoma, regardless of histologic subtype.[15-17] Cytogenetic and molecular techniques help to confirm the diagnosis and have been utilized recently as an additional way of predicting clinical outcome.[18,19] Cytogenetic investigation was not performed in our case. Large tumor size, poorly differentiated histology, and high mitotic counts have been shown to be strongly negative prognostic factors in synovial sarcoma.[5,18] In Krane's series of seven cases of myxoid synovial sarcoma, high mitotic rate (>10 mitoses per 10 high-power fields) was found to correlate with poor outcome.[4] In the present case, there was no evidence of recurrence or metastasis upon follow-up at 12 months.

In conclusion, we have described a case of synovial sarcoma with a massive myxoid feature arising in the left upper thigh. Synovial sarcoma with massive myxoid feature should be considered in the differential diagnosis of other myxoid soft tissue neoplasms.

REFERENCES

1. Fisher C, de Bruijin DRH, Geurts van Kessel A. Synovial sarcoma. In: Fletcher CD, Unni K, Mertens F. World Organization Classification of Tumours. Pathology and Genetics of Tumours of Soft Tissue and Bone. Lyon, France: IARC Press, 2002; 200-4.
2. Weiss SW, Goldblum JR. Enzinger and Weiss' Soft Tissue Tumors. 4th ed. St. Louis: Mosby, 2001; 1483-509.
3. King ES. Tissue differentiation in malignant synovial tumours. J Bone Joint Surg Br 1952; 34: 97-115.
4. Krane JF, Bertoni F, Fletcher CD. Myxoid synovial sarcoma: an underappreciated morphologic subset. Mod Pathol 1999; 12: 456-62.
5. Graadt van Roggen JF, Hogendoorn PC, Fletcher CD. Myxoid tumours of soft tissue. Histopathology 1999; 35: 291-312.
6. Wakely PE Jr. Myxomatous soft tissue tumors: correlation of cytopathology and histopathology. Ann Diagn Pathol 1999; 3: 227-42.
7. Moffatt EJ, Liu K, Layfield LJ. Demonstration of myxoid change in fine-needle aspiration of synovial sarcoma: a case report. Diagn Cytopathol 1998; 18: 188-91.
8. Bokemeyer C, Franzke A, Hartmann JT, *et al*. A phase I/II study of sequential, dose-escalated, high dose ifosfamide plus docorubicin with peripheral blood stem cell support for the treatment of patients with advanced soft tissue sarcomas. Cancer 1997; 80: 1221-7.
9. Kampe CE, Rosen G, Eilber F, *et al*. Synovial sarcoma. A study of intensive chemotherapy in 14 patients with localized disease. Cancer 1993; 72: 2161-9.
10. Rosen G, Forscher C, Lowenbraun S, *et al*. Synovial sarcoma. Uniform response of metastases to high dose ifosfamide. Cancer 1994; 73: 2506-11.
11. Lopes JM, Bjerkehagen B, Holm R, Bruland O, Sobrinho-Simoes M, Nesland JM. Immunohistochemical profile of synovial sarcoma with emphasis on the epithelial-type differentiation. A study of 49 primary

tumours, recurrences and metastases. Pathol Res Pract 1994; 190: 168-77.
12. Abenoza P, Manivel JC, Swanson PE, Wick MR. Synovial sarcoma: ultrastructural study and immunohistochemical analysis by a combined peroxidase-antiperoxidase/avidin-biotin-peroxidase complex procedure. Hum Pathol 1986; 17: 1107-15.
13. Ordonez NG, Mahfouz SM, Mackay B. Synovial sarcoma: an immunohistochemical and ultrastructural study. Hum Pathol 1990; 21: 733-49.
14. Weidner N, Goldman R, Johnston J. Epithelioid monophasic synovial sarcoma. Ultrastruct Pathol 1993; 17: 287-94.
15. Guillou L, Coindre J, Gallagher G, *et al*. Detection of the synovial sarcoma translocation t(X;18)(SYT;SSX) in paraffin-embedded tissues using reverse transcriptase-polymerase chain reaction: a reliable and powerful diagnostic tool for pathologists. A molecular analysis of 221 mesenchymal tumors fixed in different fixatives. Hum Pathol 2001; 32: 105-12.
16. Pelmus M, Guillou L, Hostein I, Sierankowski G, Lussan C, Coindre JM. Monophasic fibrous and poorly differentiated synovial sarcoma: immunohistochemical reassessment of 60 t(X;18)(SYT-SSX)-positive cases. Am J Surg Pathol 2002; 26: 1434-40.
17. Renwick PJ, Reeves BR, Dal Cin P, *et al*. Two categories of synovial sarcoma defined by divergent chromosome translocation breakpoints in Xp11.2, with implications for the histologic sub-classification of synovial sarcoma. Cytogenet Cell Genet 1995; 70: 58-63.
18. Chan JA, McMenamin ME, Fletcher CD. Synovial sarcoma in older patients: clinicopathological analysis of 32 cases with emphasis on unusual histological features. Histopathology 2003; 43: 72-83.
19. de Silva MV, McMahon AD, Paterson L, Reid R. Identification of poorly differentiated synovial sarcoma: a comparison of clinicopathological and cytogenetic features with those of typical synovial sarcoma. Histopathology 2003; 43: 220-30.