

CASE REPORT

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Synovial sarcoma of the tibial nerve - case report of a rare tumor in a rare location requiring early diagnosis

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Abstract

Background We present the case of a patient with a rare synovial sarcoma (SS) of the tibial nerve. So far, only 4 cases of patients with SS originating from the tibial nerve have been described in the literature, and our patient is only the second patient whose limb was saved during treatment. Synovial sarcomas are malignant mesenchymal tumors, i.e., tumors arising from connective tissue. Synovial sarcomas account for 5–10% of all soft tissue sarcomas. However, the name synovial sarcoma is misleading, because the tumor does not originate from synovial cells, but rather from primitive mesenchymal cells. The name most likely originated from the localization around the large joints on the limbs, more often on the lower ones, in the area of the knee joints.

We point out the aspects of correct and quick diagnosis and subsequent treatment, which has very important effect on the patient's prognosis. Primary less radical excision without prior biopsy verification leads to a higher risk of local recurrence, even if a proper reexcision was performed immediately after biopsy verification of the sarcoma.

Case presentation A woman born in 1949 began to suffer at the end of 2020 with escalating pain under the left inner ankle with a projection to the sole and fingers. Her personal, family work and social history were insignificant. After the initial neurological examination, the patient was sent for an ultrasound examination of the ankle, which showed a lobular mass measuring 50 × 22 × 16 mm and according magnetic resonance imaging, the finding appeared to be a suspicious neurinoma of the tibial nerve. The tumor was surgically excised, without prior biopsy verification: a 50 × 20 mm tumor was dissected in the distal part of the tarsal canal, which grew through the structure of the tibial nerve and in some places into the surrounding area and appeared intraoperatively as a neurofibroma. But histologically the tumor was classified as monophasic synovial sarcoma. The patient was indicated for a wide reexcision of the skin with the subcutaneous tissue of size 91 × 20 × 15 mm. Now the patient is being treated with external radiotherapy to the tumor bed and she is able to walk.

Conclusion This report draws attention to a rare type of malignant nerve tumor, which both clinically and radiologically can mimic benign peripheral nerve sheath tumors. Synovial sarcoma should be considered in very painful resistances, typically located around the joints of the lower limbs, the growth of which can be slow. Because the size of the tumor is a negative prognostic factor, it is necessary to make a timely diagnosis using MR imaging and a biopsy with histological examination and to start treatment quickly. Surgical treatment should take place only after a biopsy with histological examination of the tumor so that it is sufficiently radical and does not have to undergo an additional reoperation, as happened in the case of our patient.

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Keywords Synovial sarcoma, Rare tumor, Tibial nerve, Case report

Background

We present the case of a patient with a rare synovial sarcoma (SS) of the tibial nerve. So far, only 4 cases of patients with SS originating from the tibial nerve have been described in the literature, and our patient is only the second patient whose limb was saved during treatment [1–4].

Case presentation

A woman born in 1949 began to suffer at the end of 2020 with escalating pain under the left inner ankle with a projection to the sole and fingers, which therefore corresponded to the sensitive innervation region of the tibial nerve. The pain was severe, she could hardly touch the area around her ankle because of the palpation sensitivity. It worsened when she stepped on it, forcing her to walk on her tiptoes. If we were to evaluate the pain using a numerical scale (Numeric Rating Scale, NRS) with a range of 0–10, or 0–100, where “+” means “no perceived pain” and 10 (or 100) represents “worst imaginable pain”, the patient’s reported value was around 8.

So far, the patient has been treated for arterial hypertension, bronchial asthma, and diabetes mellitus type II, gastroduodenal ulcer disease, in 1985 she underwent right nephrectomy for clear cell carcinoma and in 1999 hysterectomy with adnexectomy for myomatous uterus.

The patient’s mother died of an unspecified gynecological malignancy. Otherwise, the family history was negative oncologically. Work and social history were insignificant.

After the initial neurological examination, the patient was sent for an ultrasound examination of the ankle, which showed a lobular mass measuring $50 \times 22 \times 16$ mm. After supplementing the magnetic resonance imaging, the finding appeared to be a suspicious neuroinoma of the tibial nerve (Fig. 1A).

The tumor was surgically excised, without prior biopsy verification: a 50×20 mm tumor was dissected in the distal part of the tarsal canal, which grew through the structure of the tibial nerve and in some places into the surrounding area and appeared intraoperatively as a neurofibroma. The nerve fascicles were freed from the tumor and the tumor was radically resected. Histologically, it was a spindle cell mesenchymal affection consisting of cells in poorly defined fascicles, with variably collagenized stroma (Fig. 2A). The cells had a uniform appearance, with nuclei with fine chromatin, small nucleoli, without significant cytological atypia, with well-identifiable mitotic activity (Fig. 2B, mitosis indicated by

an arrow). Most cells were positive for epithelial membrane antigen (Fig. 2C) and isolated cells for cytokeratin AE1/3 (Fig. 2D) and S100 protein. Using a break-apart FISH probe, a break in the SS18 gene, a genetic alteration

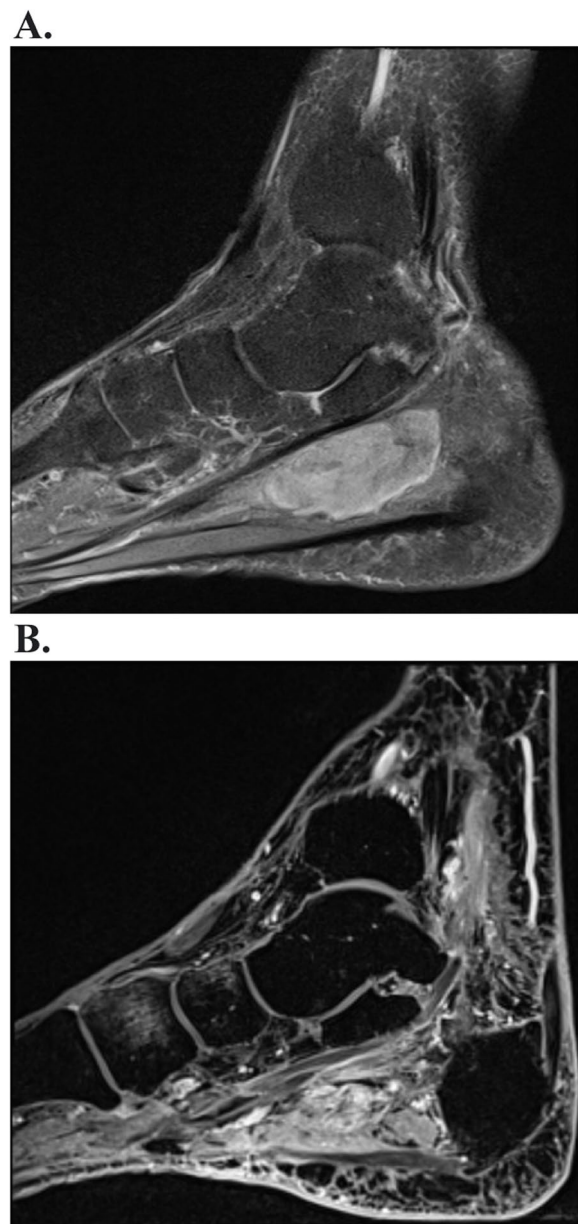


Fig. 1 **A** Preoperative MR examination of the left ankle. Imaging in the sagittal plane (PD TSE sequence) with the finding of an oval-shaped soft tissue tumorous mass along the course of the tibial nerve. **B** Postoperative MR examination of the left ankle. Imaging in the sagittal plane (T1 VIBE sequence, after administration of contrast material) showing postoperative changes, without evidence of macroscopic residual tumor

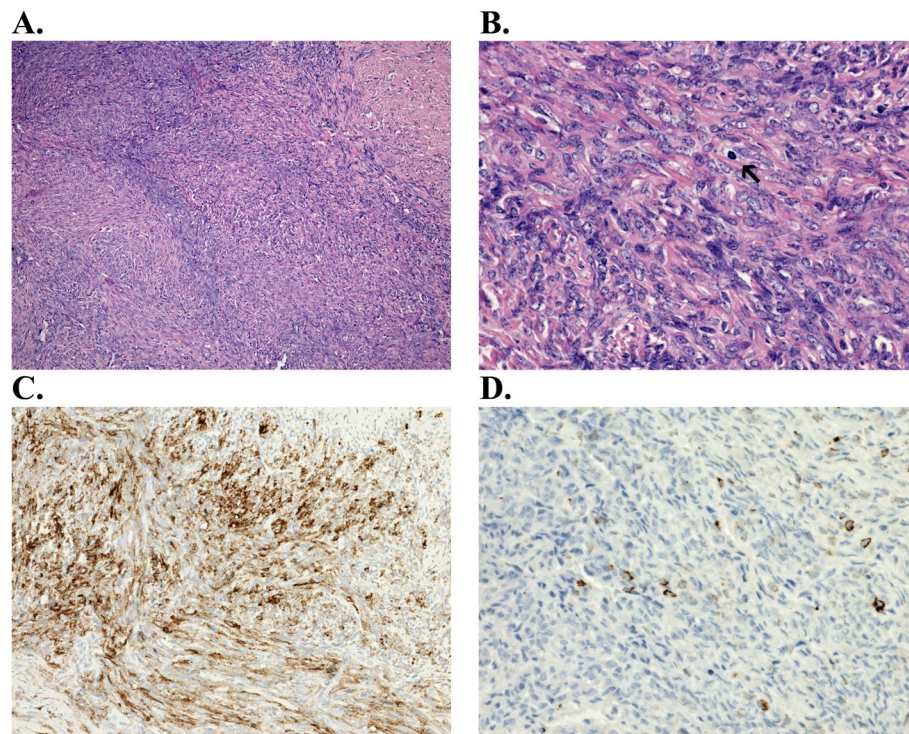


Fig. 2 **A** Histological evidence of a spindle cell mesenchymal affection consisting of cells in poorly defined fascicles, with variably collagenized stroma. **B** Uniform appearance of the cells, with nuclei with fine chromatin, small nucleoli, without significant cytological atypia, with well-identifiable mitotic activity (mitosis indicated by an arrow). **C** Positivity in the epithelial membrane antigen test. **D** Single positivity in the detection of cytokeratin AE1/3

diagnostic for synovial sarcoma, in this case classified as monophasic synovial sarcoma, was demonstrated in the tumor. Tumor structures reached the resection margin; however, the tumor sample was fragmented and the assessment of the resection margin was not reliably possible for these reasons. Subsequently, a control MRI was performed, where postoperative changes, edema and scarring were displayed on the medial surface of the foot, no nodular solid tumor residue was found (Fig. 1B). For the histological findings and therefore the possible microscopic residue, the patient was indicated for a wide reexcision of the skin with the subcutaneous tissue of size $91 \times 20 \times 15$ mm, which took place in January 2022. Histologically, the sarcoma structures were no longer found in the resection margins. CT of the body was without signs of disease dissemination. After the removal of the tumor, the patient was significantly relieved of pain. Two months after the second procedure, an electromyographic examination was completed, where a low summation muscle potential (CMAP) amplitude of the tibial nerve (1 mV) was measured on the left. Otherwise the findings were normal, thus indicating a partial axonal lesion of the tibial nerve. Now the patient is being treated with external radiotherapy to the tumor bed. The

mobility of the leg lying on the bed is unimpaired and the tibial paresis is not convincingly expressed. The surgical wounds healed well (Fig. 3). The patient is now starting to try walking with her feet.

Discussion and conclusions

Synovial sarcomas are malignant mesenchymal tumors, i.e., tumors arising from connective tissue. Benign mesenchymal tumors include, for example, fibroma, lipoma, chondroma, osteoma, myoma (leiomyoma or rhabdomyoma), angioma. Malignant mesenchymal tumors are called sarcomas.

Each peripheral nerve consists of axons that wrap around Schwann cells (here schwannomas, neurofibromas, or malignant tumors arise from the sheath of the peripheral nerve). The first protective covering, the endoneurium, is found around the Schwann cell, made of reticular and collagen fibers. Several bundles of such fibers are then enveloped by a second envelope, a perineurium formed from epithelioid cells, from which, for example, perineurinomas can arise. The last sheath is the epineurium, formed by a fibrous sheath of fibrous tissue, which wraps the bundles of fibers and fills them with mesenchymal cells, and from where sarcomas can



Fig. 3 In the upper part, a healed surgical wound, in the lower part, a high-quality execution of plantar and dorsiflexion

originate [5]. Synovial sarcomas account for 5–10% of all soft tissue sarcomas [6]. However, the name synovial sarcoma is misleading, because the tumor does not originate from synovial cells, but rather from primitive mesenchymal cells [7]. The name most likely originated from the localization around the large joints on the limbs, more often on the lower ones, in the area of the knee joints [8].

There are generally two types of synovial sarcoma. Monophasic sarcoma, i.e., made up of only one type of cells, namely spindle or glandular cells, and biphasic sarcoma made up of both types of cells. Soft tissue sarcomas are usually fast-growing, painless tumors, but synovial sarcomas often grow more slowly, are painful, can cause joint contractures, swelling, and the average time from the onset of symptoms to the established diagnosis is 2 years [9]. Pain was the dominant symptom in our patient as well. It took approximately a year from the first symptoms to establish the diagnosis. Another distinguishing feature of synovial sarcomas from other sarcomas is the younger age at the time of the first symptoms - it often appears in adolescents and young adults, and affects both sexes equally [10, 11]. The basis for diagnosis is a magnetic resonance examination and then a biopsy, which should be performed before surgery so that a sufficiently radical procedure can then be performed.

Cytogenetically, synovial sarcoma is characterized by the chromosomal translocation $t(X;18)(p11.2;q11.2)$, which leads to the fusion of two genes - SS18 (SYT) on chromosome 18 and SSX on chromosome X, and to the formation of SYT-SSX fusion transcripts (SS18-::SSX1, SS18-::SSX2 and rarely SS18-::SSX4). Even in our patient, FISH analysis confirmed a break in the SS18 gene, testifying to this chromosomal translocation.

The immunohistochemical profile of synovial sarcomas characteristically shows signs of epithelial differentiation, even in the case of the monophasic form. The detection of pancytokeratins, positive in up to 90% of cases [12], and the expression of the epithelial membrane antigen (EMA) are typical. Both of these markers can be commonly identified in the vast majority of epithelial tumors and for example, also in rare epithelioid sarcomas [13]. Positivity in the context of monomorphic spindle cell sarcoma is, however, completely typical for synovial sarcoma. EMA positivity itself is non-specific in soft tissue pathology and can be encountered, for example, in perineuriomas or low-grade myxoid fibrosarcoma. The same is true of pancytokeratins, which can often be identified in, for example, angiosarcomas, chordomas, leiomyosarcomas and other soft tissue tumors [14]. For these reasons, it is necessary to assess the immunoprofile always

in the context of the morphological findings. A relatively specific and sensitive immunohistochemical marker of synovial sarcoma is TLE1 [15], while immunohistochemical detection of other proteins (Bcl2, CD56 and CD99) is currently only of limited importance due to low specificity. Conversely, the absence of STAT6 immunoreactivity, typical for solitary fibrous tumors with pathognomonic NAB2::STAT6 fusion, is significant. Potentially problematic in the differential diagnosis is the focal positivity of the S100 protein, which can be identified in approximately 1/3 of synovial sarcomas [16]. S100 protein is a typical marker of neuroectodermal tumors and a similar focal positivity (in contrast to the diffuse positivity characteristic of malignant melanomas, neurofibromas and schwannomas) is often observed in malignant tumors from peripheral nerve sheaths, which also share a similar spindle cell morphology with synovial sarcomas. The most reliable means to distinguish between the two units is the proof of a break in the SS18 gene using FISH, RT-PCR or the massively parallel sequencing method [7].

The main treatment of synovial sarcoma is surgical treatment, which should take place only after a biopsy with histological examination of the tumor so that it is sufficiently radical and does not have to undergo an additional reoperation, as happened in the case of our patient.

Primary less radical excision without prior biopsy verification leads to a higher risk of local recurrence, even if a proper reexcision was performed immediately after biopsy verification of the sarcoma [17, 18].

Neoadjuvant radiotherapy is recommended especially for larger tumors (> 5 cm) or in cases where the resection margin has been reduced, for example due to an ongoing vessel, nerve or bone [19]. However, radiotherapy seems to prolong the overall survival of patients [20–22].

Synovial sarcomas appear to be more chemosensitive than other soft tissue sarcomas. In general, chemotherapy is recommended for younger patients, in whom it is expected to have a greater effect or for patients with unresectable or already generalized sarcomas [23–25].

Patient's prognosis is uncertain. It is generally reported that the five-year survival is around 30–50% and only 10% of patients survive more than ten years. Negative prognostic factors include tumor invasion into bone or blood vessels, advanced age, larger tumor size, and less radical excision [26–28]. And as was written above, primary insufficiently radical excision, even with subsequent re-excision, increases the risk of local recurrence and thus worse prognosis.

This case report draws attention to a rare type of malignant nerve tumor, which both clinically and radiologically can mimic benign peripheral nerve sheath tumors. Synovial sarcoma should be considered in very painful

resistances, typically located around the joints of the lower limbs, the growth of which can be slow. Because the size of the tumor is a negative prognostic factor, it is necessary to make a timely diagnosis using MR imaging and a biopsy with histological examination and to start treatment quickly.

Abbreviation

SS Synovial sarcoma

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Authors' contributions

PH, HM and MV analyzed and interpreted the patient data and were and was a major contributors in writing the manuscript. MK performed tumor extirpation. JS performed the histological examination of the tumour. JJ performed the radiological description of MRI. All authors read and approved the final manuscript.

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Not applicable.

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Competing interests

The authors declare that they have no competing interests.

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References

1. Spielmann A, Janzen DL, O'Connell JX, et al. Intraneural synovial sarcoma. *Skeletal Radiol.* 1997;26(11):677–81.
2. Scheithauer BW, Amrami KK, Folpe AL, et al. Synovial sarcoma of nerve. *Hum Pathol.* 2011;42(4):568–77.
3. Larque AB, Bredella MA, Nielsen GP, et al. Synovial sarcoma mimicking benign peripheral nerve sheath tumor. *Skeletal Radiol.* 2017;46(11):1463–8.

4. Hashimoto K, Nishimura S, Fujii K, et al. Intraneural synovial sarcoma of the tibial nerve. *Rare Tumors*. 2018;10:2036361318776495. <https://doi.org/10.1177/2036361318776495>.
5. Belakhova SM, Rodriguez FJ. Diagnostic pathology of tumors of peripheral nerve. *Neurosurgery*. 2021;88(3):443–56. <https://doi.org/10.1093/neuros/nyab021>.
6. Toro JR, Travis LB, Wu HJ, et al. Incidence patterns of soft tissue sarcomas, regardless of primary site, in the surveillance, epidemiology and end results program, 1978–2001: an analysis of 26,758 cases. *Int J Cancer*. 2006;119(12):2922–30. <https://doi.org/10.1002/ijc.22239>.
7. WHO Classification of Tumours Editorial Board. Soft tissue and bone tumours. WHO classification of tumours series, vol. 3. 5th ed. Lyon: International Agency for Research on Cancer; 2020. p. 290–3.
8. Sultan I, Rodriguez-Galindo C, Saab R, et al. Comparing children and adults with synovial sarcoma in the Surveillance, Epidemiology, and End Results program, 1983 to 2005: an analysis of 1268 patients. *Cancer*. 2009;115(15):3537–47. <https://doi.org/10.1002/cncr.24424>.
9. Chotel F, Unnithan A, Chandrasekar CR, et al. Variability in the presentation of synovial sarcoma in children. *J Bone Jt Surg Br Vol*. 2008;90:1090–6. <https://doi.org/10.1302/0301-620X.90B8.19815>.
10. De Silva MV, Barrett A, Reid R. Premonitory pain preceding swelling: a distinctive clinical presentation of synovial sarcoma which may prompt early detection. *Sarcoma*. 2003;7(3–4):131–5. <https://doi.org/10.1080/13577140310001644788>. PMID: 18521377; PMCID: PMC2395526.
11. Aytakin MN, Öztürk R, Amer K, et al. Epidemiology, incidence, and survival of synovial sarcoma subtypes: SEER database analysis. *J Orthop Surg (Hong Kong)*. 2020;28(2):2309499020936009. <https://doi.org/10.1177/2309499020936009>. PMID: 32618221.
12. Miettinen M, Limon J, Niezabitowski A, et al. Patterns of keratin polypeptides in 110 biphasic, monophasic, and poorly differentiated synovial sarcomas. *Virchows Arch*. 2000;437(3):275–83. <https://doi.org/10.1007/s004280000238>. PMID: 11037348.
13. Michal M. Základní imunohistochemický panel pro diagnostiku nádorů měkkých tkání. *Čes -slov Patol*. 2021;57:12–8.
14. Miettinen M. Immunohistochemistry of soft tissue tumours - review with emphasis on 10 markers. *Histopathology*. 2014;64(1):101–18. <https://doi.org/10.1111/his.12298>.
15. Foo WC, Cruise MW, Wick MR, et al. Immunohistochemical staining for TLE1 distinguishes synovial sarcoma from histologic mimics. *Am J Clin Pathol*. 2011;135(6):839–44. <https://doi.org/10.1309/AJCP45SSNAOPXYXU>.
16. Pelmus M, Guillou L, Hostein I, et al. Monophasic fibrous and poorly differentiated synovial sarcoma: immunohistochemical reassessment of 60 t(X;18)(SYT-SSX)-positive cases. *Am J Surg Pathol*. 2002;26(11):1434–40.
17. Chandrasekar R, Wafa H, Grimer RJ, et al. The effect of an unplanned excision of a soft-tissue sarcoma on prognosis. *J Bone Jt Surg Br Vol*. 2008;90:203–8. <https://doi.org/10.1302/0301-620X.90B2.19760>.
18. Potter BK, Adams SC, Pitcher JD Jr. Local recurrence of disease after unplanned excisions of high-grade soft tissue sarcomas. *Clin Orthop Relat Res*. 2008;466:3093–100. <https://doi.org/10.1007/s11999-008-0529-4>.
19. von Mehren M, Randall RL, Benjamin RS, et al. Soft tissue sarcoma, version 2.2016, NCCN clinical practice guidelines in oncology. *J Natl Compr Cancer Netw*. 2016;14:758–86. <https://doi.org/10.6004/jnccn.2016.0078>.
20. Gingrich AA, Marrufo AS, Liu Y, et al. Radiotherapy is associated with improved survival in patients with synovial sarcoma undergoing surgery: a national cancer database analysis. *J Surg Res*. 2020;255:378–87. <https://doi.org/10.1016/j.jss.2020.05.075>.
21. Naing KW, Monjzab AM, Li CS. Perioperative radiotherapy is associated with improved survival among patients with synovial sarcoma: a SEER analysis. *J Surg Oncol*. 2015;111:158–64. <https://doi.org/10.1002/jso.23780>.
22. Song S, Park J, Kim HJ, et al. Effects of adjuvant radiotherapy in patients with synovial sarcoma. *Am J Clin Oncol*. 2017;40:306–11. <https://doi.org/10.1097/COC.0000000000001148>.
23. Canter RJ, Qin LX, Maki RG, et al. A synovial sarcoma-specific preoperative nomogram supports a survival benefit to ifosfamide-based chemotherapy and improves risk stratification for patients. *Clin Cancer Res*. 2008;14:8191–7. <https://doi.org/10.1158/1078-0432.CCR-08-0843>.
24. Vletterie M, Litière S, Rizzo E, et al. Outcome of chemotherapy in advanced synovial sarcoma patients: review of 15 clinical trials from the european organisation for research and treatment of cancer soft tissue and bone sarcoma group; setting a new landmark for studies in this entity. *Eur J Cancer*. 2016;58:62–72. <https://doi.org/10.1016/j.ejca.2016.02.002>.
25. Spurrell EL, Fisher C, Thomas JM, et al. Prognostic factors in advanced synovial sarcoma: an analysis of 104 patients treated at the Royal Marsden Hospital. *Ann Oncol*. 2005;16:437–44. <https://doi.org/10.1093/annonc/mdi082>.
26. De Silva MV, McMahon AD, Reid R. Prognostic factors associated with local recurrence, metastases, and tumor-related death in patients with synovial sarcoma. *Am J Clin Oncol*. 2004;27(2):113–21.
27. Trassard M, Le Doussal V, Hacène K, et al. Prognostic factors in localized primary synovial sarcoma: a multicenter study of 128 adult patients. *J Clin Oncol*. 2001;19(2):525–34.
28. Kawai A, Woodruff J, Healey JH, et al. SYT-SSX gene fusion as a determinant of morphology and prognosis in synovial sarcoma. *N Engl J Med*. 1998;338(3):153–60.

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