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### MINIREVIEWS

- 2413** Multifocal G1-G2 gastric neuroendocrine tumors: Differentiating between Type I, II and III, a clinicopathologic review  
*Algashaamy K, Garcia-Buitrago M*
- 2420** Attention deficit hyperactivity disorder and comorbidity: A review of literature  
*Gnanavel S, Sharma P, Kaushal P, Hussain S*

### ORIGINAL ARTICLE

#### Case Control Study

- 2427** Dietary manipulation and testosterone replacement therapy may explain changes in body composition after spinal cord injury: A retrospective case report  
*Gorgey AS, Lester RM, Ghatas MP, Sistrun SN, Lavis T*

#### Retrospective Study

- 2438** Risk factors, clinical features, and short-term prognosis of spontaneous fungal peritonitis in cirrhosis: A matched case-control study  
*Huang CH, Pang LT, Xu LC, Ge TT, Xu QM, Chen Z*
- 2450** Incidence of portal vein thrombosis after splenectomy and its influence on transjugular intrahepatic portosystemic shunt stent patency  
*Dong F, Luo SH, Zheng LJ, Chu JG, Huang H, Zhang XQ, Yao KC*

#### Observational Study

- 2463** Multiplex gene expression profile in inflamed mucosa of patients with Crohn's disease ileal localization: A pilot study  
*Giudici F, Lombardelli L, Russo E, Cavalli T, Zambonin D, Logiodice F, Kullolli O, Giusti L, Bargellini T, Fazi M, Biancone L, Scaringi S, Clemente AM, Perissi E, Delfino G, Torcia MG, Ficari F, Tonelli F, Piccinni MP, Malentacchi C*

#### Prospective Study

- 2477** Analysis of the postoperative hemostatic profile of colorectal cancer patients subjected to liver metastasis resection surgery  
*Perez Navarro G, Pascual Bellosta AM, Ortega Lucea SM, Serradilla Martín M, Ramirez Rodriguez JM, Martinez Ubieta J*

### SYSTEMATIC REVIEW

- 2487** Systematic review of ablative therapy for the treatment of renal allograft neoplasms  
*Favi E, Raison N, Ambrogi F, Delbue S, Clementi MC, Lamperti L, Perego M, Bischeri M, Ferraresso M*

## CASE REPORT

- 2505** Subcutaneous sarcoidosis of the upper and lower extremities: A case report and review of the literature  
*Mehrzaad R, Festa J, Bhatt R*
- 2513** Atypical cutaneous lesions in advanced-stage Hodgkin lymphoma: A case report  
*Massaro F, Ferrari A, Zendri E, Zanelli M, Merli F*
- 2519** Characteristics of multiple nodules in a patient with pulmonary Langerhans cell histiocytosis: A case report  
*Kanaji N, Tokunaga Y, Ishikawa R, Watanabe N, Kadowaki N*
- 2526** Impact of continuous local lavage on pancreatic juice-related postoperative complications: Three case reports  
*Hori T, Ogawa K, Yamamoto H, Harada H, Matsumura K, Yamamoto M, Yamada M, Yazawa T, Kuriyama K, Tani M, Yasukawa D, Kamada Y, Aisu Y, Tani R, Aoyama R, Nakayama S, Sasaki Y, Nishimoto K, Zaima M*
- 2536** Adult intussusception caused by colonic anisakis: A case report  
*Choi YI, Park DK, Cho HY, Choi SJ, Chung JW, Kim KO, Kwon KA, Kim YJ*
- 2542** Robotic-assisted resection of ovarian tumors in children: A case report  
*Xie XX, Wang N, Wang ZH, Zhu YY, Wang JR, Wang XQ*
- 2549** Synovial sarcoma in the plantar region: A case report and literature review  
*Gao J, Yuan YS, Liu T, Lv HR, Xu HL*
- 2556** Severe serous cavity bleeding caused by acquired factor V deficiency associated with lymphatic leakage in a hemodialysis patient: A case report  
*Zhao WB, Chen YR, Luo D, Lin HC, Long B, Wu ZY, Peng H*
- 2562** Supermicrosurgery in fingertip defects-split tibial flap of the second toe to reconstruct multiple fingertip defects: A case report  
*Wang KL, Zhang ZQ, Buckwalter JA, Yang Y*
- 2567** Ultrasound-guided fascia iliaca compartment block combined with general anesthesia for amputation in an acute myocardial infarction patient after percutaneous coronary intervention: A case report  
*Ling C, Liu XQ, Li YQ, Wen XJ, Hu XD, Yang K*
- 2573** Rare spontaneous intrahepatic portosystemic shunt in hepatitis B-induced cirrhosis: A case report  
*Tan YW, Sheng JH, Tan HY, Sun L, Yin YM*
- 2580** Imaging of mixed epithelial and stromal tumor of the kidney: A case report and review of the literature  
*Ye J, Xu Q, Zheng J, Wang SA, Wu YW, Cai JH, Yuan H*
- 2587** Allogenic tooth transplantation using 3D printing: A case report and review of the literature  
*Xu HD, Miron RJ, Zhang XX, Zhang YF*

## REVIEW

- 2597 Fecal microbiota transplantation as an effective initial therapy for pancreatitis complicated with severe *Clostridium difficile* infection: A case report  
*Hu Y, Xiao HY, He C, Lv NH, Zhu L*

## CASE REPORT

- 2605 Organ-associated pseudosarcomatous myofibroblastic proliferation with ossification in the lower pole of the kidney mimicking renal pelvic carcinoma: A case report  
*Zhai TY, Luo BJ, Jia ZK, Zhang ZG, Li X, Li H, Yang JJ*
- 2611 Treating aplasia cutis congenita in a newborn with the combination of ionic silver dressing and moist exposed burn ointment: A case report  
*Lei GF, Zhang JP, Wang XB, You XL, Gao JY, Li XM, Chen ML, Ning XQ, Sun JL*
- 2617 Cause of postprandial vomiting - a giant retroperitoneal ganglioneuroma enclosing large blood vessels: A case report  
*Zheng X, Luo L, Han FG*
- 2623 Carcinoma ex pleomorphic adenoma of the trachea: A case report  
*Gao HX, Li Q, Chang WL, Zhang YL, Wang XZ, Zou XX*
- 2630 Wilson disease associated with immune thrombocytopenia: A case report and review of the literature  
*Ma TJ, Sun GL, Yao F, Yang ZL*
- 2637 Calcifying fibrous tumor of the mediastinum: A case report  
*Qi DJ, Zhang QF*
- 2644 Brachiocephalic artery stenting through the carotid artery: A case report and review of the literature  
*Xu F, Wang F, Liu YS*
- 2652 An extremely rare pedunculated lipoma of the hypopharynx: A case report  
*Sun Q, Zhang CL, Liu ZH*

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## Synovial sarcoma in the plantar region: A case report and literature review

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### Abstract

#### BACKGROUND

Synovial sarcoma (SS), a rare malignant soft tissue tumor whose histological origin is still unknown, often occurs in limbs in young people and is easily misdiagnosed.

#### CASE SUMMARY

We report a 24-year-old man who sought treatment for plantar pain thought to be caused by a foot injury that occurred 4 years prior. Currently, he had been seen at another hospital for a 1-wk history of unexplained pain in the left plantar region and was treated with acupuncture, a kind of therapy of Chinese medicine, which partly relieved the pain. Because of this, the final diagnosis of biphasic SS was made after two subsequent treatments by pathological evaluation after the last operation. SS is rarely seen in the plantar area, and his history of a left plantar injury confused the original diagnosis.

#### CONCLUSION

This study shows that pathological and imaging examinations may play a vital role in the early diagnosis and treatment of SS.

**Key words:** Imaging examination; Pathological examination; Plantar; Synovial sarcoma; Case report

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**Core tip:** A young male patient suffered from plantar pain for 1 wk. The symptoms were relieved after a kind of Chinese traditional invasive treatment. After that, the hemogram showed infection and magnetic resonance imaging showed that there was a soft tissue



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mass with a clear boundary in the plantar region. Rare location, complex medical history, invasive treatment, and auxiliary examination were easy to mislead doctors' judgments. Finally, the diagnosis was confirmed as synovial sarcoma by pathological examination. This case suggests that when soft tissue mass is encountered, biopsy is always the gold standard and must not be missed.

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## INTRODUCTION

Synovial sarcoma (SS) was first reported by Knox in 1936, who believed that SS originated from synovial cells<sup>[1]</sup>. In 1938, Berger defined SS as a tumor that occurred in the synovium, bursa, and tendon sheath<sup>[2]</sup>. Later, in 2013, the World Health Organization classified SS as a tumor of indefinite origin<sup>[3]</sup> that could be divided into single phase, double phase, and poorly differentiated lesions based on its pathological characteristics. SS is the fourth most common soft tissue sarcoma<sup>[4]</sup>, accounting for 5%-10% of soft tissue sarcomas<sup>[5]</sup>. It often occurs in boys and men aged 15-35 years old<sup>[6,7]</sup>, with a male/female ratio of about 1.2:1.0<sup>[8,9]</sup>. SS is commonly found in soft tissues around the large joints of limbs, especially in soft tissues near the knee joint<sup>[10]</sup>. A plantar SS is rare. The 5-year survival of SS patients is 61%-80%, and the 10-year survival is 10%-30%<sup>[11,12]</sup>.

It has been found that SS correlates closely with translocation of chromosomes 18 and X, which generates the SYT-SSX fusion gene now existing in no other disease but SS. Therefore, the molecular cytogenetic examination of T (x; 18) (p11.2; q11.2) and SS18-SSX fusion gene transcripts has been considered the most important evidence for diagnosing SS<sup>[13]</sup>. According to reported research<sup>[14]</sup>, the sensitivity of fluorescence *in situ* hybridization (FISH) and reverse transcription-polymerase chain reaction (RT-PCR) for identifying SS are, respectively, about 80.0% and 83.8%, and their combined sensitivity is about 92.9%.

At present, there is no effective cure for SS<sup>[15]</sup>. A timely, correct diagnosis and the proper surgical treatment at an early stage are essential for a good prognosis. Kartha and Bumpous<sup>[16]</sup> reported that performing an operation to remove the tumor with a diameter < 5 cm is the treatment of choice for SS. For an SS with a diameter > 5 cm, radiotherapy is needed prior to the surgery<sup>[16,17]</sup>. In addition, Eilber *et al*<sup>[18]</sup> reported a randomized controlled trial showing that radiotherapy after surgery for SS increased the survival rate.

In 2016, Vlenterie *et al*<sup>[10]</sup> analyzed 3711 SS patients, among whom 313 had advanced-stage SS. They found that about 56% of the SSs at an advanced stage originated from limbs, and pulmonary metastasis was commonly detected (80%). Compared with other soft tissue sarcomas, metastasis of SS begins at an earlier age (median age, 40 years), and men more often experience metastasis than women at the same age (male/female = 191:122).

SS is sensitive to chemotherapy and has a better prognosis than other sarcomas at the same stage<sup>[9]</sup>. Recent research showed that chemotherapy for metastatic SS tumor with ifosfamide or doxorubicin could protract patients' lives, whereas radiotherapy had no positive effect on patients' prognosis<sup>[19]</sup>. Trabectedin, a novel, targeted anti-tumor, cytotoxic drug, has been approved in Europe for treating advanced liposarcomas and leiomyosarcomas<sup>[20]</sup>. Japanese researchers have shown that trabectedin plays a prominent role in repressing the growth of SS cells and has potential for use clinically in the treatment of SS<sup>[21]</sup>. Surgery combined with chemotherapy or radiotherapy as comprehensive treatment for SS in current clinical practice may hopefully improve the survival rate of patients with SS.

We describe herein a case of SS in the plantar region of the foot misdiagnosed due to the patient's complicated history of plantar trauma and repeated treatment for this atypical manifestation. The patient was misdiagnosed in different hospitals as having plantar fasciitis, soft tissue infection, and inflammatory granuloma. We assess the reason for these misdiagnoses and finally conclude that when a patient's symptoms are not typical and evidence of the imaging examination is insufficient, a pathological examination is essential for a timely, correct diagnosis, which should be established as

early as possible.

## CASE PRESENTATION

### **Chief complaints**

A 24-year-old man had a 4-year history of a left plantar injury from which he recovered within several days without treatment and with no mobility obstacles.

### **History of present illness**

Currently, the patient suffered unexplained pain during walking in his left plantar region for almost a week. He noted some swelling in the left plantar area but no fever, chills, or pain. He took some nonsteroidal anti-inflammatory drugs, which partly relieved his walking-induced pain. The pain recurred within 3 d, however, at which time he visited a hospital where he was treated with acupuncture. The pain was once again relieved, although 2 d later it returned, hampering his mobility. He was brought to our hospital in an armchair (Peking University People's Hospital).

### **History of past illness**

Since the onset of his walking pain, the patient had experienced no problems with his mental state, diet, sleeping, or weight.

### **Personal and family history**

The family history was unremarkable.

### **Physical examination upon admission**

Physical examination showed some swelling in his left plantar region and ecchymosis (1.5 cm × 1.5 cm) with accompanying tenderness at that site. When he back-stretched his left foot, the fourth toe had sharp pain. No mass was found in his left plantar area.

### **Laboratory examinations**

Routine blood examination showed a white blood cell count of  $10.06 \times 10^9/L$  and C-reactive protein level was 9.51 mg/L.

### **Imaging examination**

Plain radiography of his left plantar was normal (Figure 1). Color Doppler ultrasonography showed an inhomogeneous mass in the plantar area of the left foot (Figure 2), and magnetic resonance imaging (MRI) suggested that it could be a benign tumor or tumor-like lesion, such as inflammatory granulation or a giant cell tumor in the tendon sheath (Figure 3).

## FINAL DIAGNOSIS

Taking into account the patient's disease history, symptoms, and examination findings, however, his suspected diagnosis was a soft tissue infection in the left plantar area.

## TREATMENT

He was treated with antibiotics (cefuroxime, 1500 mg, bid, *i.v.*) for 3 d, which relieved the walking-induced pain, and his laboratory values returned to normal, with a white blood cell count of  $6.90 \times 10^9/L$  and erythrocyte sedimentation rate of 7 mm/h. He was discharged from the hospital on postoperative day 7 and continued to take cefuroxime orally as directed.

On day 11 after his discharge, his pain recurred, and he was again admitted to our hospital, this time demanding that we remove the mass in his left plantar region. Physical examination showed a swelling in the left plantar area and ecchymosis (1.5 cm<sup>2</sup> × 1.5 cm<sup>2</sup>) in the left plantar region with accompanying tenderness (Figure 4). The mass had no clear margins with its surroundings, and the blood supply and nerves of the left plantar area were normal. We removed the mass on day 2 after admission, then used cefuroxime infusion as his last hospital stay. The lesion measured 3.0 cm × 1.5 cm × 1.5 cm and was elliptical, lobulated, yellowish gray, and soft (like adipose tissue). It had been located between the foot plantar flexion tendons and metatarsal with clear boundaries.

Postoperative pathological examination showed a focal adenoid structure,





**Figure 1** Plain radiography of the patient's left plantar. Both of the front view and foot oblique view show nothing abnormal in bones.

composed partly of interstitial fibrosis and multinucleated giant cells with scattered hemosiderin deposition. The HE staining showed a sign of tumor cell type (Figure 5). Immunohistochemical staining showed the following: CK (adenoid area) (+), CK7 (adenoid area) (+), desmin (-), CD34 (blood vessels) (+), TLE1 (+), S100 (-/+), P63 (-), KP-1 (coenocytes) (+), and KP-1 (+5%). The pathological diagnosis was SS (bipolar).

## OUTCOME AND FOLLOW UP

This patient received postoperative chemotherapy with doxorubicin and cyclophosphamide for 2 mo, after which no metastasis was found.

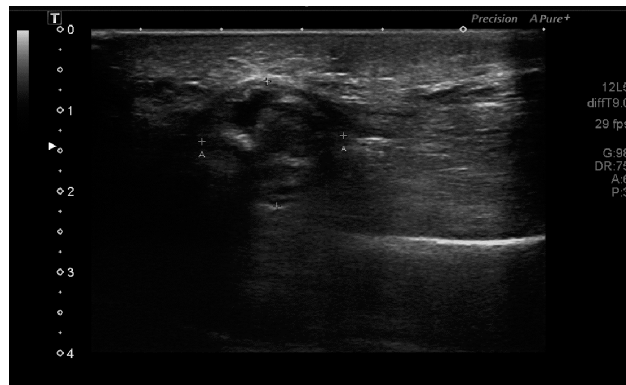
## DISCUSSION

This case of SS, with a 4-year history of plantar trauma, the inflammatory symptoms during the treatment, and the indication of a benign mass without a clear boundary on imaging, was easily misdiagnosed. Typical SSs are commonly found in deep soft tissue and manifest as a large mass with slow growth. In addition, they most often are accompanied by focal pain or tenderness. The average incubation of SS is 2-4 years, with some even reaching 20 years<sup>[22]</sup>. The patient discussed herein had an SS in his left plantar region after having experienced plantar trauma 4 years prior. In addition, his symptoms had not presented until about 2 wk before his first visit to the hospital complaining of plantar pain.

Walking-induced pain in the left plantar region in a patient with a history of plantar trauma 4 years prior is not commonly related to a malignant tumor, which caused the misdiagnosis at his first visit. When he was admitted to our hospital, the laboratory and imaging examinations suggested a benign mass due to infection that may have been caused by his prior acupuncture treatment. Thus, he was misdiagnosed as having a left plantar infection, which was relieved by the prescribed antibiotic treatment. When he returned a few days later, combined with the surgical findings, he was misdiagnosed a second time as having an inflammatory granuloma in the left plantar region. The patient was finally diagnosed correctly during the pathological examination as having SS. Without a pathological examination, SS of this kind could easily be misdiagnosed, which could cause a great loss of the patient's quality of life.

The mechanism of SS is not fully understood. A few cases have been reported in which SS may have a correlation with the use of radiotherapy<sup>[23,24]</sup>, and some believe that calcified SS may be related to trauma. Murphey *et al*<sup>[4]</sup>, however, argued that trauma has nothing to do with SS and that SS causes some clinical symptoms that might increase the possibility of discovering it after trauma. Regrettably, in this case, the patient did not seek for medical help immediately, so no imaging details were available to study whether the plantar trauma that occurred 4 years prior was related to the development of the SS.

To better understand SS, we searched PubMed for articles about SS published from 1953 to 2017. We found that, except liposarcoma, almost all other soft tissue sarcomas lack peculiar manifestations during imaging examinations, and the diagnostic rate for SS is just 25%<sup>[25]</sup>. The images of SS have no apparent specificity, although there are



**Figure 2** Doppler ultrasonography showed an inhomogeneous mass in the plantar area of the left foot.

some peculiar manifestations<sup>[26,27]</sup>. SS commonly manifests on computed tomography (CT) as a heterogeneous mass with low density and inapparent boundaries compared with the normal surrounding tissues. These characteristics may be intensified by different degrees with enhanced CT. On MRI, SS manifests as having clear boundaries and swelling around the mass, mainly equivalent signals on T1-weighted images (mixed with some higher signals) and compound signals in T2-weighted images<sup>[4,28]</sup>, and this is one of the reasons for misdiagnosing SS as a benign tumor. Therefore, whether there is a clear boundary cannot be regarded as proof for distinguishing whether a mass is benign or malignant or the degree of histological differentiation<sup>[29,30]</sup>.

## CONCLUSION

The MRI results in this case conform to the characteristics reported above (*i.e.*, a round mass with a clear boundary and compound signals on T2-weighted images), ensuring its easy diagnosis as a benign tumor. Under such a circumstance, CT should be performed to further determine if it might be SS. If the results do not clearly indicate that it is SS, a pathological examination for the correct diagnosis is needed.



Figure 3 Magnetic resonance imaging suggested that the lesion could be a benign tumor or tumor-like lesion, such as inflammatory granulation or a giant cell tumor in a tendon sheath.



Figure 4 Physical examination showed a swelling in the left plantar area and ecchymosis ( $1.5 \text{ cm}^2 \times 1.5 \text{ cm}^2$ ) in the left plantar region with accompanying tenderness.

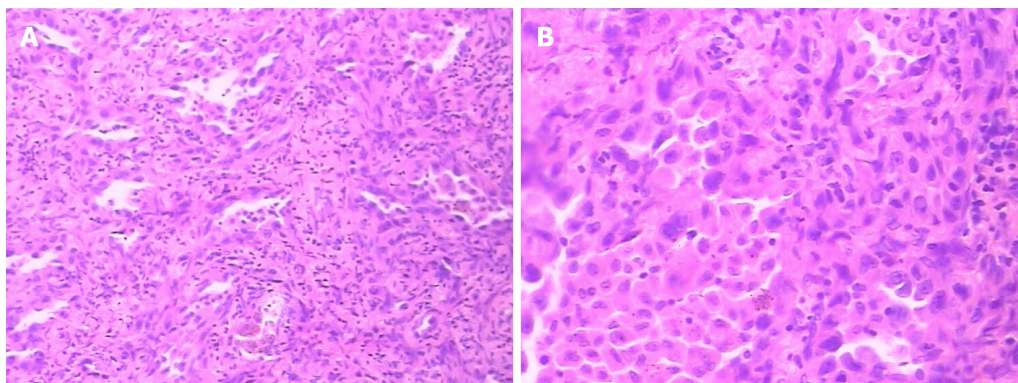


Figure 5 Hematoxylin-eosin staining showed a sign of tumor cell type. A: Magnification is 100 times; B: Magnification is 200 times.

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