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Case Report

Intra-Abdominal Malignant Solitary Fibrous Tumor with Peritoneal Dissemination: A Case Report

Vivian Ma[1*], Lawrence Turner[1], Robert van Wiltenburg[2], Conrad D Oja[3,4], Ananta Gurung[5] and Shawn MacKenzie[1]

[1]*Department of General Surgery, University of British Columbia, Canada*
[2]*Department of Radiology, University of British Columbia, Canada*
[3]*Department of General Internal Medicine, University of British Columbia, Canada*
[4]*Department of Medical Oncology, BC Cancer Agency, Canada*
[5]*Department of Pathology, University of British Columbia, Canada*

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ABSTRACT

Solitary fibrous tumor (SFT) is a rare mesenchymal tumor primarily found in the pleura, with occasional presentations in extra-pleural locations. SFTs are typically diagnosed based on compressive symptoms due to their large size. Most SFTs are benign with a low recurrence rate, with an overall good prognosis with an overall 5-year survival of over 90%. Approximately 12-22% of SFTs are malignant and are associated with a higher recurrence rate of up to 78%. Given the low incidence and sparse case series literature, no adjuvant therapies have demonstrated a survival benefit. We present the first case of abdominal malignant SFTs with peritoneal dissemination, describing the presentation, histopathology, treatment planning and surveillance.

Introduction

SFTs are rare mesenchymal tumors first histologically described in the 1870's by Wagner and later by Klemperer and Rabin in 1931 [1, 2]. Historically, SFTs have been a unique diagnostic challenge due to overlapping histological features, leading to various historical nomenclatures such as hemangiopericytomas, benign or localized mesothelioma, and solitary fibrous mesothelioma [2]. SFTs are characterized by cells with oval to spindle-shaped nuclei and minimal cytoplasm and intervening collagen bands [3]. The cells demonstrate both hypercellular and hypocellular areas with a high proportion of stromal collagen [3]. The tumors have pronounced vascularity, described as 'staghorn' blood vessels and perivascular sclerosis. The immunohistochemical marker CD34 is expressed in 83-95% of SFTs with malignant or dedifferentiated SFTs having lower CD34 positivity [3]. They can be differentiated from other stromal tumors by the absence of CD117/c-KIT and DOG-1 [3]. The NAB2-STAT6 fusion gene has also been demonstrated to be present in 98% of SFTs [3]. Other markers which are typically positive in SFTs include vimentin, CD99, BCL2, nuclear ß-catenin and EMA [3].

While the exact incidence is unknown, SFTs make up approximately 2% of soft tissue masses with pleural solitary fibrous tumors estimated to have a prevalence of 2.8 per 100,000 [2]. 60-70% of SFTs are intrathoracic, with the second most common site being intra-abdominal, followed by less common locations including the trunk, extremities, head and neck and intracranial [2, 4]. Extrathoracic SFTs are typically slow-growing lesions affecting middle-aged individuals with an equal incidence between males and females [1]. Diagnosis typically occurs when symptoms develop due to the large size of the tumor, causing compressive symptoms [1]. While the tumor size at presentation varies according to the site, the median size has been reported to be between 7 to 10 cm. Rarely, SFTs present with a paraneoplastic syndrome called Doege-Potter syndrome where non-islet cell hypoglycemia is the most commonly reported symptom [1, 2]. Doege-Potter syndrome is due to

[*]*Correspondence to: Vivian Ma, Department of General Surgery, Faculty of Medicine, University of British Columbia, 2775 Laurel Street, 11th floor, Vancouver, BC Canada V5Z 1M9, Canada; Tel: 6048081938; E-mail: vivianma@alumni.ubc.ca*

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tumor production of insulin-like growth factor (IGF), particularly IGF-II [2]. Tumors discovered due to paraneoplastic syndromes are typically malignant with a poor prognosis [2]. 78 to 88% of SFTs are benign with an approximate 12 to 22% malignant rate [5]. While benign SFTs have an overall good prognosis with recurrence rates of 8% following surgical resection, malignant solitary fibrous tumors have a much higher 63% recurrence rate, with a median survival rate of 59 months [4-6]. As such, patients with malignant SFTs may undergo adjuvant chemotherapy and/or radiation. Given the paucity of research trials, it is unknown whether adjuvant therapy provides a survival benefit.

While over one hundred SFT case reports and case series can be found in the literature, describing tumor locations, histological features, outcomes, and treatment plans, these case series only describe a solitary lesion found at the first presentation or multiple lesions at the time of recurrence. To our knowledge, there are no case reports describing multiple intra-abdominal lesions at first presentation. We present the first reported case of multiple intra-abdominal malignant SFT, consisting of a single large lesion with peritoneal dissemination of multiple smaller lesions.

Case Report

A 55-year-old previously healthy male who after experiencing 2 weeks of mild vague lower abdominal pain, presented to the emergency department. The patient reported no other gastrointestinal and/or constitutional symptoms. An IV contrast CT scan of the abdomen and pelvis was performed, which demonstrated a 20 x 17 x 13cm lobulated mesenteric mass located within the central abdomen, with soft tissue density peripherally and low central density. There is also evidence of a non-enhancing central area of necrosis (Figure 1). The tumor demonstrated tortuous veins anterior to the mass. Smaller peritoneal masses were seen in the left iliac fossa and in the right iliac fossa by the appendix, with the largest of these lesions measuring 2 cm. A nonspecific nodule was also seen in the left internal obturator region and along the dome of the right liver. An ultrasound-guided biopsy was performed of the large mass, revealing pathology consistent with a cellular tumor suggestive of solitary fibrous tumor. Subsequent STAT6 immunohistochemical testing showed diffuse nuclear positivity within the lesion, confirming the diagnosis of solitary fibrous tumor. The case was discussed at multidisciplinary tumor rounds where the consensus was to proceed with upfront resection of the mass.

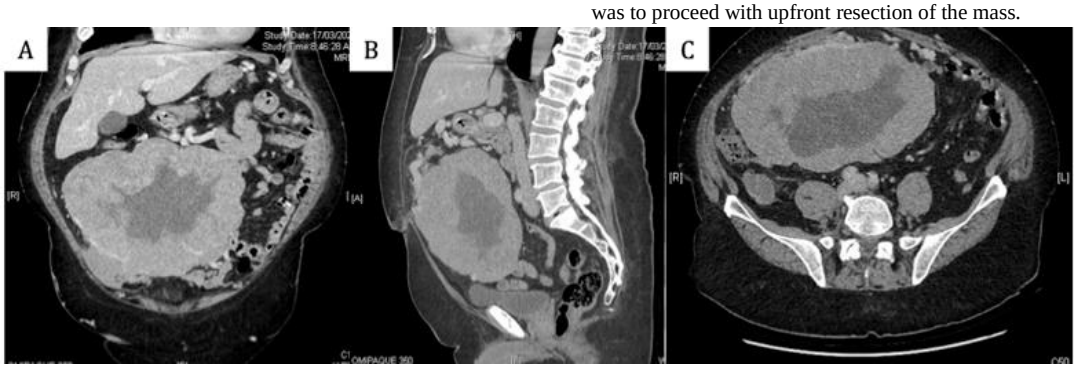

Figure 1: CT Scan with intravenous contrast demonstrating a 20 x 17 x 13cm lobulated mass with soft tissue density peripherally and central hypodensity in the central abdomen. The mass demonstrates central necrosis with associated tortuous veins. This figure presents the mass in the **A)** coronal view, **B)** sagittal view and **C)** axial view.

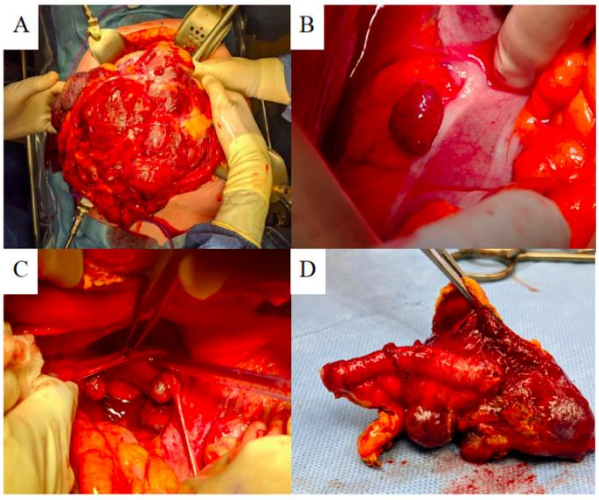

Figure 2: Intraoperative findings. **A)** The primary mass is seen to arise from the transverse mesocolon with tortuous varices arising from the greater omentum. Several smaller lesions were found throughout the abdominal cavity including **B)** adjacent to the sigmoid colon, **C)** within the pelvis, and **D)** in the right paracolic gutter, involving the appendix.

The patient was brought to the operating room and underwent a midline laparotomy, given the size of the mass. The 20-25cm mass was seen to arise from the retroperitoneal colonic mesocolon with significant varices within the omental blood vessels (Figures 2A-2C). The mass was resected off the mesocolon/omentum using a LigaSure energy device. Further examination revealed multiple smaller masses that appeared to arise from the peritoneum. There were three pelvic lesions (2 in the left, 1 in the right), two lesions in the right paracolic gutter one of which was intimately adherent to the appendiceal tip, a single suprahepatic mass, three lesions in the left paracolic gutter and several smaller lesions on the mesentery and a single peritoneal nodule. The satellite lesions ranged in size from 0.5 cm to 6 cm. Postoperatively, the patient did well and was discharged home on postoperative day #3. At follow-up 2 weeks after discharge, the patient was doing well at home with no concerns. The patient had no 30 or 90 day postoperative complications.

Pathology

The largest mass arising from the omentum measured 29 x 22 x 14.5 cm and weighed 4044g, with the sixteen smaller lesions measuring between 0.5 cm to 5.5 cm. The largest mass had a smooth multinodular external

surface. The cut surface of this mass demonstrated a heterogeneous solid tumor with extensive areas of hemorrhage and necrosis (95%). Focally (5%) there were fleshy white areas which corresponded to viable tumor (Figure 3A). Histologic examination (Figures 3B-3D) revealed a highly cellular lesion exhibiting a "patternless pattern" of cells arranged randomly in ill-defined fascicles. Dilated and branching vessels were seen scattered throughout the tumor, with a classic staghorn configuration. On high-powered microscopy, the mass was composed of tightly packed round, oval, and fusiform spindle cells. Approximately 8 mitotic figures per high power field (HPF) were identified. These histologic findings were consistently seen in the remaining resected lesions.

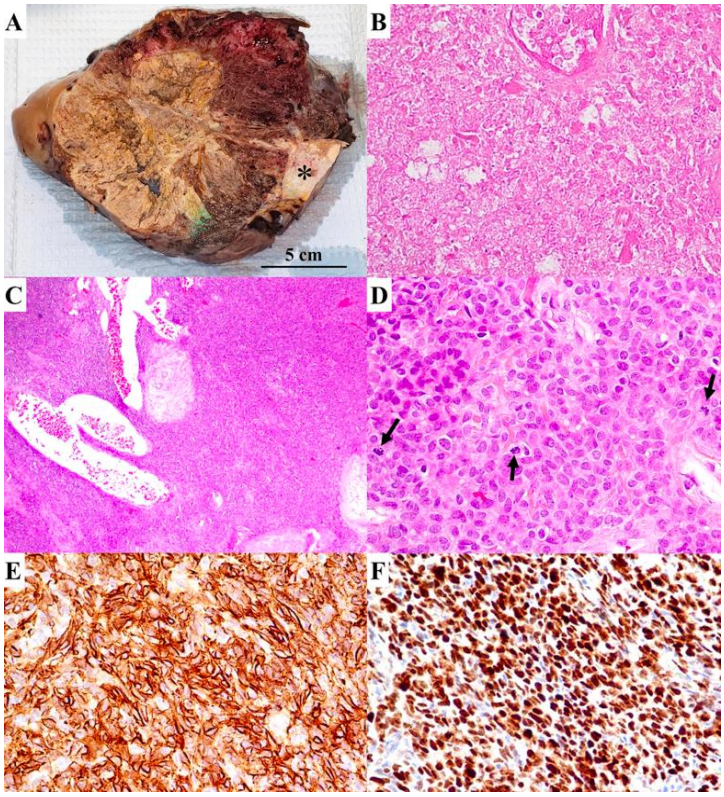

Figure 3: Gross and microscopic pathologic findings. **A)** The cut surface of the 29 cm omental tumor demonstrated **B)** a heterogenous solid mass with extensive areas of hemorrhage and necrosis (400X, H&E). Focally (asterisk), there were more fleshy white areas that corresponded to viable tumor. **C)** Sections from the viable areas of tumor show a very cellular lesion arranged randomly in ill-defined fascicles with dilated and branching vessels (40X, H&E). **D)** The tumor is composed of tightly packed round, oval and fusiform spindle cells (400X, H&E) which are mitotically active (arrows highlight mitotic figures). The lesional cells were positive for **E)** CD34 (400X) and **F)** STAT6 (400X).

A panel of immunohistochemical stains was performed on the largest mass as well as on the core needle biopsy specimen. The lesional cells were diffusely and strongly positive for CD34 (Figure 3E), STAT6 (Figure 3F), and vimentin. Patchy positivity was also seen with BCL2. The cells were negative for CD31, D2-40, calretinin, CK5/6, CD117, DOG-1 AE1/AE3, claudin-4, CEA, desmin, and S100. The constellation of histologic findings (size of the largest tumor 29 cm, >4 mitotic figures per 10 high power field, presence of tumor necrosis and increased cellularity) are consistent with a diagnosis of malignant solitary fibrous tumor.

Discussion

The prognosis for SFT is generally favourable, with a 5-year overall survival between 59 to 100% depending on various histological characteristics of the tumor [2]. Multiple studies have attempted to define features predictive of malignant potential and recurrence [7-9]. Common features investigated include size > 10cm at presentation, > 4 mitoses/10HPFs, tumor necrosis or hemorrhage, and increased cellularity. Unfortunately, at this time, there is no consensus for predicting malignant type SFT [7-9]. Given the size (29 cm), presence of tumor necrosis, high mitotic activity (8 mitoses/10 HPF) in the largest lesion and the presence of multiple other peritoneal lesions with similar features, the overall findings in our patient are that of an intra-abdominal malignant solitary fibrous tumor with peritoneal dissemination.

We present the first known case of malignant solitary fibrous tumor with multiple lesions at the first presentation for surgical resection. This provides an interesting therapeutic dilemma following resection in terms of adjuvant therapy and surveillance, given that the multiple lesions may indicate peritoneal spread already and a higher burden of disease. Based on the extent of the patient's disease with peritoneal dissemination at the index presentation and its malignant histology, there is a high rate of recurrence. Wilky *et al.* performed a retrospective cohort study evaluating factors that affected recurrence [6]. Extra-thoracic SFTs were found to have a higher rate of recurrence compared to intra-thoracic SFTs (22 versus 4%) [6]. Similarly, malignant histology with any feature of England's criteria – major criteria include mitotic changes >4/10

HPFs, tumor necrosis and hemorrhage, nuclear pleomorphism and metastasis with minor criteria being tumor size >10cm and cellular atypic – conferred a higher risk of recurrence [6]. Our patient not only demonstrated both of these features for a higher rate of recurrence, but already had evidence of peritoneal spread at the index resection. This emphasizes the importance of ongoing surveillance, but little literature exists surrounding surveillance following resection. Small case series have shown a local recurrence rate as low as 8% for benign SFTs, but they have also been reported to occur up to 17 years after resection [5, 10]. Furthermore, malignant SFTs have been demonstrated to metastasize to the lung, pleura, liver, bones, and peritoneum [11]. Brain, abdominal, or chest wall metastases were less common [5, 11]. A baseline CT chest, abdomen, and pelvis was performed at 2 months postoperative and showed two heterogeneous, hypo-enhancing geographic areas in the liver lesion not previously seen, these were ill defined and not discretely mass-like and will be followed on subsequent imaging. There was no evidence of pulmonary lesions or recurrent lesions intra-abdominally. Repeat imaging is planned for every 4 months during the first 2 years of follow-up, subsequently every 6 months through year 5.

While surgical resection continues to be the initial modality for treating malignant solitary fibrous tumors, the utility of adjuvant chemotherapy or radiation is still unknown given that most data is based on small case series. Adjuvant radiation has been studied in CNS SFTs, with overall survival rates of 93% for those treated with surgery and adjuvant radiation versus 88% for those treated with surgery alone [12]. Little literature exists for radiation treatment for SFTs outside of the nervous system. Several case reports show promising responses to radiation for metastatic SFT of the pelvis or pleural SFTs. Similarly, there is a paucity of literature examining various adjuvant chemotherapy agents and their effects on SFTs. Multiple retrospective studies have assessed the effectiveness of doxorubicin-based treatments, but typically there are low response rates of less than 20% [13, 14]. Targeted therapy with temozolomide and bevacizumab retrospectively studied in 14 pretreated patients at MD Anderson demonstrated a partial response (PR) in 79% of patients using the Choi criteria, with only 14% PR using RECIST, median PFS 9.7 month and a 78.6% progression-free rate at 6 months [14]. Given the resistance to standard chemotherapy and benefits of pazopanib in multiple other soft-tissue sarcomas, the effect of various types of Tyrosine Kinase Inhibitors on SFT has also been studied with varying results [15]. A single-institution Phase II single-arm study of 35 patients with malignant and dedifferentiated solitary fibrous tumors showed 51% PR and 26% SD with only 23% progressing. Dedifferentiated solitary fibrous tumor patients showed rapid progression, so further patients were limited to malignant SFTs [16]. In a retrospective patient case series of mostly pretreated patients, sunitinib showed a 48% PR in 29 patients, with a median PFS of 6 months [17]. A single-arm Phase II 17 patient trial of progressing patients using Axitinib demonstrated an overall response rate of 41.2%, increased to 54% when dedifferentiated/high-grade SFT were excluded, a difference seen also in the pazopanib study. This population included responses in 4 of 7 patients pretreated with Pazopanib, suggesting a possible role for sequential TKIs. Median overall survival was 25.3 months [18]. There is also literature supporting resection of local recurrences, but 80% of re-excisions develop subsequent local or distant relapse. More study is needed to determine the best options for treatment in these rare tumors, but recent advances using TKIs and similar targeted agents are optimistic.

Conclusion

Solitary fibrous tumors are rare mesenchymal tumors that typically have benign pathology. Malignant SFTs represent a small subset of discovered SFTs and we present the first known case of multiple intra-abdominal SFTs at first presentation. This provides an interesting therapeutic dilemma following upfront surgical resection and ongoing surveillance given that little literature exists regarding adjuvant therapy, ongoing surveillance, and prognosis on even solitary malignant SFTs.

Conflicts of Interest

None.

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