

## Case Report

# <sup>18</sup>F-fluorodeoxyglucose PET/CT features and correlations with histopathologic characteristics in sclerosing epithelioid fibrosarcoma

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**Abstract:** Sclerosing epithelioid fibrosarcoma (SEF) is a clinicopathologically distinct variant of fibrosarcoma that is capable of recurrence and metastasis. Awareness of imaging features and histopathologic characteristics will be helpful for differential diagnosis from other common tumors. Here, we report a case of SEF metastasizing to the pancreas as a solitary mass mimicking primary pancreatic cancer, and summarize the reported cases with FDG PET/CT from the literature (n=4). PET/CT showed abnormal FDG accumulation (n=2), mild FDG uptake (n=1), or photopenic (n=1). The FDG PET/CT features are closely related to histopathologic characteristics regarding its differentiation and aggressiveness.

**Keywords:** Sclerosing epithelioid fibrosarcoma, pancreas, FDG, PET/CT

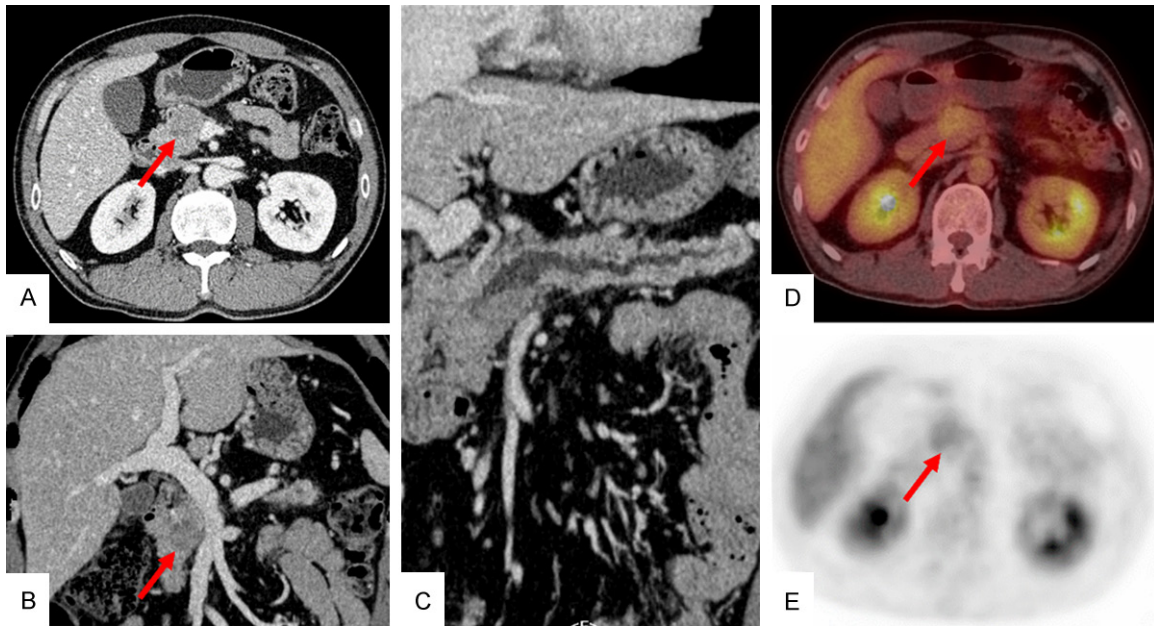
## Introduction

Sclerosing epithelioid fibrosarcoma (SEF) is a very rare mesenchymal neoplasm that exhibits a predilection for deep soft tissues, occurring most frequently in the extremities, limb girdles, trunk, and head and neck with fully malignant potential [1, 2]. It was first characterized by Meis Kindblom et al. [3] who described a series of 25 cases in 1995. Since then 37 reports on 120 patients concerned with SEF with a main focus on histopathologic and immunohistochemical features have been reported. Histologically, the tumor is characterized by a predominant population of small to medium size epithelioid cells, arranged in nests, cords and sheets, embedded in a hyalinized collagenous stroma. The tumor cells are diffusely and strongly staining positive for vimentin [1, 3-21]. The imaging features just are mentioned in few cases and lacks detail. To the best of our knowledge, only 3 cases have reported the fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) finding of SEF.

We recently encountered a case of SEF primary in the buttock and metastasized to the pancreas as a solitary mass 6 years after primary tumor resection. The purpose of this essay was to investigate the relations of histopathologic features and FDG PET/CT presentations of this tumor, and review the FDG PET/CT features of SEF from the literature.

## Case report

A 42-year-old man presented with a one month history of upper abdominal pain. He denied nausea, diarrhea, jaundice, fever, or weight loss. Abdominal ultrasonography disclosed an approximately 2.0 cm well delineated hypoechoic lesion in the head of the pancreas. Serum amylase, carbohydrate antigen 19-9, carcinoembryonic antigen, alpha-fetoprotein, and carbohydrate antigen 242 were within normal ranges. CT also confirmed a solid lesion measuring 2.3×2.9 cm in the head of the pancreas, with homogenous and progressive enhancement after contrast administration (**Figure 1A**). Three dimensional reconstruction showed the lesion



**Figure 1.** A. Portal venous phase of contrast enhanced CT shows a light enhanced mass in the head of the pancreas. B. Curved planar reformation shows the mass is adjacent to the portal vein without gross invasion. C. The distal pancreatic duct is obviously dilated. D, E. Mild FDG signal within the mass in PET/CT scan.

was adjacent to the superior mesenteric vein and the portal vein, without apparent vascular invasion or encasement (**Figure 1B**). Dilation of the distal pancreatic duct was noted (**Figure 1C**). The lesion was lightly radioactive in FDG PET/CT image, which was indeterminate for diagnosis, with an average and maximum standardized uptake value (SUV) being 1.5 and 2.4, respectively (**Figure 1D** and **1E**). The delayed PET/CT images acquired two hours after dose administration remained unchanged. No other hypermetabolic lesion was noted.

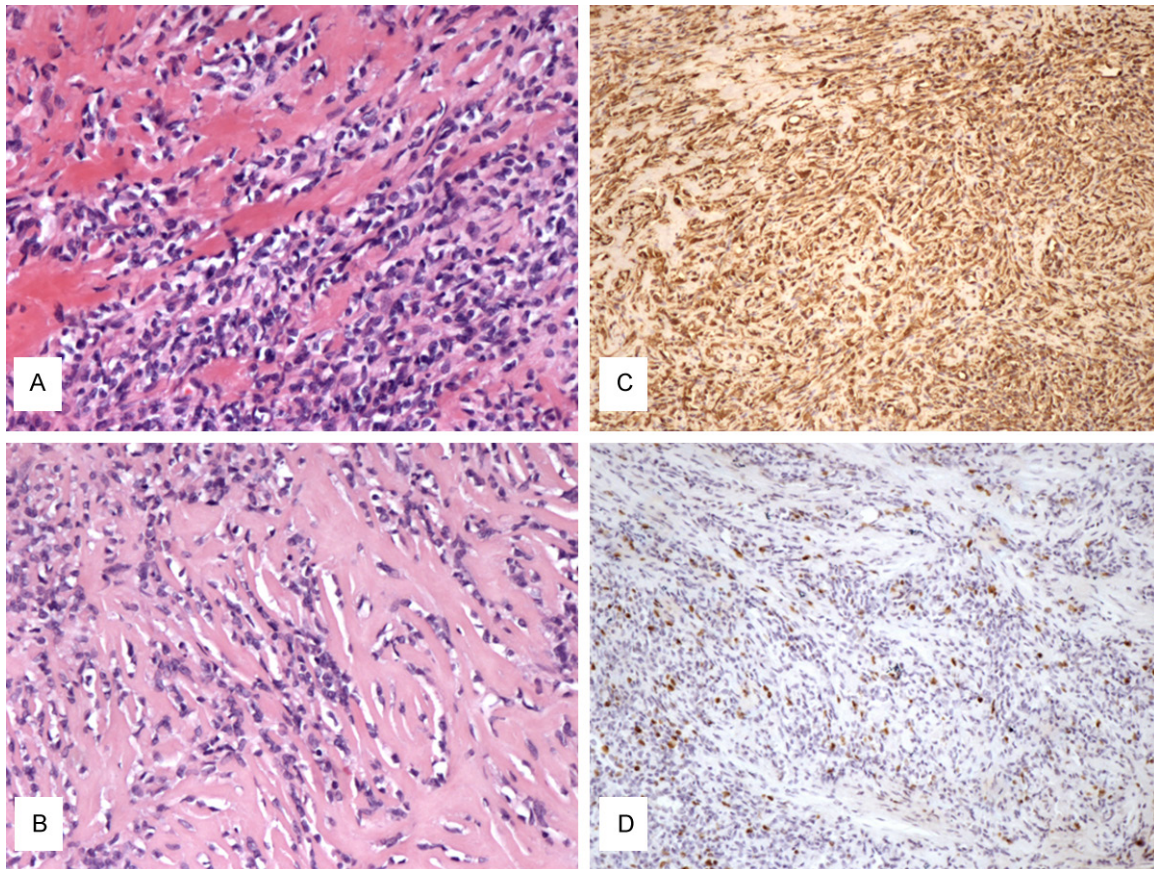
With a preoperative diagnosis of primary malignant pancreatic tumor, pancreaticoduodenectomy was performed. The tumor was successfully excised with a clear margin. Grossly, the tumor appeared multinodular and well circumscribed, with a firm and white cut surface. Histologically, the tumor cells were arranged in distinct nests, cord, and clusters, surrounded by a prominent sclerotic collagen matrix. The tumor cells were small, bland and epithelioid, and had a moderate amount of pale or clear cytoplasm (**Figure 2A** and **2B**). Little nuclear pleomorphism was observed. Mitotic figures were present at a rate of 8 mitoses per 10 high power fields (HPF) at  $\times 400$  magnification. No necrosis was noted. Immunohistochemically, the tumor cells showed strong cytoplasmic positiv-

ity for vimentin (**Figure 2C**). Staining for AE1/AE3, chromogranin, synaptophysin, smooth muscle actin (SMA), desmin, CD117, S-100 protein, HMB45, CD21, CD35, and bcl-2 were negative. Ki67 proliferation index was 15% in tumor cells (**Figure 2D**). Based on the results of histopathological examination and immunohistochemical patterns, the tumor was finally diagnosed as SEF.

Interestingly, we noted that a soft tissue tumor in the right buttock which was considered as fibrosarcoma in a local hospital was surgically removed six years ago. The specimen of the tumor was submitted to our hospital for further consultation. Retrospective histological examination revealed that the lesion was consistent with SEF. Thus, we established the diagnosis of pancreatic metastatic SEF, which was primary of the gluteal soft tissue.

The patient was treated postoperatively with two cycles of chemotherapy. However, this chemotherapy was discontinued because of adverse event including severe vomiting and weight loss. At the recent follow-up PET/CT 16 months after the pancreatic surgery, he remains in good condition, with no evidence of disease.





**Figure 2.** A, B. The tumor is composed of small to medium size epithelioid cells with pale or clear cytoplasm. The tumor cells are arranged in nests, cords and clusters, and are embedded in a dense hyalinized collagenous matrix. C. The tumor cells show diffuse and strong reactivity for vimentin. D. Ki-67 labeling index is 15%.

## Results

We summarize the prior reported cases of SEF with FDG PET/CT features. In our review, there are 4 cases in total including our case. The clinical features and follow-up of all cases are detailed in **Table 1**. All the patients are middle-aged male. The primary lesions were located in the abdominal wall, liver, lung, and gluteal region. Apart from surgical resection of the primary lesion, all of 4 patients received chemotherapy or radiotherapy. Two patients experienced local recurrences, and successful surgical removal of the relapsed lesions were achieved. All of 4 patients had metastasis at various time point in the course of disease, and the patient with hepatic SEF presented with intrahepatic metastases and tumor thrombus in portal vein at the time of primary diagnosis. The patients were followed up for several months to 12 years, and all of 4 patients were surviving for alive till the time of follow up.

FDG PET/CT was performed at the time of primary diagnosis in 2 patients, and another 2 patients underwent the procedure during follow up. All the FDG PET/CT and histopathological features of the SEF lesions are summarized in **Table 2**. The size of the tumor was from 2.5 cm to 6.8 cm. The accurate size of the bone lesion was not documented, but they were restricted to the humerus and rib and did not invade the adjacent soft tissue. The lesions showed quite different FDG uptake. Abnormal accumulation of FDG was noted in the bone metastases which occurred 12 years after primary diagnosis [22], and the huge hepatic lesion with intrahepatic metastasis also showed increased FDG uptake [23]. However, the pulmonary SEF was FDG negative [20].

In our case, only mild FDG signal within the pancreatic lesion was noted, which was in accordance to its low grade histological features: the tumor cells showing little pleomorphism were

embedded in a dense hyalinized collagenous stroma, mitosis were present but not numerous, Ki-67 index was 15%, and necrosis was absent. In contrast to our case, the reported FDG-avid lesion in the bone well corresponded to its aggressive histological appearance with the following aspects: the tumor was composed of significantly hypercellular dysplastic cells, with high nuclear/cell rate and prominent nuclear polymorphism, mitosis was 30 to 40 cells per 10 HPF, and Ki-67 index was 60%. In addition, necrosis was frequently found within the lesion [22]. In another FDG-positive SEF primary in the liver, intrahepatic metastasis, tumor thrombi in the portal vein, and peripheral invasion, that suggest the aggressive biological behavior were histologically identified [23]. The FNCLCC grade of the lung lesion was grade 2, score 5 (3, 1, 1), and the lesion was photopenic in FDG PET/CT image [20]. The poor differentiation of the tumor cells and FDG negativity seems to be discrepant, but the hypocellularity with apparent sclerosing fibrosis and hyalinosis of the lung lesion is an explanation. The disease then spread to mediastinum, bone, and kidney 8 months later, and the follow up PET/CT showed all the metastatic lesions were FDG-avid, which is consistent with its poor differentiation [20].

## Discussion

SEF was previously viewed as a relatively indolent malignant neoplasms, because of the quite long median survival time with being 11 years, and its low grade histopathological classification [3-5, 24]. However, it is fully malignant and capable of metastases and recurrences, often several months to years after surgical removal [1, 3-6, 8, 24]. According to literature to date, the pooled metastasis, recurrence and mortality rates of the reported SEFs with available follow up data were 65.1%, 46.6%, and 27.9%, respectively [1-8, 10-16, 18-20, 22-34]. Only 33.0% of the patients were with no evidence of disease in reported follow-ups (average 52 months, range 1 month to 17 years) [2-4, 7, 8, 12, 14, 16, 23, 25, 29, 32, 33]. The frequent metastases were to the lung [1, 3, 6, 8, 9, 11, 13, 15, 19, 20, 24, 27, 30, 32, 34, 35], skeleton [3, 6, 8, 10, 15, 16, 18, 20, 22, 31, 32], chest wall/pleura [3, 4, 6, 16, 22, 28, 30, 31, 36], liver [1, 10, 17, 18, 27, 31], and regional lymph node [3, 8, 15, 20, 31, 32]. Other possible sites were peritoneum/omentum [1, 27, 31,

32], pericardium [3], brain/dural [3, 26], breast [8], soft tissue [1, 8, 11], kidney [15, 20], and stomach [15]. SEF metastasizing to the pancreas has never been reported yet.

Diagnosing SEF preoperatively with imaging modality is challenging. It is due to its rare occurrence and confusing imaging characteristics. In fact, SEF can mimic other common soft tissue tumor, moreover, the diagnosis of SEF primarily in visceral organs is even more difficult. Therefore, imaging and histopathology of SEF should be well known, and at least the correct diagnosis of malignancy should be achieved due to its discouraging recurrent and metastatic rates. FDG PET/CT is a widely used imaging modality for the workup of neoplasms. In our study, we find the FDG uptake of SEF is various from photopenic to abnormal increased uptake. Furthermore, the FDG uptake of SEF is closely associated with its histopathologic features regarding differentiation and aggressiveness. Such difference of FDG uptake perfectly reveals the heterogeneity of each lesion. The high-grade SEF is probably FDG-avid, and the low-grade one is likely to show less FDG uptake.

Although there are no established treatment regimens of SEF due to its rareness, surgical resection is the only generally acknowledged preferable treatment [2]. However, radical excision of solitary metastasis of SEF has not been reported in the literature, let alone exceedingly rare pancreatic metastasis. In our case, FDG PET/CT played an essential role in re-staging, to confirm that the patient was free of distant metastasis except for the solitary pancreatic lesion. Thus, radical excision for pancreatic metastasis could be an optimizing treatment choice. The patient remains in good health with no evidence of disease in the follow up 16 months after excision of the pancreatic metastasis. The value of adjuvant therapy in the control of SEFs remains unclear [1-3, 6, 18, 24, 29].

The prognosis of patients with SEF varies. Some patients experienced progressive disease and died within 1 year [10, 32], and some survived more than 15 years [3, 16]. With respect to location, Bilsky et al. [6] reported SEF arising in the neuraxis appear to display a more aggressive course, as these patients developed local recurrences and distant metastasis shorter than those in soft tissues. A systemic

## FDG PET/CT and histopathologic characteristics in SEF

**Table 1.** Reported cases of SEF with FDG PET/CT procedure

Gender/ Age	Primary location	Treatment	Local recur- rence	metastases	PET/CT time point	Follow-up	Author
M/30	abdominal wall	Resection of the primary, chemo- and radiotherapy	5 yr*	Bone, pleural	12 yr* after primary diag- nosis	12 yr AWD*	Kanno et al. [22]
M/39	Liver	Resection of the primary and recurrence, chemotherapy	7 mo*	Liver, portal vein	primary diagnosis	18 mo NED*	Tomimaru et al. [23]
M/54	Lung	Resection of the primary, chemo- and radiotherapy	no	mediastinum, bone, kidney	primary diagnosis	Months AWD*	Leisibach et al. [20]
M/42	gluteal region	Resection of the primary and metastasis, chemotherapy	no	pancreas	6 yr* after primary diagnosis	7.5 yr NED*	Present case

\*mo, month; yr, year; AWD, alive with disease; NED, no evidence of disease.

**Table 2.** FDG PET/CT and histopathologic features of SEF

location	Size (cm)	PET	Histological features						Ki-67	
			Local invasion	cellularity	Mitosis (10/HP)	Atypia/differen- tiation	necro- sis			
Humerus, rib (metastasic)	NR*	abnormal FDG accumulation	NR*	hyper	30-40	significant atypia	frequent	60%	Kanno et al. [22]	
Liver (primary)	6.8×5.4	abnormal FDG accumulation	IVC*, diaphragm, tumor thrombi	NR*	NR*	NR*	NR*	30%	Tomimaru et al. [23]	
Lung (primary)	2.5	FDG negative	none	hypo with zones of fibrous	0-9	undifferentiated	<50%	NR*	Leisibach et al. [20]	
Pancreas (metastatic)	2.9	Mild FDG uptake	none	some hyper area	8	little atypia	no	15%	Present case	

\*NR, not reported; IVC, inferior vena cava.



review showed that SEF of the head and neck had worse prognosis compared with primaries in other locations [2]. FDG PET/CT can be used to evaluate the metabolic tumor burden affecting the whole body, and the metabolic indices of the tumor have been shown to be an independent prognostic factors in many neoplasms, e.g., lung cancer [37, 38], head and neck cancer [39], gastrointestinal carcinoma [40, 41], ovarian cancer [42], lymphoma [43], and soft tissue sarcoma [44]. It is possible that SEF behave in the same way, however, there is not enough data for such study in SEF due to its rareness.

In conclusion, SEF is a fully malignant tumor that is capable of recurrence and metastases, and the morbidity and mortality are discouraging, despite low-grade histological appearance. FDG PET/CT findings of SEF are dependent upon the histological features, and the different FDG uptake in SEF lesions suggests the heterogeneity of the tumor. In addition, FDG PET/CT could become part of proceedings of monitoring and follow up of tumor. Further research on treatment of recurrent and metastatic SEF, and predictive value of FDG PET/CT for prognosis will be necessary.

#### Disclosure of conflict of interest

None.

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