Intraneural synovial sarcoma of the tibial nerve

Kazuhiko Hashimoto[1], Shunji Nishimura[1], Kousuke Fujii[2], Ryosuke Kakinoki[1] and Masao Akagi[1]

Abstract

Synovial sarcomas are malignant soft tissue tumors that carry a metastatic potential and portend poor prognoses. We report a very rare synovial sarcoma arising from the tibial nerve and describe its successful treatment including limb preservation. To the best of our knowledge, this is the 40th reported incident of intraneural synovial sarcoma, and only the fourth arising from the tibial nerve. Extensive resection of synovial sarcoma arising in the popliteal region is difficult, particularly when limb preservation is desired. Ours is the first reported patient treated for tibial nerve-derived synovial sarcoma whose limbs were preserved.

Introduction

Synovial sarcomas are malignant soft tissue tumors that account for approximately 10% of all soft tissue sarcomas. These tumors can produce distant metastasis, and the 5-year survival rate is only 50%−60% despite aggressive treatment (including extended surgical resection and local radiation therapy) and a fairly high response rate to chemotherapy.[1] Although reported in patients of all ages, synovial sarcomas commonly occur in adolescents and young adults with an apparent male predominance.[1,2]

Because of their periarticular location, synovial sarcomas were originally believed to arise from the synovium. However, they can occur anywhere in the body; in fact, less than 5% are continuous with the synovium.[1,2] Current consensus is that these tumors arise from primitive undifferentiated mesenchymal cells.[1] While the majority of synovial sarcomas occur in the skeletal muscle and supporting connective tissue of the extremities (most often the legs),[1,2] they have also been reported in many other anatomical locations such as the mediastinum, head, neck, esophagus, pleura, heart, small intestine, and lungs.[3–6]

Herein, we report an extremely rare synovial sarcoma arising from the tibial nerve. To our knowledge, this is the 40th reported incidence of intraneural synovial sarcoma and only the fourth in the tibial nerve. Importantly, our patient is the first to have been diagnosed with synovial sarcoma in the tibial nerve and whose limbs were preserved via wide resection with revascularization.

Case report

An 11-year-old girl with no significant medical or family history presented with sharp pain in the popliteal fossa of her left knee and was admitted to our hospital in January 2014. She had noted a mass in this region for the past

[1]Department of Orthopedic Surgery, Kindai University Hospital, Osaka-Sayama City, Japan
[2]Department of Cardiovascular Surgery, Kindai University Hospital, Osaka-Sayama City, Japan

Corresponding author:
Kazuhiko Hashimoto, Department of Orthopedic Surgery, Kindai University Hospital, 377-2 Ohno-Higashi, Osaka-Sayama City 589-8511, Japan.
Email: hazzhiko@med.kindai.ac.jp

2 years that had gradually grown in size. Moreover, she had complained of claudication for the past year.

On physical examination, an approximate 5×5 cm moderately tender mass was noted on the back of the left knee (Figure 1(a)). The surface of the skin was smooth, as was the mobility between the skin and tumor as well as between the base and body of the tumor. Tinel's sign was positive over the lower region of the left leg and medial plantar. All lower limb manual muscular strength tests were normal (grade 5). Radiography of the left knee showed no calcification in the popliteal region (Figure 1(b)). Magnetic resonance imaging showed a $4.7 \times 2.95 \times 3.35$ cm fusiform homogeneous mass arising within the tibial nerve (Figure 1(c)). The mass was lower in intensity than the skeletal muscle on T1-weighting (Figure 1(c)) but higher on T2-weighting (Figure 1(d)). Contrast-enhanced computed tomography revealed that the tumor was in contact with the popliteal artery and vein (Figure 1(e)). 18F-fluorodeoxyglucose positron emission tomography showed slight accumulation of the isotope in the tumor (maximum standardized uptake value, (SUVmax) = 1.48) (Figure 1(f)). A whole-body scan revealed no metastases.

Histopathology of a needle biopsy sample showed dense spindle-shaped cells with oval nuclei with fine chromatin on hematoxylin-eosin staining (Figure 2(a)). Nuclear pleomorphism was mild. Suspected diagnoses included synovial sarcoma, schwannoma, and malignant peripheral nerve sheath tumor (MPNST); hence, immunohistochemistry was performed to distinguish between these possibilities. The spindle-shaped cells were positive for vimentin (Figure 2(b)) and CD99 (Figure 2(c)), but negative for epithelial membrane antigen (EMA) (Figure 2(d)), S-100 (Figure 2(e)), and keratin. Moreover, reverse transcription polymerase chain reaction showed expression of *SYT-SSX* fusion gene transcripts in the resected specimen. Based on these histopathological findings, monophasic synovial sarcoma was diagnosed.

Because a malignant neoplasm was diagnosed, three courses of neoadjuvant chemotherapy (ifosfamide, actinomycin D, and vincristine) were administered in accordance with Japan Clinical Oncology Group 0304 guidelines. Tumor size and the internal signal were not changed (stable disease). Wide resection was performed after chemotherapy. The saphenous vein was harvested from the right leg, and the popliteal vein and tumor (the tibial nerve) in the left leg were excised en bloc; the tumor margin was 3 cm both proximally and distally. The left common peroneal nerve was preserved. Finally, we rebuilt the popliteal vein in the left leg using the saphenous vein from the right leg (Figure 2(f)). Although the left sural nerve was harvested for reconstruction of the left tibial nerve, this was abandoned owing to the length of the defect. The macroscopic margin was tumor-free (Figure 2(g)). The resected specimen showed an elastic, hard yellowish-white cut tumor surface (Figure 2(h)). No obvious vascular invasion was observed.

Anticoagulation therapy was administered via infusion for 2 weeks after surgery, and two courses of chemotherapy were administered according to the Japan Clinical Oncology Group 0304 guidelines. No recurrence or metastasis was observed at the 40-month follow-up visit. Although paresthesia of the plantar surface remained, claudication had almost disappeared. Postoperative manual muscle testing of the gastrocnemius and flexor hallucis longus muscles showed that their strengths had declined to grades 2 and 1, respectively.

Discussion

Intraneural synovial sarcomas are extremely rare, with only 39 cases published to date.[5] Moreover, there are only three previous reports of synovial sarcoma originating in the tibial nerve (Table 1). We present the fourth case, in the youngest patient reported thus far. We describe in detail how limb preservation with revascularization was achieved for the first time via wide resection.

A primary synovial sarcoma of the nerve can mimic a benign peripheral nerve sheath tumor (BPNST) clinically and on imaging; hence, it should be considered a differential diagnosis for tumors arising from peripheral nerves as previously recommended.[5] In a previous study, approximately 80% of synovial sarcomas were homogeneous on T2-weighted images, approximately, 40% had a high signal intensity on both T1- and T2-weighted images (consistent with hemorrhage), and approximately 20% had fluid–fluid levels due to intratumoral hemorrhage or necrosis.[6] Moreover, 35% of tumors had a triple-signal intensity owing to a mixture of solid, cystic, fibrous, and hemorrhagic elements. Similar to a BPNST, the tumor in our patient was internally homogeneous on magnetic resonance imaging. It also had a low maximum standardized uptake value (SUVmax) of 1.48 compared with the mean SUVmax of synovial sarcomas (5.2; range, 0.8–25.0).[8] A cutoff SUVmax of 4.0 is used to distinguish between a BPNST and an MPNST, with a sensitivity and specificity of 1.0 and 0.94, respectively.[9]

Synovial sarcomas are composed of spindle-shaped cells derived from the mesenchyme and have a unique tendency to differentiate from mesenchymal to epithelial tissues to various extents.[1,2] Histopathologically, three types of synovial sarcoma are recognized: biphasic (distinct epithelial cells in gland-like arrangements along with fibroblast-like spindle cells in varying proportions), monophasic (entirely composed of spindle cells), which is the most common type[10] and dominant in intraneural synovial sarcomas,[7] especially those originating in the tibial nerve (Table 1); and poorly differentiated. In our case, the tumor was monophasic. Synovial sarcomas can easily be distinguished from schwannomas via histology and immunohistochemistry: the former the epithelial markers keratin and EMA, and sparsely express S-100, whereas schwannomas are diffusely S100-positive.[7] However,
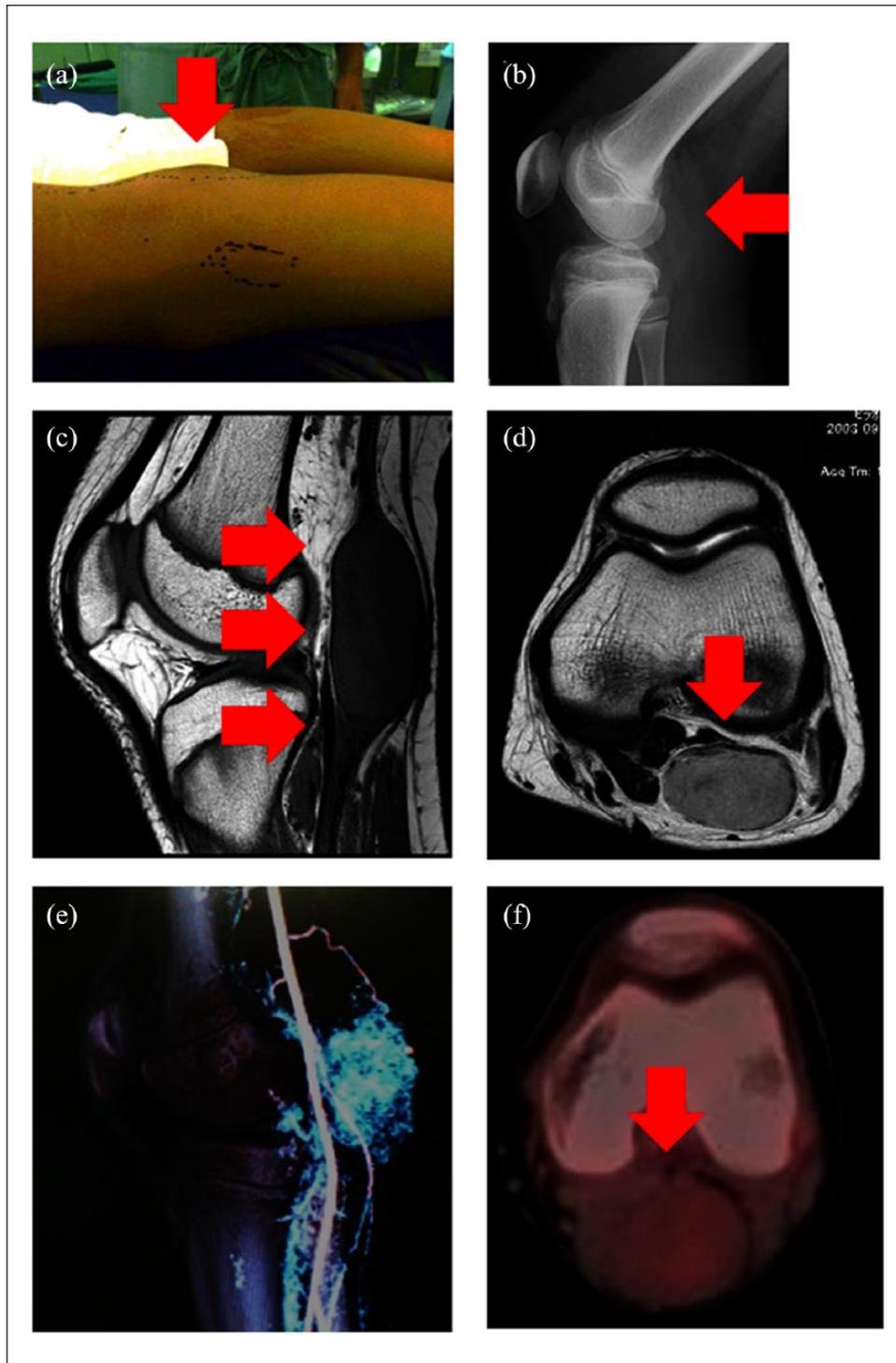
Figure 1. Photograph showing the tumor on the left leg (a). X-ray image (sagittal view) of the left knee, (b) T1-weighted magnetic resonance image of the left knee (sagittal view), (c) T2-weighted magnetic resonance image of the left knee (coronal view), (d) contrast-enhanced computed tomography scan of the left knee, (e) 18F-fluorodeoxyglucose positron emission tomography scan of the left knee (coronal view), and (f).the red arrows indicate the location of the tumor.

distinguishing monophasic synovial sarcomas and MPNSTs is more challenging owing to oftentimes very focal staining of epithelial markers in monophasic synovial sarcoma, and because S100 expression is highly variable and sometimes absent in MPNST.[11] CK7 and CK19 are expressed in almost all synovial sarcomas, but are not expressed in MPNSTs,[12] and are sometimes useful for distinguishing these neoplasm. Approximately 60% of synovial sarcomas also express
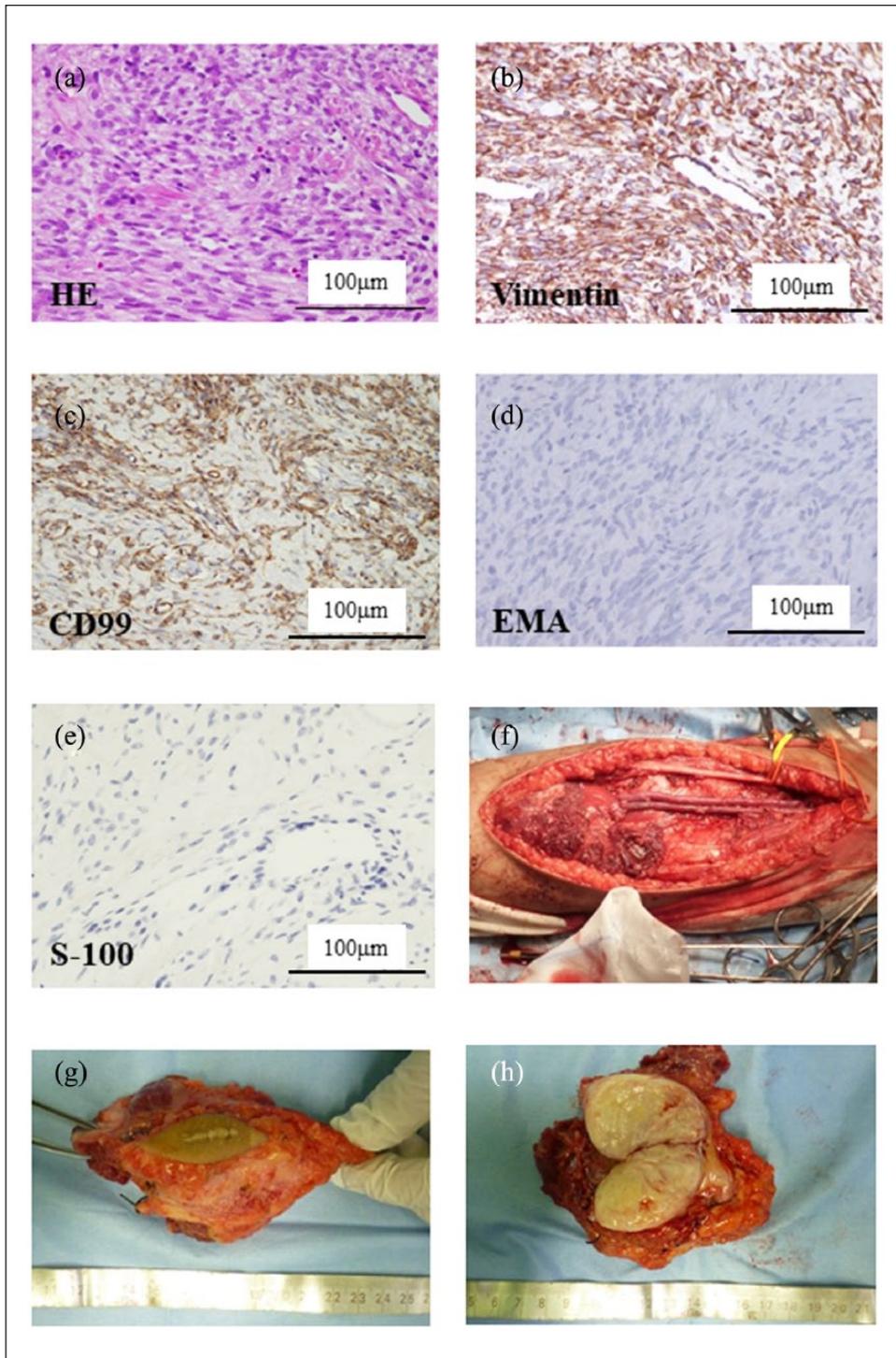
Figure 2. (a) Hematoxylin and eosin staining of a tumor sample, (b) Immunohistochemical staining of vimentin, (c) CD99, (d) epithelial membrane antigen (EMA), (e) S-100, (f) popliteal region after revascularization, (g) appearance of the excised specimen, and (h) appearance of the cut surface of the excised specimen.

CD99.[13] Although CD99 can be expressed in MPNSTs, the staining pattern is less diffuse and lacks cytoplasmic membrane staining compared to synovial sarcomas.[11] Although the tumor in our patient resembled an MPNST, its expression of the CD99 and lack of S100 expression favored synovial

sarcoma rather than an MPNS. Previous report has shown that Transducer-like enhancer of split 1 (TLE1) will be useful for distinguishing synovial sarcoma from MPNST since it is stronger and more diffuse in synovial sarcoma (82%) compared to MPNST (15%).[14] A recent report also suggests that

Table 1.

Author (Year)	Age (years)	Sex	Nerve	Histology	EMA	KRT	S-100	CD99	Cytogenesis	Surgery
Spielmann et al.[3] (1997)	43	M	Posterior tibialis	Monophasic	+	+	−	+	SYT-SSX	A
Scheithauer et al.[7] (2011)	13	F	Tibial	Monophasic	+	N/A	+	N/A	SYT-SSX2	ER
Larque et al.[5] (2017)	50	M	Tibial	Biphasic	+	+	−	N/A	SYT-SSX	GT
Current case	13	F	Posterior tibialis	Monophasic	−	−	−	+	SYT-SSX	ER

EMA: epithelial membrane antigen; ER: extended resection; KRT: keratin; GR: gross total.

the SOX10 transcription factor, a putative marker of neural crest differentiation, may be useful for distinguishing between MPNSTs and synovial sarcomas.[15]

A specific gene translocation between chromosome 18 and the X chromosome has been identified in synovial sarcoma.[16] Approximately 90% of synovial sarcomas harbor the *SYT-SSX* fusion gene as a result of the translocation.[17] There are two *SYT-SSX* variants, *SYT-SSX1*, and *SYT-SX2*, which are present in 100% and 50% of biphasic synovial sarcomas, respectively.[16,18] Hence, this gene is useful for obtaining a definitive diagnosis, as exemplified in a previous study[19] as well as ours.

Because synovial sarcomas are high-grade malignant soft tissue tumors, extended resection is desirable; in our patient, wide excision and revascularization ensured wide margins. Synovial sarcomas in the popliteal region are in close proximity to the neurovascular bundle, which portends a poor prognosis.[20] Radiation therapy is not necessary for a favorable outcome.[21,22] Although chemotherapy is effective for the local control of synovial sarcomas, its effect on overall survival is unknown.[21,22] Ifosfamide is primarily used to treat synovial sarcoma worldwide, but no convincing evidence of its efficacy has been reported.[21,22] The effect of chemotherapy was unclear in our patient.

The prognosis of patients with synovial sarcoma is relatively poor. The 5-year survival rate is 30–50 %, while the 10-year survival rate is approximately 10%.[21,22] Adverse prognostic factors include a tumor diameter greater than 5 cm, patient age greater than 40 years, and poorly differentiated status.[18,21,22] SYT-SSX1 and SYT-SSX2 have not been shown to have prognostic value in synovial sarcoma.[23] In our patient, there was no recurrence or metastasis as of 4 years post-treatment. Because synovial sarcomas progress slowly, a long follow-up period should be required to monitor for local recurrence.

Conclusion

We described a patient with a very rare synovial sarcoma originating in the tibial nerve in whom the limb was preserved via revascularization.

Informed consent

The patient provided written informed consent.

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