Case Report

rare tumors

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The management of pancreatic metastasis from synovial sarcoma of the soft tissue: A case report

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Abstract

Pancreatic metastases are rare, accounting for 2%–3% of pancreatic tumors. The pancreas represents an unusual metastatic site of synovial sarcoma (SS) outside the usual localizations (regional nodes, lung, bone, and liver). The diagnosis is evoked by the personnel medical history of SS and imaging then confirmed by histological examination of the guided pancreatic biopsy. Its therapeutic management is mainly surgical with extensive removal of the lesion. So far only four cases have been reported in the English literature. We reported the case of a male aged 30-year-old who was admitted to our Institute for a local recurrence of SS of the left thigh which was initially treated by surgical excision. The patient underwent a wide surgical excision followed by chemotherapy and radiotherapy. About 15 months later, he experienced a pancreatic metastasis of his SS. He had a caudal splenopancreatectomy with partial resection of the transverse colon followed by chemotherapy. This report highlights the diagnostic difficulties of this rare localization and therapeutic challenge.

Keywords

Pancreatic, metastasis, synovial sarcoma, therapeutics

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Introduction

Soft tissue sarcoma is a rare mesenchymal neoplasm, accounting for approximately 1% of all adult cancers.[1] Synovial sarcoma (SS), a malignant soft tissue tumor, forms up to 10% of sarcomas in soft tissue.[2–4] Indeed, metastasis occurs in approximately 50% of patients due to its aggressive potential. Lung, lymph nodes, and bone are respectively the most common sites of metastasis.[5] Pancreatic SS metastasis is very rare, and they are mostly detected in the autopsy. In the majority of cases, the disease can affect several organs at the same time, and even though they were detected before death, there is no surgical treatment.[6] Isolated pancreatic SS metastasis can be treated by surgery, in rare cases. In this article, we present a case of surgically treated solitary pancreatic metastasis from SS, and we discuss the clinical, radiological, and treatment characteristics of SS pancreatic metastasis.

Case report

We report the case of a 30-year-old male patient who was treated initially in another facility for SS of the left thigh. He underwent wide excision with free margins. The tumor measured 3 cm in its greatest diameter. Anatomopathological examination showed: a monophasic spindle cell synovial sarcoma in a fascicular arrangement. Immunohistochemistry showed positivity for bcl2, cytokeratin, epithelial membrane antigen

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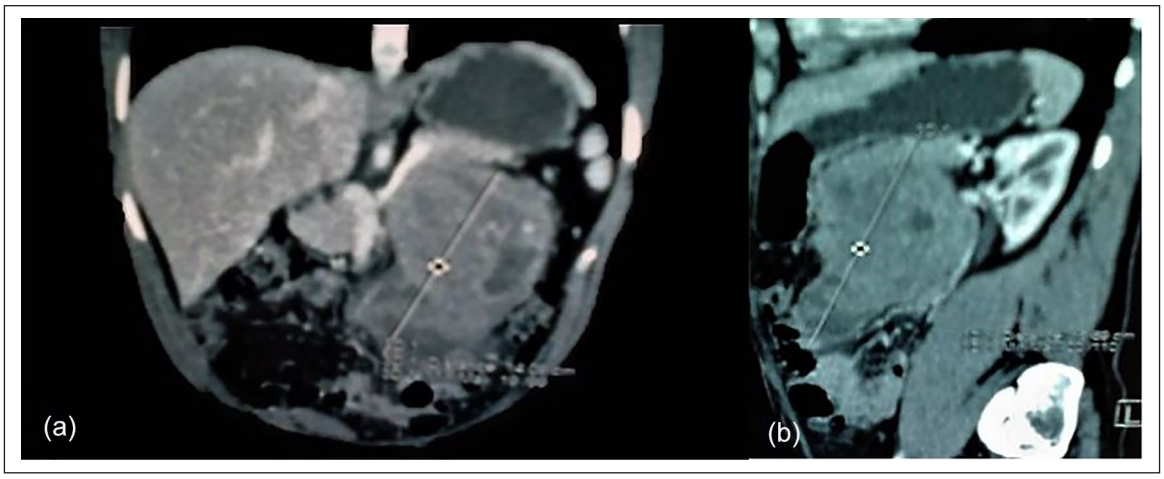

Figure 1. (a) Cross-section, and (b) sagittal section CT scan showing a large, solid, and heterogeneous mass located on the tail of the pancreas. This mass was enhanced after the injection of the contrast agent.

(EMA), CK, and negativity for chromogranin A, synaptophysin, and vimentin. About 6 months later, he was admitted to our institute for a local recurrence confirmed by biopsy. A thoracic-abdominopelvic computed tomography (CT) scan was performed and didn't reveal any secondary locations. The patient underwent a wide excision, with a vascular replacement of the femoral artery and coverage with a flap of the left rectus abdominis muscle. The following operations were straightforward. The Surgical limits were free. The search for the SYT-SXX fusion transcript was not completed. The patient underwent six cycles of ifosfamide-based chemotherapy followed by adjuvant external radiotherapy at a dose of 54 Gy. After 15 months of regular clinical and radiological follow-up, the patient presented a pancreatic mass diagnosed on a CT scan. The mass was located on the tail of the pancreas. It was heterogeneous, solid, enhanced after the injection of the contrast agent. Tumor markers: ACE, CA19-9, and NSE were negative. A biopsy under CT scan was performed and the histologic exam confirmed the metastatic nature of the pancreatic mass. The patient was reluctant to surgical treatment, and he was lost of view for 4 months. Due to the onset of transfixing abdominal pain and the increase in abdominal volume, the patient consulted after 4 months. An abdominal ultrasound showed an increase in the size of the lesion to 15 cm. The thoracic-abdominopelvic CT scan was performed and it showed a pancreatic mass invading the transverse colon without any other metastatic localizations (Figure 1). The patient underwent a laparotomy. Upon exploration, a mass of the tail and body of the pancreas was discovered invading the transverse colon. There was no ascites or carcinosis. The rest of the abdominal cavity was free of sarcomatosis (Figure 2). The procedure consisted of a caudal splenopancreatectomy with partial resection of the transverse colon.

Pathological examination showed a pancreatic localization of the previously diagnosed monophasic synovial sarcoma with free surgical margins (Figures 3 and 4). He underwent four cycles of first-line metastatic chemotherapy

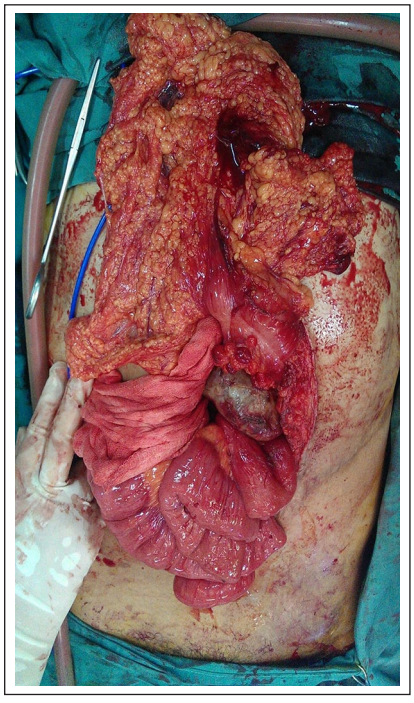

Figure 2. Intraoperative image showing a large greyish pancreatic mass invading the transverse colon.

with high-dose ifosfamide and doxorubicin. The patient developed an endocrine pancreatic insufficiency requiring insulin therapy. The patient died 6 months later due to a diabetic coma.

Discussion

Sarcoma is a malignant tumor arising from mesenchymal tissue. It is less common than carcinoma and occurs mainly in young people.[1] SS, a malignant soft tissue tumor, forms up to 10% of sarcomas in soft tissue.[2–4] Owing to its

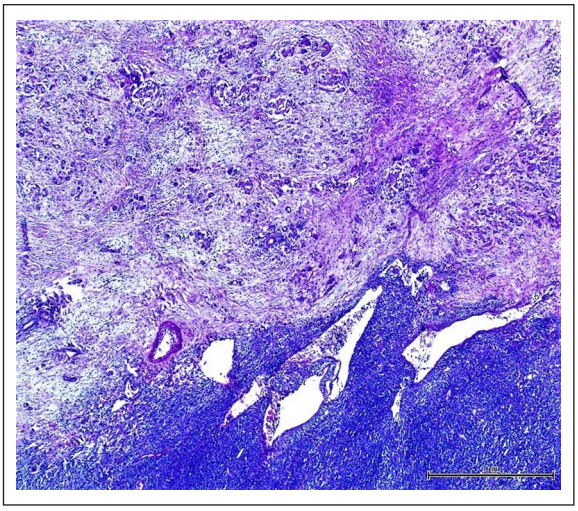

Figure 3. Magnification in hematoxylin–eosin staining ×50: infiltration of the pancreas at low magnification; normal pancreatic tissue at the top and tumor proliferation at the bottom.

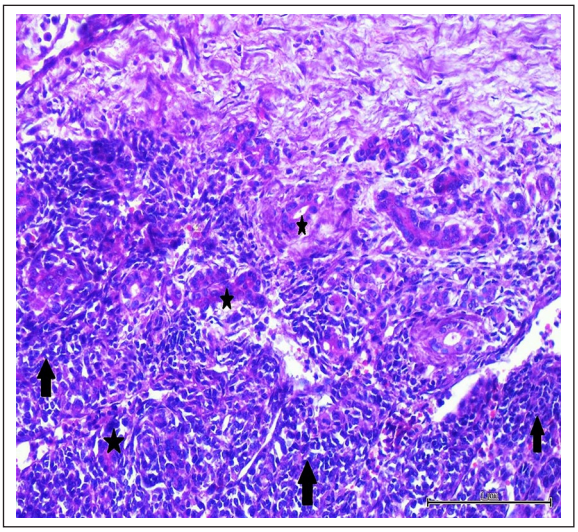

Figure 4. Magnification in hematoxylin–eosin staining ×400: infiltration of the pancreas at pancreatic acini (asterisk) tumor proliferation (arrows).

aggressive potential, metastasis occurs in around 50% of patients. The most common sites of metastasis are respectively: lungs, lymph nodes, and bone.[5]

The pancreas is an uncommon metastatic site, accounting for around 2% of pancreatic cancers.[7–9] The most usual primary malignancy of pancreatic metastasis is renal cell cancer, colorectal cancer, melanoma, and lung cancer, while pancreatic metastasis from the synovial soft tissue sarcoma is extremely rare, with only four cases recorded worldwide to date.[10–13]

We present the fifth case of pancreatic metastasis from soft tissue SS.

The metastases of sarcomas are preferentially propagated by the hematogenous pathway.[5]

The isolated pancreatic metastasis is still unclear. Reviewing the reported cases of pancreatic metastasis of SS resumed in Table 1, we notified that in all the cases, the primary tumor was located in the lower limbs. This observation mays lead to think about the presence of a shunt between the lower limbs and the pancreas. This theory has to be confirmed by autopsy to look for abnormal vascularization that may explain the isolated pancreatic metastasis.

With the presented patient, the pancreatic metastasis was asymptomatic initially, and then the patient developed symptoms such as pain and an increase in abdomen volume. Clinically, we can observe non-specific symptoms in the pancreatic metastasis from SS like pain, jaundice, nausea, anorexia, weight loss, and palpable abdominal mass as a primary pancreatic tumor.[10–13] In the reported cases the pancreatic metastasis was discovered incidentally in three cases and symptomatic in two cases.

Tumors markers in pancreatic metastasis are often negative when they were reported.

The diagnosis of pancreatic metastasis remains difficult. Imaging findings can not differentiate between the pancreatic metastasis and the primary pancreatic carcinoma.[10–13]

The imaging characteristics of synovial sarcoma pancreatic metastasis have a wide variety of differential diagnoses, as primary pancreatic cancer, pancreatic neuroendocrine tumors, pancreatic metastases from renal cell carcinoma (RCC), and other rare pancreatic tumors.[14,15]

In endoscopic ultrasonography, Krishna et al.[12] reported a cystic appearance of the mass.

In computed tomography scan (CT), the mass was heterogeneous, hypervascular, enhanced after injection of contrast product. The microcalcifications were inconstant. The dilatation of the intra and extrahepatic ducts depends on the pancreatic localization.[10,11,13]

Makino et al reported a heterogeneous enhancement on contrast-enhanced ultrasonography. The MRI features of the pancreatic metastasis showed a heterogeneous mass and were described as a hypo-, hyper-, and hyper-intense lesion on T1-, T2-, and diffusion-weighted images, respectively.[13]

18 F fluoro-2-deoxy-D-glucose (18F-FDG) positron emission tomography/computed tomography (PET/CT) in high-grade bone and soft tissue sarcoma may bring significant benefit to routine CT/MRI staging. The benefit consists of upstaging tumors and to detect any microfocus metastasis that not have been detected in the routine imaging.[16]

To date, only Makino et al performed a PET scan to stage the tumor, and there was no abnormal uptake in the whole body.[13] In our case, we didn't perform a PET scan due to a lack of availability at the moment of diagnostic.

Table1. The characteristics of the primary tumor of reported cases and our case of pancreatic metastasis from synovial sarcoma.

Author	Sex	Age (Y)	Location	treatment	Recurrence	Interval of recurrence	Recurrence location	Treatment of recurrence
Yamamoto et al.[10]	F	26	Right thigh	Surgical resection	Yes	24 months	Local + lungs	Surgical resection
Patel et al.[11]	F	34	Left thigh	Wide resection + RT	No	–	–	–
Krishna et al.[12]	M	37	Right ilium + left glenoid	NT	–	–	–	–
Makino et al.[13]	M	32	Left pelvis + femur	Wide resection + CT + RT	No	–	–	–
Our case	M	30	Left thigh	Surgical resection	Yes	6 months	Local	Wide resection + CT + RT

F: female; M: male; Y: years; RT: radiotherapy; CT: chemotherapy.

Table 2. Radiologic characteristics of reported cases and our case of pancreatic metastasis from synovial sarcoma.

Authors	Imaging methods	Size (mm)	location	Description
Yamamoto et al.[10]	CT	UF	Head	Heterogenous
Patel et al.[11]	CT	80	Head	Heterogenous, dilatation of the intrahepatic and extrahepatic ducts to the level of the pancreas.
Krishna et al.[12]	CT/EUS	19, and 12	Tail	Cystic appearance, septated, and had a thick wall.
Makino et al.[13]	CT/CEUS/MRI/ PET CT	35	Body	CT: Heterogeneous, enhanced hypervascular mass. CEUS: Heterogeneous enhancement MRI: hypo-, hyper-, and hyper-intense lesion on T1, T2-, and diffusion-weighted images, respectively PET CT: low uptake
Our case	CT	150	Tail	CT: Heterogeneous, enhanced mass.

CT: computed tomography scan; EUS: Endoscopic ultrasound; CEUS: Contrast-enhanced ultrasonography, MRI: Magnetic resonance imagery; PET CT: positron emission tomography-computed scan; UF: unspecified.

We summarized the radiologic characteristics in the table below of the reported cases (Table 2).

As we have reported there is no pathognomonic clinical, radiological or biological sign of pancreatic metastasis from SS. However, the diagnosis of pancreatic SS metastasis still relies on medical SS history and histological findings.

We performed a CT guided biopsy to confirm the diagnosis of pancreatic metastasis from SS. Diagnostic confirmation can be was obtained by biopsy either under CT scan control or under echoendoscopy.[11–13] in one case the diagnosis of pancreatic metastasis from SS was obtained after pancreatectomy (Table 3).[10]

Histological findings of pancreatic metastasis from SS are similar to the primary tumor.

Histologically, SS is subdivided into three subtypes: Monophasic type consisting only of spindle cells (50%–60%), biphasic type consisting of both epithelial and spindle cell components (20%–30%), and poorly differentiated type (15%–20%).[3,4] The prognostic of monophasic and biphasic SS is similar.[2] However, the poorly differentiated type clinical path seems to be aggressive with early recurrence and metastasis.[20]

In four of the reported cases, the histological subtype of SS was monophasic.

On immunohistochemistry, synovial sarcoma is positive for keratins and EMA, bcl-2, and transducin-like enhancer of split-1, and negative for desmin and a-SMA, and CD34.[3,17,21,22] However, the sensitivity and specificity of these markers are insufficient.[17–19]

SS is characterized by the presence of a pathognomonic translocation between chromosomes X and 18, t(X;18) (p11.2;q11.2), which results in several SS18:SSX fusion proteins expression. The most common of which are SS18-SSX1, SS18:SSX2, and much more rarely, SS18:SSX4. In 95% of patients, fusion is detectable and constitutes an effective diagnostic tool.[23]

In our case we identified the same histologic features of the primary SS (monophasic), however, the genetic identification of the SS18-SSX1 or SS18-SSX2 fusion gene wasn't performed.

The standardized treatment of primary localized SS consists of wide surgical resection of the tumor followed by radiotherapy in high-risk patients (i.e. tumor $>$ 5 cm, grade 3, and deeply located).[24,25]

Doxorubicin and ifosfamide regimen are also considered for patients with localized SS in both the neoadjuvant and adjuvant settings.[24–26]

SS is generally considered a high-grade sarcoma, characterized by a poor prognosis, with expected 5-year survival

Table 3. Diagnosis and treatment modalities of reported cases and our case of pancreatic metastasis from synovial sarcoma and outcomes.

Author	Biopsy	Histological subtype	Interval between primary/last recurrence and PM, Y	Number of PM	Treatment	Adjuvant therapy	Prognosis
Yamamoto et al.[17]	ND	NA	2	1	PPPD	No	DFS 6 years
Patel et al.[18]	CT-GB	Monophasic	10	1	Biliary drainage	NA	NA
Krishna et al.[19]	EUS-FNA	Monophasic	0	2	NA	NA	NA
Makino et al.[13]	EUS-FNA	Monophasic	4	1	Laparoscopic DP	CT: AI + ICE	DFS 30 months
Our case	CT-GB	Monophasic	1.25	1	DP + splenectomy + partial resection of the transverse colon.	CT: ID	DFS 6 months

ND: not done; NA: not available; Y: years; CT-GB: computed tomography-guided biopsy; EUS-FNA: endoscopic ultrasound-guided fine-needle aspiration; PM: pancreatic metastasis; DP: distal pancreatectomy; PPPD: pylorus-preserving pancreaticoduodenectomy; CT: chemotherapy; AI: adriamycin/ifosfamide; ICE: ifosfamide, carboplatin, and etoposide; ID: ifosfamide and doxorubicin; DFS: disease-free survival.

ranging from 50% to 60% in adult patients and 5-year metastatic disease-free survival (DFS) ranging from 40% to 60%.[27,28]

The treatment of SS metastasis remains non-codified. To date, there are only 4 cases of pancreatic metastasis from SS, and only 2 cases had a surgical treatment.[10–13]

We had an isolated pancreatic metastasis, therefore we have opted for a wide surgical resection: a caudal splenopancreatectomy with partial resection of the transverse colon followed by 4 cycles of high-dose ifosfamide and doxorubicin.

Due to the rarity of the pancreatic metastasis from SS, there is no evidence of treatment guidelines, and the therapeutic strategy has been extrapolated from the treatment of pulmonary metastases from SS and treatment of isolated pancreatic metastasis from other cancer types.[7–9,29,30]

In the case of pulmonary metastasis from SS, long-term survival was observed in the case of complete resection of the metastasis.[29,30] Moreover, the efficacy of pancreatic metastasectomy in different cancer forms such as RCC has been demonstrated.[7–9]

Strobel et al. defined four factors associated with a good prognosis after resection for pancreatic metastases from different malignant tumors: primary RCC, a >3-year interval between resection of the primary tumor and development of pancreatic metastases, isolated pancreatic metastases, and no prior recurrence.[9]

There were only two cases that have been treated surgically (Table 3). The first case met one criterion, she had a pancreaticoduodenectomy without adjuvant chemotherapy and the patient achieved a disease-free survival period of >6 years after resection.[10] the fourth case met 3 criteria, he underwent laparoscopic distal pancreatectomy followed by chemotherapy and the patient achieved 30 months disease-free.[13] Our case met one criterion of the Strobel factors.

The standard frontline chemotherapy in SS is anthracycline in advanced SS, whereas the combination of an anthracycline with ifosfamide is a heated topic that is mostly a histology-driven decision.[31]

Thus, in first-line chemotherapy for patients with advanced disease, the options are anthracycline as a single agent or combined with ifosfamide, provided that the regimen associated with the best expected antitumor effect is the combination, with an expected response rate (RR) ranging between 25% and 60%.[31–33]

Trabectenid has demonstrated an antitumor effect in patients resistant to anthracycline.[34–36]

Tyrosine kinase inhibitors have some activity in SS, but pazopanib is the only one approved for the treatment of SS. Metabolic therapy, molecular targets, and immunotherapy for advanced SS are under investigation.[26]

In conclusion, we have presented a rare entity of pancreatic metastasis from SS that was treated by splenopancreatectomy with partial resection of the transverse colon followed by chemotherapy. Within our presented case we have highlighted the importance of monitoring late postoperative complications. However pancreatic metastasectomy can be a therapeutic approach if the metastasis is unique.

Further cases are needed to establish the treatment guidelines of this rare entity.

Authors' contributions

Concepts: Chargui Riadh; Design: Bouhani Malek; Definition of intellectual content: Bouhani Malek; Literature search: Jaidane Olfa; Clinical studies: Bouhani Malek; Experimental studies: none; Data acquisition: Slimene Maher; Materials: Sakhri Saida/ Kamoun Salma; Data analysis: Jaidane Olfa; Statistical analysis: None; Manuscript preparation: Bouhani Malek; Manuscript editing: Bouhani Malek; Manuscript review: Khaled Rahal; Guarantor/ Supervision: Khaled Rahal.

Declaration of conflicting interests

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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References

1. Clark MA, Fisher C, Judson I, et al. Soft-tissue sarcomas in adults. *N Engl J Med* 2005; 353: 701–711.
2. Takenaka S, Ueda T, Naka N, et al. Prognostic implication of SYT-SSX fusion type in synovial sarcoma: a multi-institutional retrospective analysis in Japan. *Oncol Rep* 2008; 19: 467–476.
3. Murphey MD, Gibson MS, Jennings BT, et al. From the archives of the AFIP: imaging of synovial sarcoma with radiologic-pathologic correlation. *Radiographics* 2006; 26: 1543–1565.
4. Bakri A, Shinagare AB, Krajewski KM, et al. Synovial sarcoma: imaging features of common and uncommon primary sites, metastatic patterns, and treatment response. *AJR Am J Roentgenol* 2012; 199: W208–W215.
5. 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: 437–444.
6. Roland CF and van Heerden JA. Nonpancreatic primary tumors with metastasis to the pancreas. *Surg Gynecol Obstet* 1989; 168: 345–347.
7. Reddy S, Edil BH, Cameron JL, et al. Pancreatic resection of isolated metastases from nonpancreatic primary cancers. *Ann Surg Oncol* 2008; 15: 3199–3206.
8. Reddy S and Wolfgang CL. The role of surgery in the management of isolated metastases to the pancreas. *Lancet Oncol* 2009; 10: 287–293.
9. Strobel O, Hackert T, Hartwig W, et al. Survival data justifies resection for pancreatic metastases. *Ann Surg Oncol* 2009; 16: 3340–3349.
10. Yamamoto H, Watanabe K, Nagata M, et al. Surgical treatment for pancreatic metastasis from soft-tissue sarcoma: report of two cases. *Am J Clin Oncol* 2001; 24: 198–200.
11. Patel S, Martins N, Yantis R, et al. Endoscopic management of metastatic synovial sarcoma to the pancreas. *Pancreas* 2006; 33: 205–206.
12. Krishna SG, Rao BB and Lee JH. Endoscopic sonography and sonographically guided fine-needle aspiration biopsy in the diagnosis of unusual pancreatic metastases from synovial sarcoma. *J Clin Ultrasound* 2014; 42: 180–182.
13. Makino Y, Shigekawa M, Kegasawa T, et al. A case report of pancreatic metastasis from synovial sarcoma successfully treated by metastasectomy with adjuvant chemotherapy. *Medicine (Baltimore)* 2016; 95(39): e4789.
14. Raman SP, Hruban RH, Cameron JL, et al. Pancreatic imaging mimics: part 2, pancreatic neuroendocrine tumors and their mimics. *AJR Am J Roentgenol* 2012; 199: 309–318.
15. Makino Y, Imai Y, Fukuda K, et al. Sonazoid-enhanced ultrasonography for the diagnosis of an intrapancreatic accessory spleen: a case report. *J Clin Ultrasound* 2011; 39: 344–347.
16. Macpherson RE, Pratap S, Tyrrell H, et al. Retrospective audit of 957 consecutive 18F-FDG PET–CT scans compared to CT and MRI in 493 patients with different histological subtypes of bone and soft tissue sarcoma. *Clin Sarcoma Res* 2018; 8(1): 9.
17. Terry J, Saito T, Subramanian S, et al. TLE1 as a diagnostic immunohistochemical marker for synovial sarcoma emerging from gene expression profiling studies. *Am J Surg Pathol* 2007; 31: 240–246.
18. Folpe AL, Schmidt RA, Chapman D, et al. Poorly differentiated synovial sarcoma: immunohistochemical distinction from primitive neuroectodermal tumors and high-grade malignant peripheral nerve sheath tumors. *Am J Surg Pathol* 1998; 22: 673–682.
19. 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: 1434–1440.
20. Changchien YC, Tátrai P, Papp G, et al. Poorly differentiated synovial sarcoma is associated with high expression of enhancer of zeste homologue 2 (EZH2). *J Transl Med* 2012; 10: 216.
21. Thway K and Fisher C. Synovial sarcoma: defining features and diagnostic evolution. *Ann Diagn Pathol* 2014; 18: 369–380.
22. Hirakawa N, Naka T, Yamamoto I, et al. Overexpression of bcl-2 protein in synovial sarcoma: a comparative study of other soft tissue spindle cell sarcomas and an additional analysis by fluorescence in situ hybridization. *Hum Pathol* 1996; 27: 1060–1065.
23. Fletcher CDM, Bridge JA, Hogendoorn P, et al, (eds.) *World Health Organization classification of tumours. Pathology and genetics of tumours of soft tissue and bone*. Lyon: IARC Press, 2013, pp.80–82.
24. 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: 8191–8197.
25. Von Mehren M, Randall RL, Benjamin RS, et al. Soft tissue sarcoma, version 2.2016, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw* 2016; 14: 758–786.
26. Stacchiotti S and Van Tine BA. Synovial sarcoma: current concepts and future perspectives. *J Clin Oncol* 2018; 36(2): 180–187.

27. Naing KW, Monjazeb AM, Li CS, et al. Perioperative radiotherapy is associated with improved survival among patients with synovial sarcoma: a SEER analysis. *J Surg Oncol* 2015; 111: 158–164.
28. Vlenterie M, Ho VK, Kaal SE, et al. Age as an independent prognostic factor for survival of localised synovial sarcoma patients. *Br J Cancer* 2015; 113: 1602–1606.
29. Billingsley KG, Burt ME, Jara E, et al. Pulmonary metastases from soft tissue sarcoma: analysis of patterns of diseases and postmetastasis survival. *Ann Surg* 1999; 229: 602–610. discussion 610–612.
30. Stanelle EJ, Christison-Lagay ER, Wolden SL, et al. Pulmonary metastasectomy in pediatric/adolescent patients with synovial sarcoma: an institutional review. *J Pediatr Surg* 2013; 48: 757–763.
31. Sleijfer S, Ouali M, van Glabbeke M, et al. Prognostic and predictive factors for outcome to firstline ifosfamide-containing chemotherapy for adult patients with advanced soft tissue sarcomas: an exploratory, retrospective analysis on large series from the European Organization for Research and Treatment of Cancer-Soft Tissue and Bone Sarcoma Group (EORTC-STBSG). *Eur J Cancer* 2010; 46: 72–83.
32. Eilber FC, Brennan MF, Eilber FR, et al. Chemotherapy is associated with improved survival in adult patients with primary extremity synovial sarcoma. *Ann Surg* 2007; 246: 105–113.
33. Spurrell EL, Fisher C, Thomas JM, et al. Prognostic factors in advanced synovial sarcoma: an analysis of 104 patients treated at the RoyalMarsden Hospital. *Ann Oncol* 2005; 16: 437–444.
34. Le Cesne A, Cresta S, Maki RG, et al. A retrospective analysis of antitumour activity with trabectedin in translocation-related sarcomas. *Eur J Cancer* 2012; 48: 3036–3044.
35. Sanfilippo R, Dileo P, Blay JY, et al. Trabectedin in advanced synovial sarcomas: a multicenter retrospective study from four European institutions and the Italian Rare Cancer Network. *Anticancer Drug* 2015; 26: 678–681.
36. Takahashi M, Takahashi S, Araki N, et al. Efficacy of trabectedin in patients with advanced translocation-related sarcomas: pooled analysis of two phase II studies. *Oncologist* 2017; 22: 979–988.