

# A case report of pancreatic metastasis from synovial sarcoma successfully treated by metastasectomy with adjuvant chemotherapy

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## Abstract

**Introduction:** Synovial sarcoma is a malignant soft tissue sarcoma which arises near joints. The most frequent metastasis sites of synovial sarcoma are the lungs, lymph nodes, and bone. Pancreatic metastasis is quite rare; only 3 cases have been reported worldwide to date. We herein present the 4th case of pancreatic metastasis from synovial sarcoma.

**Methods and Results:** A 32-year-old man underwent extended excision of synovial sarcoma in the left pelvis and femur in 2009. In 2013, follow-up contrast-enhanced computed tomography revealed a 35-mm heterogeneously enhanced mass in the pancreas body. Endoscopic ultrasound-guided fine needle aspiration of the mass revealed a diffuse proliferation of atypical spindle cells in a fascicular arrangement. Because the histology was quite similar to the resected specimen of synovial sarcoma in 2009, the mass was suspected to be a metastasis from synovial sarcoma. Laparoscopic distal pancreatectomy with adjuvant adriamycin/ifosfamide chemotherapy was subsequently performed. Synovial sarcoma-specific SS18-SSX1 (synovial sarcoma translocation, chromosome 18-synovial sarcoma X1) or SS18-SSX2 chimera mRNA was detected in the resected specimen, confirming the diagnosis of metastasis from synovial sarcoma. The patient did well for 30 months without recurrence.

**Conclusion:** This case suggests that pancreatic metastasis from synovial sarcoma can be successfully treated by metastasectomy with adjuvant chemotherapy.

**Abbreviations:** AI = adriamycin/ifosfamide, CT = computed tomography, EMA = epithelial membrane antigen, EUS = endoscopic ultrasound, FNA = fine needle aspiration, MRI = magnetic resonance imaging, RCC = renal cell carcinoma, RT-PCR = reverse transcriptase-polymerase chain reaction, SMA = smooth muscle actin, SS18-SSX1 = synovial sarcoma translocation, chromosome 18-synovial sarcoma X1.

**Keywords:** EUS-FNA, metastasectomy, pancreatic metastasis, synovial sarcoma

## 1. Introduction

Soft tissue sarcoma is a rare mesenchymal neoplasm that accounts for about 1% of all adult cancers.<sup>[1]</sup> Synovial sarcoma,

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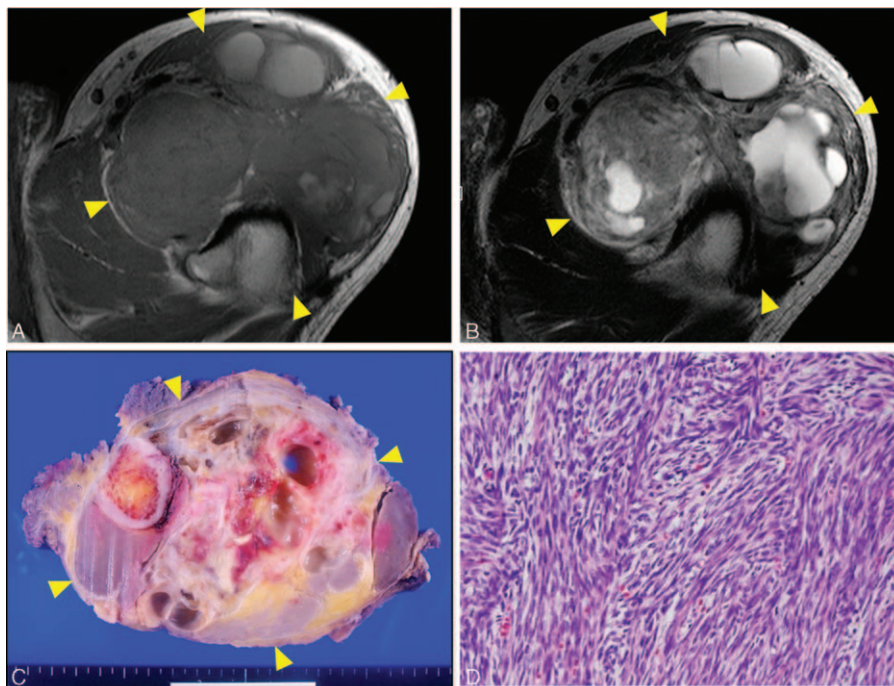
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first reported in 1893, is one of about 50 histological types of soft tissue sarcoma but accounts for approximately 10%.<sup>[2–4]</sup> It initially manifests as an indolent and palpable slowly growing mass. The long duration of symptoms and initial slow growth sometimes give a false impression of benign characteristics.<sup>[3]</sup> However, because of its aggressive potential, metastasis occurs in approximately 50% of patients, and the most frequent sites of metastasis are the lungs (74%–81%), lymph nodes (3%–23%), and bone (10%–20%).<sup>[5]</sup> Pancreatic metastasis from synovial sarcoma is quite rare, and a standard management regimen has not been established. In this report, we present a case of solitary pancreatic metastasis from synovial sarcoma that was successfully treated by radical metastasectomy with adjuvant chemotherapy.

## 2. Case report

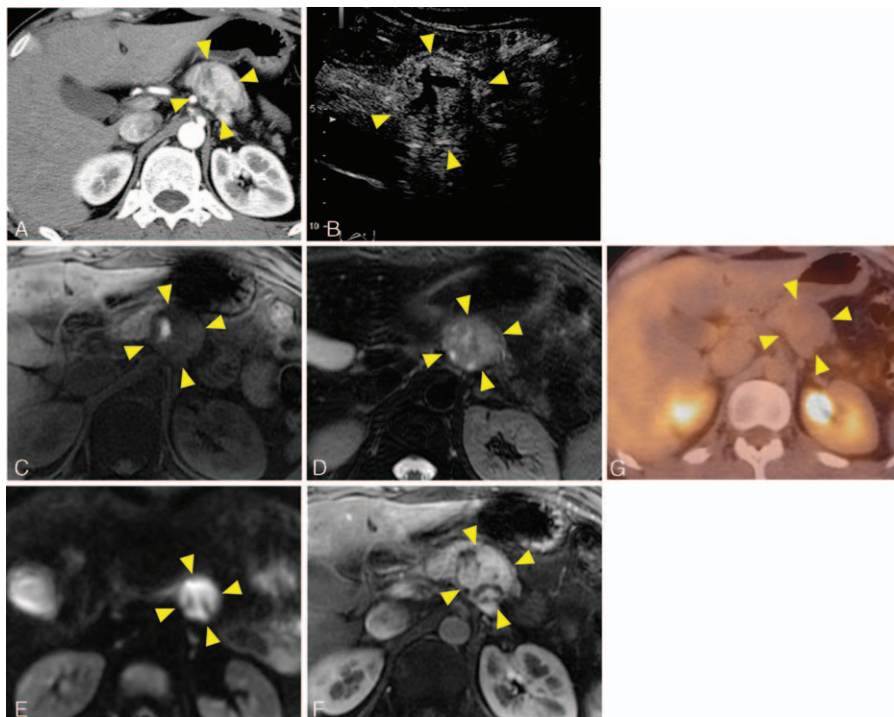
A 32-year-old man without a medical history first visited Osaka University Hospital in 2009 for the treatment of synovial sarcoma in the left pelvis and femur (Fig. 1). He underwent extended tumor resection and reconstruction with constrained total hip megaprosthesis with neoadjuvant adriamycin/ifosfamide (AI) therapy for 4 cycles, followed by adjuvant AI therapy



**Figure 1.** Synovial sarcoma (arrowheads) in the left pelvis and femur resected in 2009. (A) T1- and (B) T2-weighted images of nonenhanced magnetic resonance imaging. (C) Macroscopic and (D) microscopic appearance of the resected specimen (hematoxylin–eosin staining,  $\times 200$ ).

for 1 cycle. He was regularly followed up thereafter, and no recurrence was observed on annual computed tomography (CT) examinations until 2012.

In 2013, however, follow-up contrast-enhanced CT revealed a 35-mm heterogeneously enhanced hypervascular mass in the pancreas body (Fig. 2A). Heterogeneous enhancement was also



**Figure 2.** Imaging appearance of pancreatic metastasis from synovial sarcoma (arrowheads). (A) Arterial-phase image of contrast-enhanced computed tomography. (B) Vascular-phase image of contrast-enhanced ultrasonography. (C) T1-, (D) T2-, and (E) diffusion-weighted images and (F) arterial-phase images of gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid–enhanced magnetic resonance imaging. (G) Fluorodeoxyglucose positron emission tomography image.

observed on contrast-enhanced ultrasonography (Fig. 2B). On gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid-enhanced magnetic resonance imaging (MRI), the mass was depicted as a hypo-, hyper-, and hyper-intense lesion on T1-, T2-, and diffusion-weighted images, respectively (Fig. 2C–E). It was heterogeneously enhanced on arterial-phase images (Fig. 2F). Hepatobiliary-phase images revealed no space-occupying lesions suggesting liver metastasis. On fluorodeoxyglucose positron emission tomography, the mass showed low uptake (maximum standardized uptake value of 2.3) (Fig. 2G), and no abnormal uptake was observed in the whole body. The patient was asymptomatic, and laboratory tests of routine biochemical parameters and tumor markers including carcinoembryonic antigen, carbohydrate antigen 19–9, elastase I, and sialyl Lewis X antigen were all within their respective normal ranges.

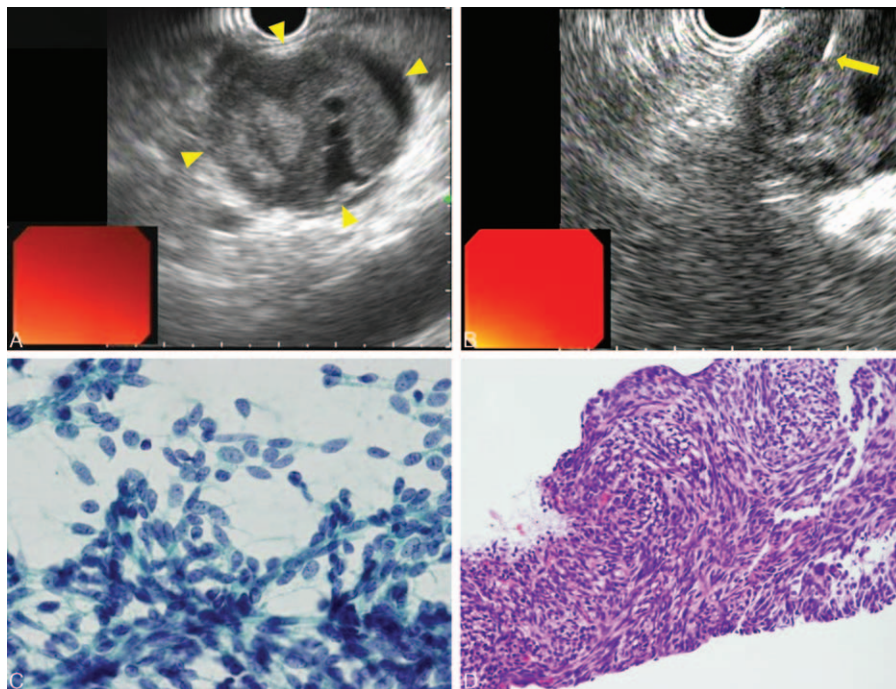
Pathological examinations included endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA). On grayscale EUS, the lesion was depicted as a well-demarcated and heterogeneous mass with abundant cystic components (Fig. 3A). Although the mass showed expansive growth and oppressed the splenic vein, no invasion was suspected. Avoiding cystic elements, a 22-gauge puncture needle was transgastrically inserted into the mass, and specimens were collected (Fig. 3B). Rapid cytological examination revealed atypical spindle-shaped cells (Fig. 3C). Histological examination revealed a uniform population of small spindle-shaped cells in a fascicular arrangement (Fig. 3D). Immunohistochemically, these cells were positive for bcl-2 and negative for pan-cytokeratin, epithelial membrane antigen (EMA), chromogranin A, synaptophysin, and vimentin. Ki-67 antigen staining was about 10% positive. Although the immunohistochemical pattern was not typical for synovial sarcoma, the mass was considered to be pancreatic metastasis from synovial sarcoma because these microscopic findings were quite similar to the resected specimen of monophasic synovial sarcoma in 2009.

We judged that the metastatic lesion could be completely resected without residual tissue and performed laparoscopic distal pancreatectomy under adequate informed consent. Although a minor pancreatic fistula occurred postoperatively, it was conservatively treated and resolved in a short period of time. The resected tumor was a well-circumscribed mass measuring 45 × 30 mm with prominent cystic changes (Fig. 4A, B). Microscopic examination revealed a monophasic appearance comprising only spindle cells, similar to the biopsy sample obtained by EUS-FNA, and glandular structures were not found (Fig. 4C). Immunohistochemistry revealed a positive reaction to bcl-2 (diffuse) and EMA (focal) (Fig. 4D, E) and a negative reaction to pan-cytokeratin,  $\alpha$ -smooth muscle actin (SMA), CD34, and c-kit. Synovial sarcoma-specific SS18-SSX1 (synovial sarcoma translocation, chromosome 18-synovial sarcoma X1) or SS18-SSX2 chimera mRNA was detected by reverse transcriptase-polymerase chain reaction (RT-PCR), which confirmed the diagnosis of pancreatic metastasis from synovial sarcoma (Fig. 4F).

The patient underwent 2 cycles of adjuvant AI chemotherapy followed by 2 cycles of ifosfamide, carboplatin, and etoposide without remarkable adverse events. At the time of this writing, he had been doing well without recurrence for 30 months postoperatively.

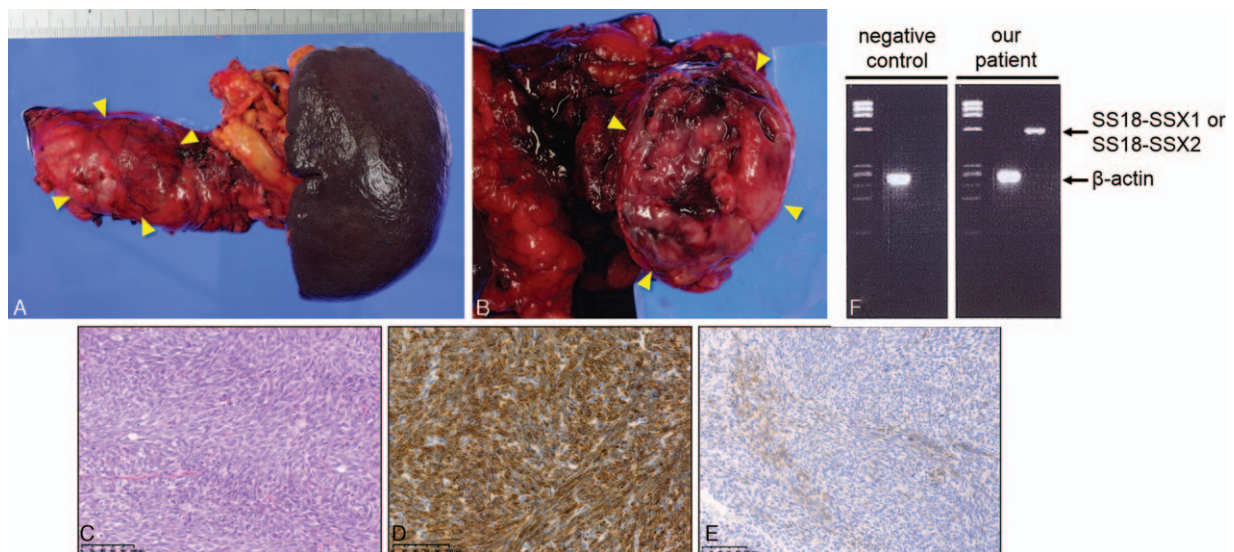
### 3. Discussion

The diagnosis of synovial sarcoma generally starts with imaging examinations. On contrast-enhanced CT/MRI, synovial sarcoma is typically depicted as a heterogeneously enhanced, well-circumscribed mass.<sup>[3,4]</sup> Because these imaging findings are not specific for synovial sarcoma, however, histological analysis is necessary for the diagnosis.<sup>[3,4,6–9]</sup> Synovial sarcoma is histologically divided into 3 subtypes: the monophasic type composed



**Figure 3.** Endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) of the pancreatic metastasis from synovial sarcoma (arrowheads). The puncture needle is indicated by an arrow. (A) Grayscale EUS, (B) FNA, (C) cytology (Papanicolaou stain,  $\times 400$ ), and (D) histology (hematoxylin–eosin staining,  $\times 200$ ) of the tumor.





**Figure 4.** Resected specimen of the pancreatic metastasis from synovial sarcoma (arrowheads). (A) Macroscopic appearance and (B) cut surface of the tumor. (C) Histology (hematoxylin–eosin staining,  $\times 200$ ). Immunohistochemistry for (D) *bcl-2* and (E) epithelial membrane antigen. (F) Electrophoresis of SS18-SSX1 (synovial sarcoma translocation, chromosome 18-synovial sarcoma X1) or SS18-SSX2 chimera mRNA in the tumor after reverse transcriptase-polymerase chain reaction. The primers used were as follows: forward primer, 5'-CAACAGCAAGATGCTACCA-3' and reverse primer, 5'-CACTTGCTATGCACCTGATG-3'.

only of spindle cells (50%–60%), the biphasic type composed of both epithelial and spindle cell elements (20%–30%), and the poorly differentiated type (15%–20%).<sup>[3,4]</sup> Among these histological subtypes, prognosis was reported to be not different between monophasic type and biphasic type.<sup>[2]</sup> Meanwhile, the clinical course of poorly differentiated type tends to be aggressive with early recurrence and metastasis.<sup>[10]</sup> On immunohistochemistry, synovial sarcoma is positive for epithelial markers (e.g., keratins and EMA), *bcl-2*, and transducin-like enhancer of split-1, and negative for skeletal muscle markers (e.g., desmin and  $\alpha$ -SMA) and CD34.<sup>[3,7–9]</sup> However, the sensitivity and specificity of these markers are insufficient.<sup>[9,11,12]</sup> Conversely, identification of the SS18-SSX1 or SS18-SSX2 fusion gene resulting from the chromosomal translocation t(X;18)(p11;q11), first published in 1994,<sup>[13]</sup> reportedly has a sensitivity of 94% and a specificity of 100% by RT-PCR.<sup>[14]</sup> Owing to this high diagnostic ability, demonstration of the SS18-SSX1 or SS18-SSX2 fusion gene is currently considered to be the gold standard diagnostic test for synovial sarcoma.<sup>[9,12–15]</sup>

The optimal treatment of synovial sarcoma is surgical resection, if the mass is resectable,<sup>[3,4,16]</sup> followed by adjuvant chemotherapy using adriamycin and ifosfamide.<sup>[17,18]</sup> For unresectable masses, systemic chemotherapy is usually

attempted.<sup>[16,19]</sup> Synovial sarcoma is an intermediate- to high-grade sarcoma, and the 5- and 10-year survival rates reportedly range from 36% to 76% and 20% to 63%, respectively.<sup>[3]</sup>

We have herein presented a case of pancreatic metastasis from synovial sarcoma. Pancreatic metastasis from synovial sarcoma is quite rare, and only 3 cases have been reported worldwide to date.<sup>[20–22]</sup> The clinical characteristics of these 3 cases and our case are summarized in Table 1. Both imaging and histological examinations were performed to achieve the correct diagnosis in all cases. However, the imaging features of pancreatic metastasis from synovial sarcoma have a broad range of differential diagnoses, including pancreatic neuroendocrine tumors, pancreatic metastases from renal cell carcinoma (RCC), gastrointestinal stromal tumors, paraganglioma, solitary fibrous tumors, pancreatic hamartoma, intrapancreatic accessory spleen, and others.<sup>[23,24]</sup> Some of these tumors have a histological appearance similar to that of synovial sarcoma, and immunohistochemistry is not always reliable.<sup>[9,11,12]</sup> Therefore, the presence of the SS18-SSX1 or SS18-SSX2 fusion gene should be investigated to confirm the diagnosis; ours is the only case in which its existence was proven. Because our case shows that SS18-SSX1 or SS18-SSX2 chimera mRNA can also be detected in pancreatic metastasis, demonstration of the SS18-SSX1 or SS18-SSX2 fusion gene in a

**Table 1**

**Characteristics of reported cases and our case of pancreatic metastasis from synovial sarcoma.**

Author	Sex	Age, y	Interval between primary and pancreatic metastasis, y	Number of pancreatic metastasis	Size, cm	Location	Method for histological diagnosis	Extrapancreatic metastasis	Treatment	Prognosis
Yamamoto H et al <sup>[19]</sup>	F	40	14	1	NA	Head	After operation	No	PPPD	DFS>6 years
Patel S et al <sup>[20]</sup>	F	44	10	1	8	Head	CT-guided biopsy	Yes	Biliary drainage	NA
Krishna SG et al <sup>[21]</sup>	M	38	1	2	1.9 1.2	Tail	EUS-FNA	Yes	NA	NA
Our case	M	36	4	1	3.5	Body	EUS-FNA	No	Laparoscopic DP	DFS 30 months

CT=computed tomography, DFS=disease-free survival, DP=distal pancreatectomy, EUS-FNA=endoscopic ultrasound-guided fine needle aspiration, NA=not available, PPPD=pylorus-preserving pancreaticoduodenectomy.

biopsy sample obtained by EUS-FNA might be the gold standard technique for the pretreatment diagnosis of pancreatic metastasis from synovial sarcoma.

We performed metastasectomy to treat the tumor in this case. For unresectable synovial sarcoma, adriamycin or ifosfamide-based chemotherapy is usually attempted.<sup>[16,19]</sup> However, sufficient evidence of drug therapy has not been established, and the effect is limited. Only in cases of pulmonary metastasis can long-term survival be expected by pulmonary metastasectomy if complete resection is achieved.<sup>[25,26]</sup> The question then arises regarding whether pancreatic metastasectomy enables long-term survival of patients with pancreatic metastasis from synovial sarcoma. Metastatic pancreatic cancer accounts for approximately 2% of pancreatic cancers.<sup>[27–29]</sup> Common primary tumors are lung cancer, breast cancer, RCC, malignant melanoma, and gastrointestinal cancers.<sup>[27–29]</sup> Although most patients with pancreatic metastasis are not usually candidates for resection because they are considered to have systemic micrometastasis, the effectiveness of pancreatic metastasectomy has been proven in specific cancer types such as RCC.<sup>[27–29]</sup> When considering surgical resection of pancreatic metastases, 4 factors are reportedly associated with a good prognosis after resection for pancreatic metastases from various 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.<sup>[29]</sup> With respect to synovial sarcoma, the effectiveness of pancreatectomy for metastatic lesions is completely unknown because only one case in which pancreatic metastasectomy was performed has been reported to date (Table 1). In that case, however, a disease-free survival period of >6 years was achieved after resection.<sup>[20]</sup> Similar to that case, the metastatic tumor in our case was solitary without extrapancreatic lesions. Additionally, our case met 3 of the 4 criteria previously reported to be associated with a good prognosis after pancreatic metastasectomy: a >3-year interval between resection of the primary tumor and development of pancreatic metastases, isolated pancreatic metastases, and no prior recurrence.<sup>[29]</sup> Therefore, we considered that long-term survival could be expected by pancreatic metastasectomy in our case as well. Actually, the metastatic lesion was successfully resected and the patient had been disease-free for 30 months at the time of this writing. This result suggests that pancreatic metastasis from synovial sarcoma can be successfully treated by metastasectomy unless apparent extrapancreatic metastasis is present.

In conclusion, we have presented a quite rare case of solitary pancreatic metastasis from synovial sarcoma that was successfully treated by radical metastasectomy with adjuvant chemotherapy. Pancreatic metastasectomy could be considered for pancreatic metastasis from synovial sarcoma without extrapancreatic metastasis. Additional cases should be accumulated to investigate the characteristics of patients who are indicated for metastasectomy and to establish pancreatic metastasectomy as a treatment option for pancreatic metastasis from synovial sarcoma.

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