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RADIOLOGY CASE REPORTS

Case Report

Metastatic extrapleural malignant solitary fibrous tumor presenting with hypoglycemia (Doege–Potter syndrome)

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ABSTRACT

We report a rare case of metastatic malignant solitary fibrous tumor (SFT) that presented with hypoglycemia because of insulin growth factor-2 production. Initial workup included computed tomography imaging that revealed a large, partially necrotic liver mass, a hypervascular pancreatic head lesion, and 2 renal lesions. Following hepatic resection, pancreatic head resection and nephrectomy, all these lesions demonstrated pathological findings that were consistent with SFT. The patient also had a history of an intracranial mass that had been previously resected and treated with gamma knife therapy at an outside institution, which was found to also be SFT. Six months after initial pancreatic head resection, the patient developed a new lesion involving the pancreatic tail that was found to represent recurrent metastatic SFT. This case emphasizes the highly aggressive nature of extrapleural SFT, while rare, and the role of imaging in follow-up for disease recurrence.

Case report

A 39-year-old male presented with an episode of altered mental status and was found to be hypoglycemic with blood glucose levels of approximately 30 mg/dL. The patient had a history of seizures with a low-grade brain tumor of unknown etiology, status post-temporal lobe lesion resection approximately 10 years before this presentation and gamma knife therapy, all performed at an outside institution. Subsequent workup for hypoglycemia included a contrast-enhanced computed tomography (CT) scan of the abdomen and pelvis after the intravenous administration of 125 cc of iopamidol-370 (Isovue-370, Bracco Diagnostics, Princeton, NJ). CT scan evaluation revealed a large, hypervascular abdominal mass replacing much of the left hepatic lobe (Fig. 1). Also, 2 left renal lesions (Fig. 2) and a hypervascular pancreatic head lesion
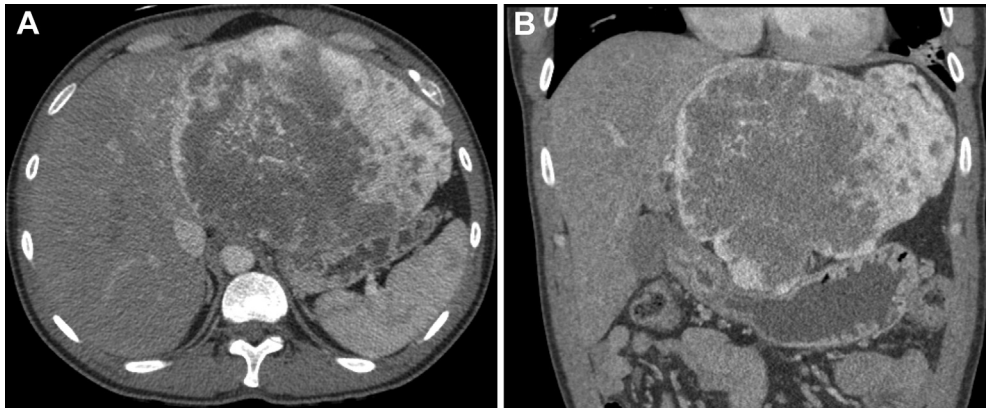
Fig. 1 — Axial (A) and coronal-reformatted (B) contrast-enhanced computed tomography (CT) images demonstrate a large, heterogeneous enhancing mass that appears to arise from the left lateral segment of the liver with associated mass effect on the stomach.

were present (Fig. 3). The preliminary clinical and radiological diagnosis was metastatic neuroendocrine tumor (possibly insulinoma given the hypervascularity of the lesions and history of hypoglycemia); metastatic fibrolamellar hepatocellular carcinoma was also considered in the differential diagnosis.

Soon after, an exploratory laparotomy was performed with left hepatic lobectomy along with enucleation of pancreatic head lesion and abdominal lymph node dissections. Surgical evaluation revealed a large upper abdominal mass arising from the left hepatic lobe that was partially adherent to the left diaphragm and abutting the spleen. Enlarged
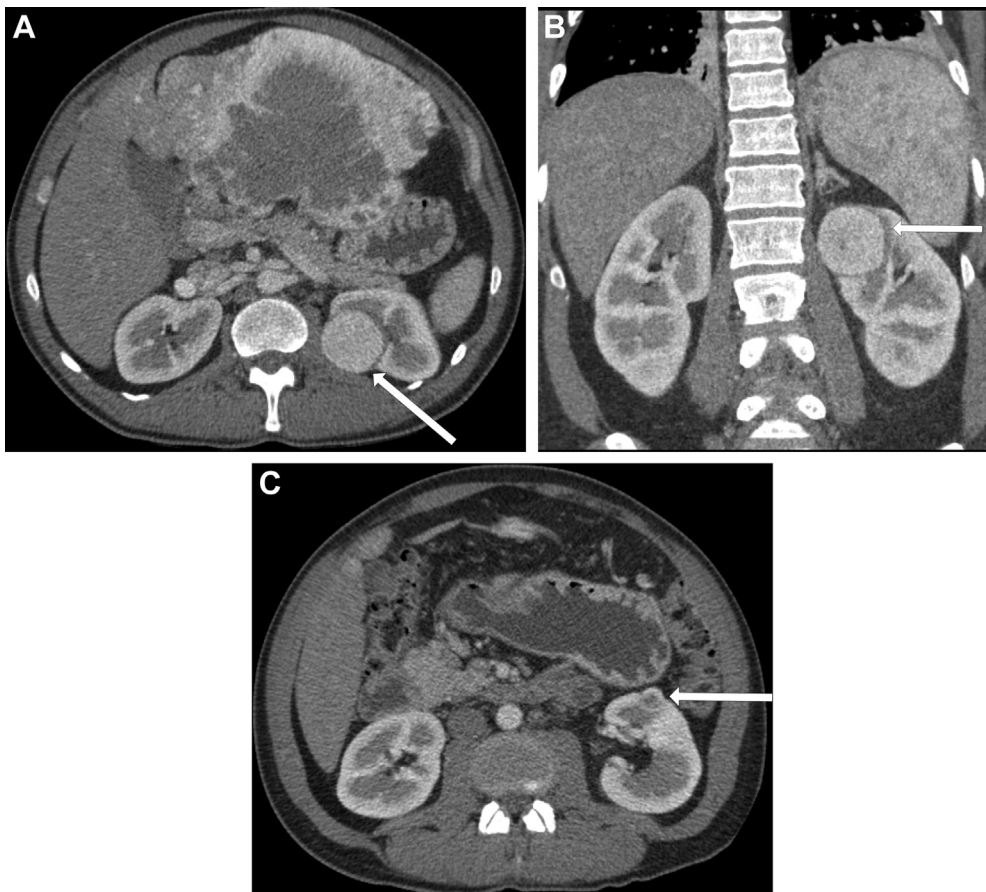

Fig. 2 — Axial and coronal contrast-enhanced CT images (A and B) demonstrate an enhancing left upper pole renal mass (arrow) measuring up to 3.9 cm. There is also a smaller inferior pole lesion located within the left renal cortex (C).
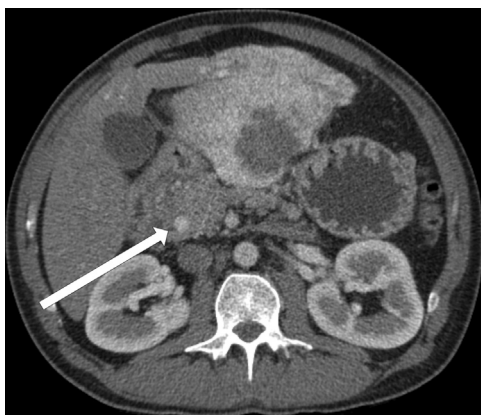
Fig. 3 – Axial contrast-enhanced CT image demonstrates a hyperenhancing lesion (arrow) within the pancreatic head in addition to the large lateral segment hepatic mass.

peripancreatic and periportal lymph nodes as well as the pancreatic head lesion were also identified on palpation and then resected.

On gross examination (Fig. 4), the large left hepatic lobe mass measured 20 × 18 × 15 cm and demonstrated focal areas of hemorrhage. Histopathological evaluation revealed spindle-shaped neoplastic cells growing in small nests surrounding the small vessels with associated luminal compression (Fig. 4). Approximately 4 mitoses per 10 high-powered fields (4/10 hpf) and increased cellularity were seen, suggesting a more aggressive tumor behavior. Tumor cells were positive to collagen 4, vimentin, calponin, Bcl-2 and STAT-6 (Fig. 4B). Histologic changes and immunophenotype of the resected pancreatic head mass appeared similar to the liver mass (Fig. 5) representing "hemangiopericytoma-like" solitary fibrous tumor (SFT).

Because of an interval increase in the size of renal lesions approximately 3 months after resection of the hepatic and pancreatic lesions, the patient underwent surgery for biopsy and possible nephrectomy with a concern that the renal lesions might represent renal cell carcinoma rather than SFT metastases. A rock-hard white-colored exophytic left upper

pole lesion was identified externally and the smaller inferior pole lesion was appreciated on palpation. Because of the multiplicity of the lesions, it was decided to proceed with radical nephrectomy.

The gross examination of the left kidney demonstrated a bulging encapsulated lesion in the superior pole of the left kidney abutting Gerota fascia (Fig. 6). Both superior pole and inferior pole renal lesions showed morphologic and immunophenotypic findings similar to the resected liver and pancreatic lesions consistent with multifocal SFT.

Given the patient's history of a low-grade brain tumor, there was a concern that the previously treated intracranial lesion could have, in fact, represented a SFT. The prior brain magnetic resonance imaging (MRI) findings from the outside hospital were not, as would be expected, consistent with a low-grade neoplasm as prior pathology reports had suggested. There was avid enhancement of a lobulated, likely extra-axial left temporal lobe lesion with associated mass effect and vasogenic edema (Fig. 7). Our pathology department reviewed the previously obtained intracranial tumor specimen from the prior left temporal lobe lesion resection (Fig. 7). A spindle-shaped neoplasm was seen with neoplastic cells growing in small nests (Fig. 7). Neoplastic cells were monomorphic with thin-walled anastomosing vessels. Therefore, both imaging and pathology reviews suggested that the patient's previously treated "low-grade brain tumor" was actually a SFT.

Approximately 6 months after the initial resection of hepatic and pancreatic head lesions, a routine follow-up contrast-enhanced CT examination was performed (Fig. 8), which observed a new 1.0 cm hypervascular pancreatic tail lesion. Spleen-preserving distal pancreatectomy was performed (Fig. 8), and pathology confirmed suspected metastatic SFT. The patient continues to be followed with clinical and imaging follow-up. His hypoglycemia has resolved following partial pancreatectomy.

Discussion

SFTs, formerly termed hemangiopericytoma, are rare mesenchymal tumors that usually present as slowly growing painless masses in middle age without any sex predilection.

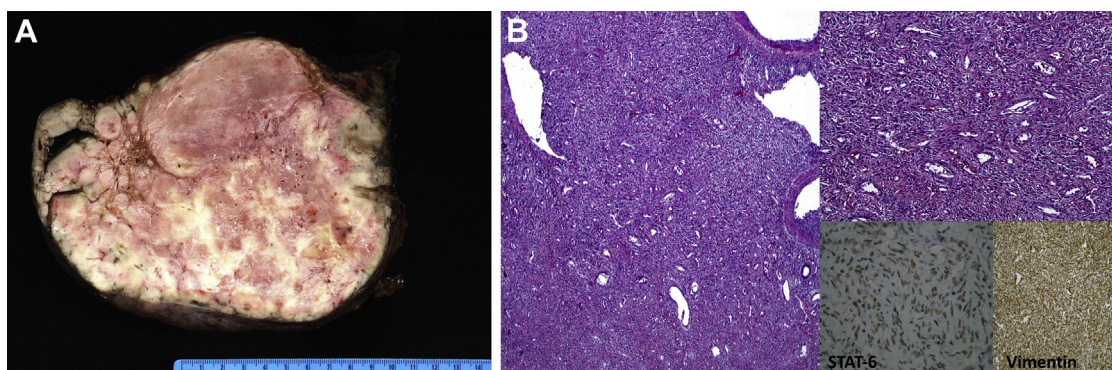
Fig. 4 – A large liver mass is demonstrated on gross pathology (A) following left hepatic lobectomy. The mass contained areas of necrosis and hemorrhage. Standard hematoxylin and eosin (H&E) stains with magnification observed spindle-shaped cells and a high mitotic index (B). STAT-6 and vimentin immunohistochemical stains were positive. Findings were consistent with solitary fibrous tumor.
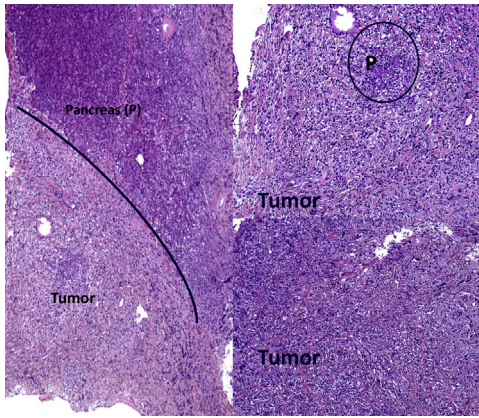
Fig. 5 – **Microscopic examination of the hypervascular pancreatic lesion demonstrated similar appearance to the large liver mass with spindle-shaped cells and immunohistochemical staining consistent with solitary fibrous tumor involving the pancreas. The tumor is seen infiltrating normal pancreatic tissue (P).**

These may also present with symptoms related to compression of adjacent structures. They may arise from any location, but SFTs are thought to most commonly involve the pleura [1]. Extrapleural SFTs were only recognized pathologically in the last 2 decades and may represent more cases than previously recognized [2]. The extrapleural SFTs more commonly involve the liver [3]. Other sites of involvement include the peritoneum, kidneys, orbits, meninges, and parotid glands [1,2,4–7].

SFT is generally associated with good prognosis with an overall 5-year survival of 84%-89% [2,8]. However, approximately 26% and 45% of cases develop metastases at 5 and 10 years, respectively [2]. The markedly aggressive nature of some extrathoracic SFTs has been increasingly recognized over the past 2 decades with approximately one-tenth of SFTs demonstrating malignant pathology and metastasis [9–12]. Larger tumors with higher mitotic indices demonstrate much greater risk of metastases and poorer outcomes [2,8]. Our case exemplifies a particularly aggressive form of SFT with intracranial, pancreatic, hepatic, and renal involvement as well as subsequent recurrence with a

pancreatic tail metastasis less than 1 year after initial surgical resection of abdominal lesions.

Some SFTs present with paraneoplastic syndromes including hypoglycemia related to the production of insulin-like growth factor 2 (IGF-2), termed Doege–Potter syndrome, that may be confused for symptoms seen with neuroendocrine tumors as was initially suspected in our case [13]. Doege–Potter syndrome is encountered in less than 5% of SFT cases and is reported in rare cases of SFT involving the liver [13–15]. Patients who have liver involvement and hypoglycemia, as in our case and others, appear to have more grave course with higher rate of metastases and recurrence; in these patients, serum IGF-2 may be helpful in assessing for recurrence in addition to surveillance imaging [15].

The etiology of SFT is attributed to mutations of the NAB2 and STAT6 genes located on chromosomal region 12q13 [16]. SFTs are generally well-circumscribed, partially encapsulated tumors. When aggressive, areas of necrosis and hemorrhage may be seen, as in our example. On histology, spindle-shaped or ovoid cells are seen with varying mitotic rates depending on aggressiveness. Classically described findings include hemangiopericytoma-like vessels and prominent stromal collagen. These lesions strongly express vimentin [1]. On immunohistochemistry, STAT-6 immunoreactivity in the nuclei is a sensitive and specific indicator of SFT. All the sampled lesions in this case demonstrated pathology findings consistent with SFT including STAT-6 staining [17].

SFTs may present in a variety of locations, usually as a single well-circumscribed large mass within the abdomen and pelvis [7,18]. They demonstrate avid enhancement on arterial phase imaging that increases progressively during venous and delayed phases [19]. There may be areas of necrosis that are hypoattenuating on CT scan and do not enhance, as noted in the large hepatic mass in our patient. Calcification within these masses, sometimes quite large, have also been reported [7].

The lesions are described to be hypo- to isointense on T_1-weighted MRI and showing heterogeneous T_2 hyperintensity [18,19]. Sonographic evaluation demonstrates heterogeneous echotexture with internal vascularity on Doppler examination [7]. Echogenicity is generally increased compared with the normal liver [7]. Large vessels may be seen
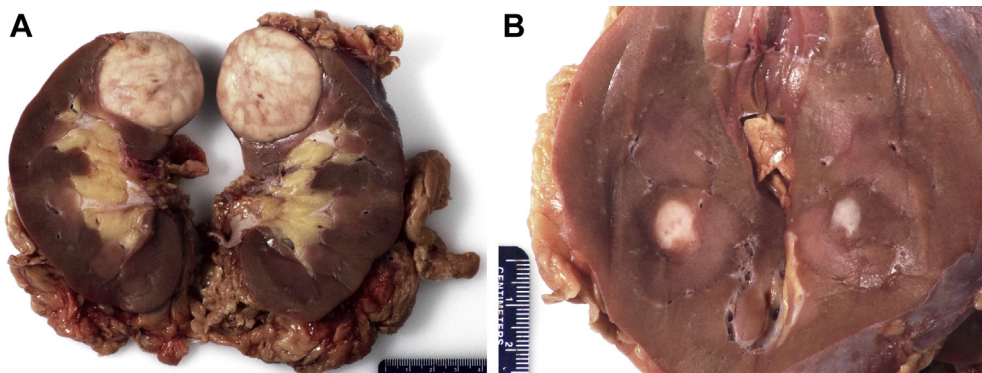

Fig. 6 – **Split gross pathological specimen (A) following radical nephrectomy demonstrates a tan solid soft tissue lesion within the upper pole of the kidney. The lower pole lesion was identified on gross examination as well (B). Microscopic examination was similar revealing spindle-shaped neoplastic cells consistent with solitary fibrous tumor.**
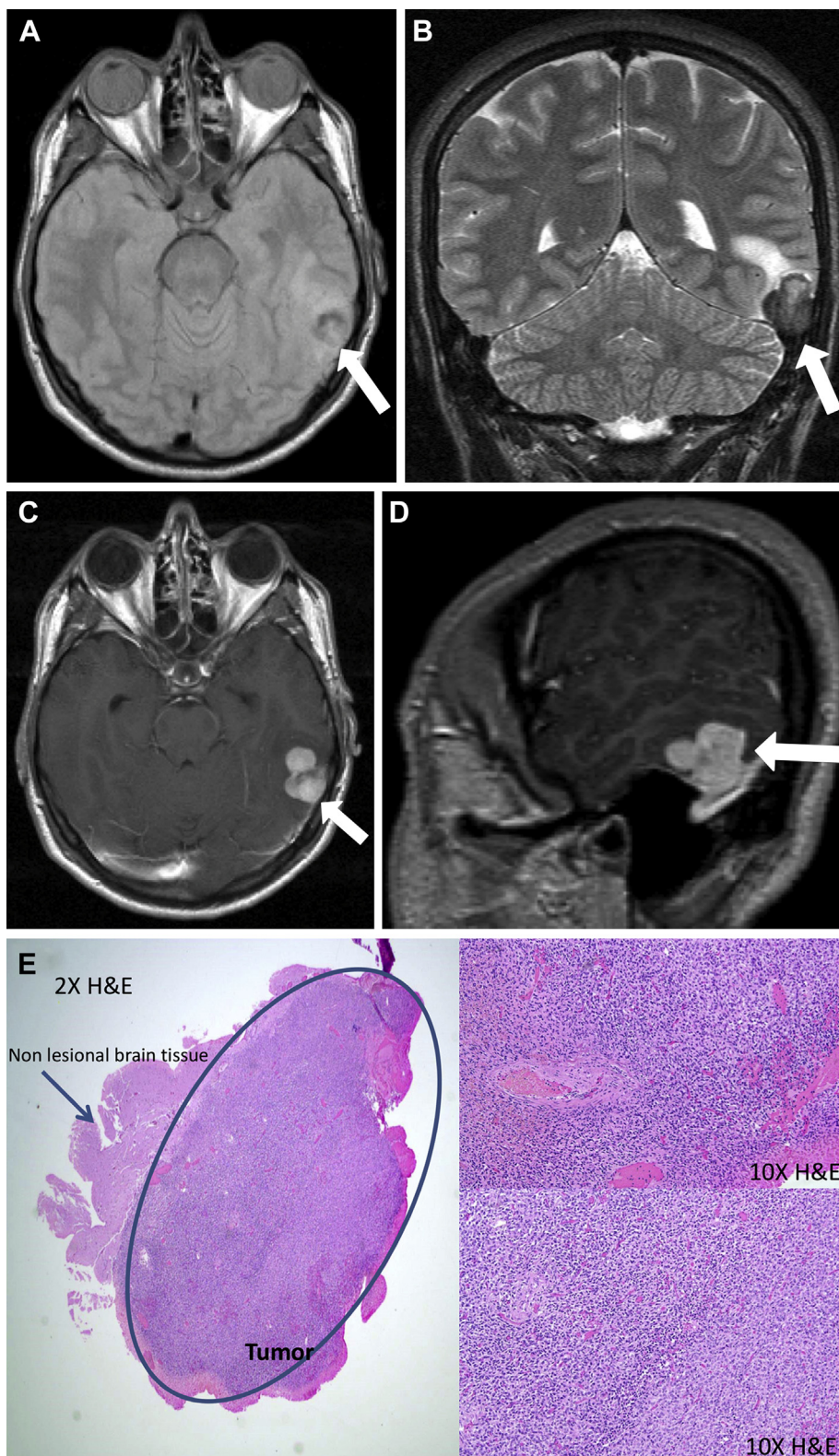
Fig. 7 – **Brain MRI (A-D) performed in this patient more than 10 years before presentation had demonstrated a tumor (arrows) in the left temporal lobe region that was thought to represent a low-grade glial tumor on pathology at the time of resection. Axial FLAIR (A) and coronal T_2-weighted (B) images show a peripherally hypointense and internally hyperintense extra-axial lesion near the posteroinferior left temporal lobe with associated mass effect and vasogenic edema. Axial (C) and sagittal (D) postcontrast T_1-weighted images demonstrate avid enhancement of this lobulated extra-axial lesion. Secondary pathological review of the previously obtained specimen (E) revealed spindle-shaped cells with moderate pleomorphism that was consistent with solitary fibrous tumor.**
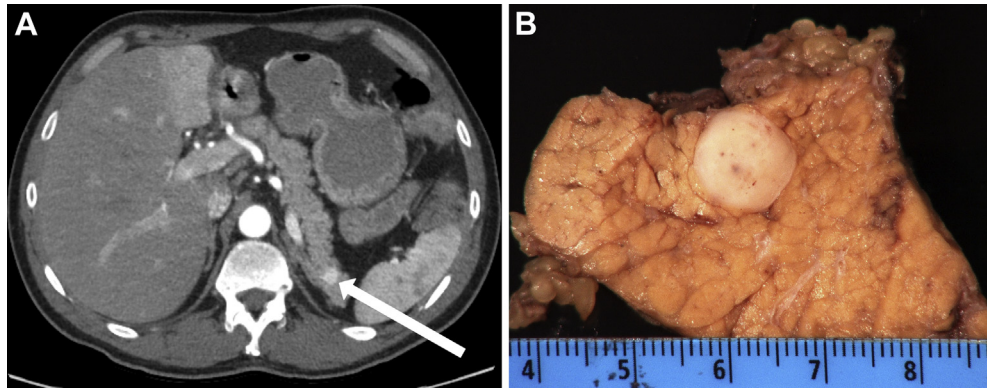
Fig. 8 – Six months after surgical resection of the large hepatic mass and pancreatic head resection, a routine follow-up CT examination was performed that showed a new enhancing pancreatic tail mass (arrow) (A). The pancreatic tail lesion was resected with spleen-preserving distal pancreatectomy (B), with pathology confirming recurrent metastatic solitary fibrous tumor.

within these tumors, which are seen as areas of flow-related signal loss on spin-echo MRI [7]. Associated imaging findings may be seen related to mass effect within the abdomen such as compression of bowel or the urinary bladder with secondary findings of obstruction.

The presentation of this case was unusual for SFT given the simultaneous presence of hepatic, pancreatic, and renal lesions (also with a history of brain tumor of unknown etiology later shown to be SFT), as well as later recurrence with a new pancreatic tail lesion. This hepatic mass raised the possibility of an atypical presentation of hepatocellular carcinoma, but this was felt to be unusual given the clinical presentation, patient age, and the absence of underlying liver disease. Alternatively, the imaging findings of a hypervascular pancreatic lesion suggested that this might represent a metastatic neuroendocrine tumor especially in conjunction with the patient's clinical presentation with hypoglycemia. The renal lesions were initially felt to represent metastatic disease over primary renal cell carcinoma, but interval enlargement of the lesions was concerning for a more aggressive neoplasm and radical nephrectomy was performed, revealing multifocal SFT. Pattern of enhancement was very atypical for lymphoid tumor. Sarcoma could also be considered within the differential diagnosis although abdominal sarcomas (liposarcoma or leiomyosarcoma) commonly arise from retroperitoneum. Ultimately, resection is required and while there are some overlapping histological features, SFT may be differentiated with the presence of spindle-shaped cells, hemangiopericytoma-like vessels, and most importantly, STAT6 immunopositivity [17].

This case highlights the utility of review of prior imaging studies and pathology specimens in cases of multiorgan tumoral involvement. As the aggressive nature of extrathoracic SFTs has been underestimated in the past, we emphasize the importance of continued clinical surveillance in patients diagnosed with SFT, even with benign pathology and no metastases on initial presentation [12]. The clinical utility of adjunctive treatment is poorly understood for these rare SFTs, and further investigation is needed to ascertain the role of chemotherapy or radiation therapy following tumor resection [8].

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