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Contents

Thrice Monthly Volume 9 Number 2 January 16, 2021

OPINION REVIEW

- 291 Continuity of cancer care in the era of COVID-19 pandemic: Role of social media in low- and middle-income countries
Yadav SK, Yadav N

REVIEW

- 296 Effect of a fever in viral infections — the ‘Goldilocks’ phenomenon?
Belon L, Skidmore P, Mehra R, Walter E
- 308 Overview of bile acid signaling in the cardiovascular system
Zhang R, Ma WQ, Fu MJ, Li J, Hu CH, Chen Y, Zhou MM, Gao ZJ, He YL

MINIREVIEWS

- 321 Gut microbiota and inflammatory bowel disease: The current status and perspectives
Zheng L, Wen XL

ORIGINAL ARTICLE

Retrospective Cohort Study

- 334 Effective immune-inflammation index for ulcerative colitis and activity assessments
Zhang MH, Wang H, Wang HG, Wen X, Yang XZ

Retrospective Study

- 344 Risk factors associated with acute respiratory distress syndrome in COVID-19 patients outside Wuhan: A double-center retrospective cohort study of 197 cases in Hunan, China
Hu XS, Hu CH, Zhong P, Wen YJ, Chen XY

META-ANALYSIS

- 357 Limb length discrepancy after total knee arthroplasty: A systematic review and meta-analysis
Tripathy SK, Pradhan SS, Varghese P, Purudappa PP, Velagada S, Goyal T, Panda BB, Vanyambadi J

CASE REPORT

- 372 Lateral position intubation followed by endoscopic ultrasound-guided angiotherapy in acute esophageal variceal rupture: A case report
Wen TT, Liu ZL, Zeng M, Zhang Y, Cheng BL, Fang XM
- 379 Perioperative mortality of metastatic spinal disease with unknown primary: A case report and review of literature
Li XM, Jin LB

- 389** Massive gastric bleeding - perforation of pancreatic pseudocyst into the stomach: A case report and review of literature
Jin Z, Xiang YW, Liao QS, Yang XX, Wu HC, Tuo BG, Xie R
- 396** Natural history of inferior mesenteric arteriovenous malformation that led to ischemic colitis: A case report
Kimura Y, Hara T, Nagao R, Nakanishi T, Kawaguchi J, Tagami A, Ikeda T, Araki H, Tsurumi H
- 403** Coil embolization of arterioportal fistula complicated by gastrointestinal bleeding after Caesarian section: A case report
Stepanyan SA, Poghosyan T, Manukyan K, Hakobyan G, Hovhannisyan H, Safaryan H, Baghdasaryan E, Gemilyan M
- 410** Cholecystoduodenal fistula presenting with upper gastrointestinal bleeding: A case report
Park JM, Kang CD, Kim JH, Lee SH, Nam SJ, Park SC, Lee SJ, Lee S
- 416** Rare case of fecal impaction caused by a fecalith originating in a large colonic diverticulum: A case report
Tanabe H, Tanaka K, Goto M, Sato T, Sato K, Fujiya M, Okumura T
- 422** Intravitreal dexamethasone implant — a new treatment for idiopathic posterior scleritis: A case report
Zhao YJ, Zou YL, Lu Y, Tu MJ, You ZP
- 429** Inflammatory myofibroblastic tumor successfully treated with metformin: A case report and review of literature
Liang Y, Gao HX, Tian RC, Wang J, Shan YH, Zhang L, Xie CJ, Li JJ, Xu M, Gu S
- 436** Neonatal isovaleric acidemia in China: A case report and review of literature
Wu F, Fan SJ, Zhou XH
- 445** Malignant solitary fibrous tumor of the greater omentum: A case report and review of literature
Guo YC, Yao LY, Tian ZS, Shi B, Liu Y, Wang YY
- 457** Paratesticular liposarcoma: Two case reports
Zheng QG, Sun ZH, Chen JJ, Li JC, Huang XJ
- 463** Sinistral portal hypertension associated with pancreatic pseudocysts - ultrasonography findings: A case report
Chen BB, Mu PY, Lu JT, Wang G, Zhang R, Huang DD, Shen DH, Jiang TT
- 469** Epstein-Barr virus-associated monomorphic post-transplant lymphoproliferative disorder after pediatric kidney transplantation: A case report
Wang Z, Xu Y, Zhao J, Fu YX
- 476** Postoperative complications of concomitant fat embolism syndrome, pulmonary embolism and tympanic membrane perforation after tibiofibular fracture: A case report
Shao J, Kong DC, Zheng XH, Chen TN, Yang TY
- 482** Double-hit lymphoma (rearrangements of MYC, BCL-2) during pregnancy: A case report
Xie F, Zhang LH, Yue YQ, Gu LL, Wu F

- 489** Is sinusoidal obstructive syndrome a recurrent disease after liver transplantation? A case report
Liu Y, Sun LY, Zhu ZJ, Wei L, Qu W, Zeng ZG
- 496** Portal hypertension exacerbates intrahepatic portosystemic venous shunt and further induces refractory hepatic encephalopathy: A case report
Chang YH, Zhou XL, Jing D, Ni Z, Tang SH
- 502** Repair of a severe palm injury with anterolateral thigh and ilioinguinal flaps: A case report
Gong HY, Sun XG, Lu LJ, Liu PC, Yu X
- 509** Indirect inguinal hernia containing portosystemic shunt vessel: A case report
Yura M, Yo K, Hara A, Hayashi K, Tajima Y, Kaneko Y, Fujisaki H, Hirata A, Takano K, Hongo K, Yoneyama K, Nakagawa M
- 516** Recurrent inverted papilloma coexisted with skull base lymphoma: A case report
Hsu HJ, Huang CC, Chuang MT, Tien CH, Lee JS, Lee PH

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Dr. Mukul Vij is Senior Consultant Pathologist and Lab Director at Dr Rela Institute and Medical Center in Chennai, India (since 2018). Having received his MBBS degree from King George Medical College in 2004, Dr. Vij undertook postgraduate training at Sanjay Gandhi Postgraduate Institute of Medical Sciences, receiving his Master's degree in Pathology in 2008 and his PDCC certificate in Renal Pathology in 2009. After 2 years as senior resident, he became Assistant Professor in the Department of Pathology at Christian Medical College, Vellore (2011), moving on to Global Health City as Consultant Pathologist and then Head of the Pathology Department (2013). (L-Editor: Filipodia)

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WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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Malignant solitary fibrous tumor of the greater omentum: A case report and review of literature

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Abstract

BACKGROUND

Malignant solitary fibrous tumors (SFTs) account for 15%-20% of all SFTs, and malignant SFTs arising from the greater omentum are extremely rare. Most malignant SFTs of the greater omentum are diagnosed *via* pathological examinations after surgery. In this study, we report a case of malignant omental SFT and review the published literature on this rare malignancy.

CASE SUMMARY

A 64-year-old female presented with an abdominal mass, and underwent exploratory surgery, during which a huge tumor originating from the greater omentum and intraperitoneal implants were identified and resected. The results of the pathological examination, immunohistochemistry staining, and gene sequencing led to the diagnosis of malignant SFT of the greater omentum. The patient died one and a half years later due to tumor recurrence and metastasis.

CONCLUSION

This is the first report of the application of gene sequencing in the diagnosis of malignant SFTs of the greater omentum.

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Core Tip: In this study, we present the rare case of a huge malignant solitary fibrous tumor (SFT) of the greater omentum. At presentation, the patient complained of an abdominal mass. After routine imaging examination, she underwent an exploratory laparotomy with a suspected diagnosis of gastrointestinal stromal tumor. Post-operative histological examination and gene sequencing indicated a malignant SFT of the greater omentum. We reviewed and discussed the pre-operative diagnosis, surgical options, and post-operative treatment of reported cases of malignant SFTs of the greater omentum. We suggest the application of gene sequencing in the diagnosis of malignant SFTs.

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INTRODUCTION

A solitary fibrous tumor (SFT) is a mesenchymal tumor, which was initially reported as an intra-pleural neoplasm by Klemperer and Coleman^[1]. Increasing interest in SFTs and their revised definition has led to the additional diagnosis of SFTs in a wide variety of extra-pleural sites, such as the orbit, thyroid gland, head, neck, and extremities. This conforms to the theory that as the tumor is derived from mesenchymal cells, SFT can occur anywhere within the human body. SFTs are generally benign; only one-fifth of all SFTs are invasive, with poor prognoses^[2]. In the abdomen, primary SFTs are mostly observed in the retroperitoneal space, and malignant SFTs arising from the greater omentum are not sufficiently documented^[3], which results in limited knowledge on SFTs and their management. We herein report a case of malignant SFT of the greater omentum in a female. For a better understanding of malignant SFTs, we also collected and summarized the data in existing reports on malignant SFTs originating from the greater omentum.

CASE PRESENTATION

Chief complaints

A 64-year-old female was admitted to our center due to an incidental mobile abdominal mass.

History of present illness

Prior to admission, the patient noticed an increase in her abdominal size, which she construed as weight gain.

Physical examination

On physical examination, a large non-tender mobile mass was palpated in the right abdomen.

Laboratory examinations

Laboratory examinations showed a cancer antigen 125 (CA125) level of 540.6 U/mL (normal range < 35 U/mL).

Imaging examinations

Contrast-enhanced abdominal computed tomography (CT) revealed a huge mass measuring 25.4 cm × 23.0 cm with a mixed density and heterogeneous enhancement (Figure 1A). CT three-dimensional (3D) reconstruction showed that the feeding arteries were from the splenic artery and celiac axis (Figure 1B). From the imaging findings, we suspected a gastrointestinal stromal tumor (GIST).

MULTIDISCIPLINARY EXPERT CONSULTATION

Guo YC, MD, PhD, Attending, Department of Gastrointestinal Surgery: The patient then underwent an exploratory laparotomy. Intraoperatively, a huge tumor originating from the greater omentum with several implant nodules on the omentum and intestinal mesentery were identified (Figure 2A and B). Tumorectomy and omentectomy with excision of the adjacent parietal peritoneum were performed, and the implanted nodules on the mesentery were also resected. The tumor weighed 4.32 kg and measured 27 cm × 21 cm × 9 cm in size (Figure 3A).

On pathological examination of the resected specimen, hypercellularity with spindle cells (Figure 3B) was observed, and the mitotic rate was 30/10 on high power field (HPF). Immunohistochemistry revealed positivity for Vimentin; weak positivity for BCL-2, DOG-1, CD99, and Ki-67 (+ 40%); negativity for CD34, Desmin, SMA, CD117, S-100, STAT6, and CK, suggesting the diagnosis of malignant SFT or GIST (Figure 3C-F).

To make an exact diagnosis, gene sequencing was performed using a paraffin section of the tumor tissue obtained during surgery. The Sanger sequencing method was used. The tumor cell content was 90%. The nucleic acid content was 152.3 ng/μL, and the ratio of OD₂₆₀/OD₂₈₀ was 1.84. We examined 4 exons of c-KIT including 9, 11, 13, and 17; and 2 exons of PDGFRA including 12 and 18. As a result, neither c-KIT nor PDGFRA had a gene mutation in their exons (Figure 4A-4F) which further excluded the probability of GIST and supported the diagnosis of a malignant SFT.

FINAL DIAGNOSIS

The final diagnosis was malignant SFT of the greater omentum.

TREATMENT

Additional treatment was not provided after the tumorectomy and omentectomy.

OUTCOME AND FOLLOW-UP

The post-operative course was unremarkable, and the patient was discharged from the hospital 8 d after surgery. However, the patient refused further medical therapy after surgery and died one and a half years later due to tumor recurrence and disseminated metastasis.

DISCUSSION

SFT accounts for approximately 5% of all sarcomas, and SFTs originating from the greater omentum are extremely rare^[4]. SFTs mainly occur at the age of 50-70 years, without gender predilection^[2]. Typically, the histological features of SFTs are characterized by a submesothelial mesenchymal neoplasm with a combination of hemangiopericytoma-like spindle cells and collagenous fibroma-like collagen bundles^[5,6]. According to the third World Health Organization classification of sarcomas, several morphologically similar tumors including extra-meningeal SFT, hemangiopericytoma (HPC), lipomatous HPC, and giant cell angiofibroma were grouped under the umbrella of extra-pleural SFT^[4]. To completely review malignant SFTs of the greater omentum, we searched all the subtypes that were classified as SFTs. As a result, we found that besides SFTs, cases were also described in patients

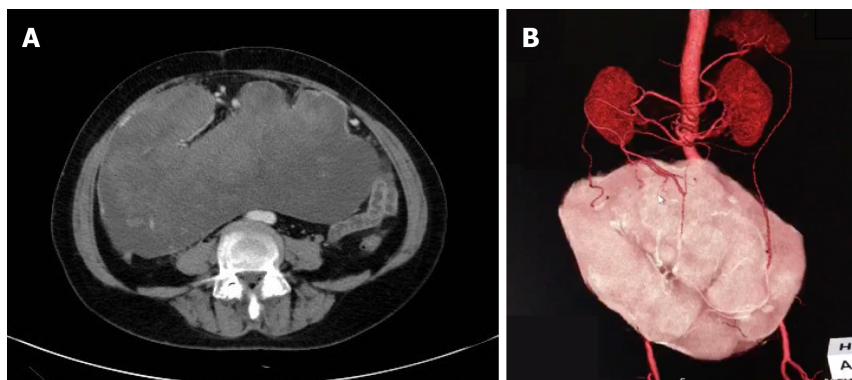


Figure 1 Imaging of the abdominal mass. A: Contrast-enhanced abdominal computed tomography (CT) scan showing a huge mass measuring 25.4 cm × 23.0 cm with mixed density and heterogeneous enhancement (arrow); B: CT 3D reconstruction showing that the feeding arteries were from the splenic artery, right colic artery, and middle colic artery (arrows).

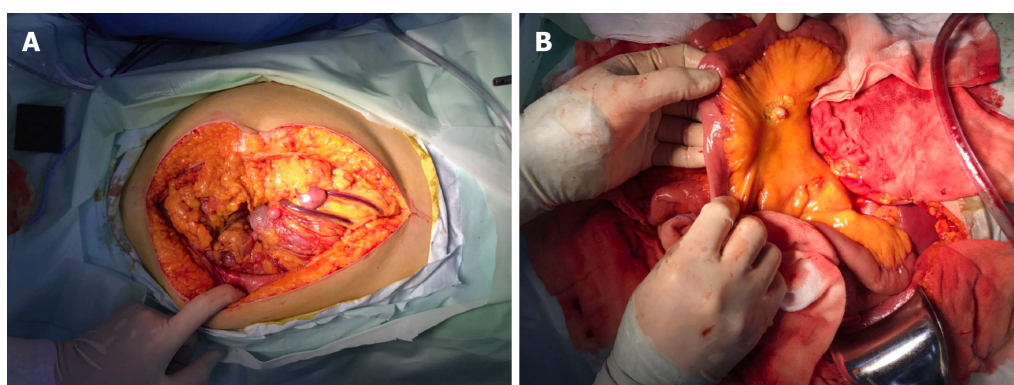


Figure 2 Intraoperative external phase of the abdominal mass. A: During the operation, a tumor originating from the greater omentum was detected, which occupied most of the space in the abdominal cavity; B: The tumor was highly invasive, and several implant nodules were identified on the intestinal mesentery and greater omentum. A mesenteric implant is shown (arrow).

with HPC, and the other subtypes of SFTs did not occur in the greater omentum. Since 1963, a total of 13 cases of malignant SFTs of the greater omentum have been reported, and our patient is the fourteenth (Table 1)^[2,7-17]. The patients (6 males and 7 females, 1 unknown) had an average age of 55 ± 10.3 years, and the shortest follow-up time was 4 mo. Of these 14 cases, 10 were recorded as HPC, which is a tumor of Zimmermann's pericyte in capillary walls and post capillary venule walls^[18]; it was confirmed as one of the SFTs in 2002, since HPCs do not encompass the origins of all HPC-like tumors^[19]. Compared with other reported malignant omental SFT cases, our case is unique. Firstly, the tumor was huge; it was the third largest malignant SFT resected from the greater omentum. Secondly, our case is the first in which satellite lesions were detected during the primary exploratory surgery. Among the reported cases, abdominal carcinomatosis at presentation was reported once by Prakash *et al*^[15], who defined the implants *via* contrast-enhanced CT and did not perform surgery. Lastly, this is the first case in which gene sequencing was used in the diagnosis.

SFT is difficult to diagnose. SFT in the abdominal cavity induces various abdominal symptoms, and the most frequent complaints are different degrees of abdominal pain with a palpable abdominal mass, and a sudden alteration of the tumor state, such as rupture, may cause a lethal acute abdomen^[20]. On CT, malignant SFTs may present with a cystic area of low attenuation, consistent with necrosis, calcification, and external invasion^[21]. Contrast-enhanced CT usually shows a highly vascularized mass. In ultrasonography, the malignancy evaluation is based on the morphological index and Doppler index together with CT findings^[22]. Although the internal structures of the mass can be assessed by CT, magnetic resonance imaging, and ultrasonography, the precise origin, type of mass, and benign-malignant nature cannot be ascertained prior to surgery, resulting in a difficult diagnostic scenario. Of the reported cases with malignant SFT of the greater omentum, some were initially diagnosed with GISTs or ovarian tumors, which to an extent affected the treatment strategy. For instance, a

Table 1 Since 1963, a total of 13 cases of malignant solitary fibrous tumors of the greater omentum have been reported, and our patient is the fourteenth

Ref.	Age/gender	Chief complaint	Suspected diagnosis	Size	Mitosis/HPF	Immunohistochemical staining	Pathological diagnosis	Surgical treatment	Chemotherapy	Follow-up	Recurrence and metastasis
Forman <i>et al</i> ^[7] , 1952	40/M	Abdominal pain, rectal and vaginal pressure	Ovarian cyst	5 cm	NA	NA	HPC	Tumor resection and partial omentectomy	No	Recurrence and metastasis in 1 year	Rectum invasion after 11 mo
Stout <i>et al</i> ^[8] , 1963	57/F	NA	NA	11 cm × 7 cm × 5 cm	2/50	NA	HPC	NA	No	NA	NA
Stout <i>et al</i> ^[8] , 1963	64/M	Pain, swelling of the abdomen	NA	28 cm × 20 cm × 15 cm	11/50	NA	HPC	Tumor resection, omentectomy, transverse colon and the gastrocolic omentum	No	Died of disease	Distant metastasis on lung and liver
Imachi <i>et al</i> ^[9] , 1990	62/F	Abdominal distension and pain, increasing abdominal girth, diarrhea, and weight loss	Malignant ovarian tumor	24 cm × 20 cm × 12 cm	12/10	Positive for vimentin, negative for S-100 protein, myoglobin, desmin, actin, and factor VIII	HPC	Tumor resection, omentectomy, and hysterectomy	Applied	Recurrence after 1 yr	Implant in the peritoneum and the mesentery were found after 1 yr
Schwartz <i>et al</i> ^[10] , 1991	40/Unknown	Abdominal pain, abdominal mass, early satiety, weight loss	NA	NA	NA	NA	HPC	Tumor resection	Applied	Tumor spread after 18 mo. Died in 2 mo	Tumor wide spread
Cajano <i>et al</i> ^[11] , 1995	49/F	Left hypochondrial abdominal pain	NA	7 cm	NA	NA	HPC	Tumor resection and omentectomy	Applied	Recurrence after 9 mo	Intraperitoneal and liver metastases after 9 mo
Ahmad <i>et al</i> ^[12] , 2004	74/F	Abdominopelvic mass	Malignant ovarian tumor	NA	NA	NA	HPC	Tumor resection	NA	Died of disease	NA
Slupski <i>et al</i> ^[13] , 2007	61/M	Left lumbar pain	NA	5, 1, and 12 cm	NA	NA	HPC	Tumor and liver segment resection, diaphragm clearance	No	Recurrence after 18 yr	Recurrence after 18 yr, 3 metastases were found
Salem <i>et al</i> ^[14] , 2008	60/M	Intermittent periumbilical pain, weight loss, abdominal distension	NA	24 cm × 19 cm × 10 cm	25	Positive for CD34 and CD99, negative for SMA, desmin, S-100 protein and C-kit	SFT	Tumor resection	No	Uneventful recovery	No
Prakash <i>et al</i> ^[15] , 2009	45/F	Lower abdominal pain and dysuria	Hemangiopericytoma	21 cm × 16 cm × 13 cm	NA	NA	HPC	No	Applied	Symptoms decreased	No
Rodriguez Tarrega <i>et al</i> ^[2] , 2016	34/F	Unremarkable	NA	6 cm	13/10	Positive for CD34, CD99, negative for SMA, desmin, kit and DOG-1	SFT	Tumor resection and omentectomy	No	Disease-free in 32-mo follow-up	No

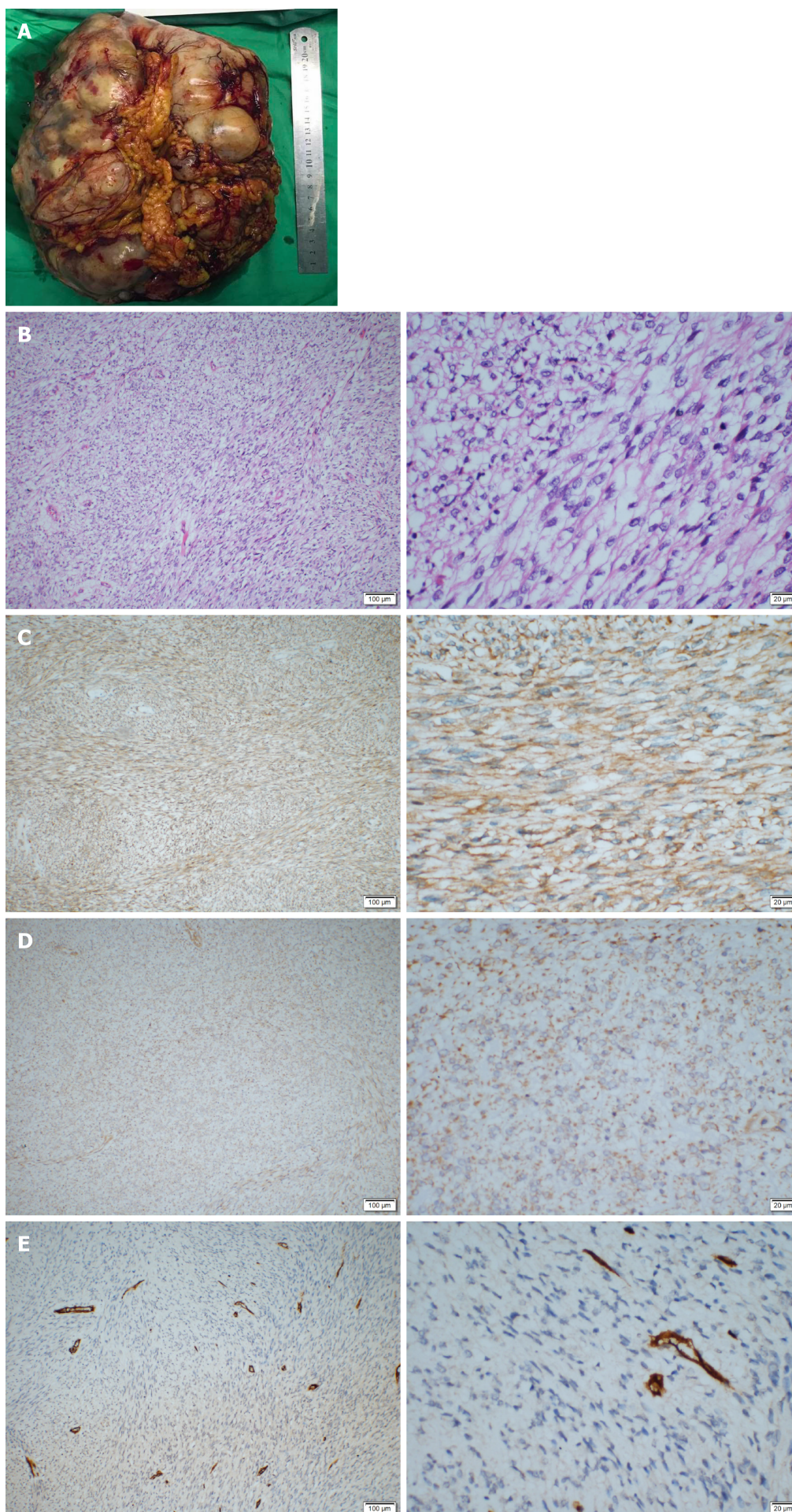
Vasdeki <i>et al</i> ^[16] , 2018	72/M	Recurrent mass of the anterior abdominal wall	NA	11 cm × 10.4 cm × 10.7 cm, 8 cm × 6.5 cm and 7.5 cm × 5.7 cm	< 4/10	Positive for vimentin, CD34 and CD99	HPC	Tumor resection and omentectomy	No	Recurrence twice in 19 yr	2 lesions in the omentum in 2011, 3 lesions in the omentum in 2018
Jung <i>et al</i> ^[17] , 2019	57/M	Asymptomatic	NA	18 cm × 11 cm × 6.2 cm	5-6/HPF	Positive for STAT6 and CD34	SFT	Tumor resection and omentectomy	No	Uneventful recovery	No
Current case		Abdominopelvic mass	GIST	27 cm × 21 cm × 9 cm	30/10	Positive for vimentin, weakly positive for DOG-1, CD99, and bcl-2; negative for STAT6, SMA, and CD34	SFT	Tumor resection, omentectomy, mesentery clearance	No	Died in 1.5 yr	Tumor recurrent and metastasis in 1.5 yr

M: Male; F: Female; HPC: Hemangiopericytoma; SFT: Solitary fibrous tumor; GIST: Gastro-intestinal stromal tumor; NA: Not available (not mentioned).

patient had a benign SFT mimicking an ovarian tumor and underwent gynecologic surgery instead of gastrointestinal surgery^[22]. Therefore, some clinicians recommend preoperative needle aspiration biopsy, which can provide preliminary pathological information.

Although SFTs are generally benign, 12-22% of SFTs are malignant. In 1976, Enzinger and Smith suggested HPC malignancy criteria by analyzing 106 cases^[23]. Later in 1989, England *et al*^[24] proposed histological malignant features of malignant fibrous tumors localized in the pleura after reviewing 223 cases. However, the diagnostic criteria of malignant SFT remains controversial. For a conclusive diagnosis, pathologists must assess all aspects of the tumor's histology. This is why in many reported cases, pathologists have only described the histological features instead of giving a clear diagnosis of benignity or malignancy. Kaneko *et al*^[25] concluded that SFT/HPC tumors ≥ 20 cm in size and a mitotic figure > 4 HPF had a poor prognosis. In the study by Demicco *et al*^[26], besides large size and high mitotic activity, they added age ≥ 55 years as another risk factor for metastasis and death. Zong *et al*^[5] suggested mitotic activity, pleomorphism, cellularity, and tumor size as predictors of SFT behavior, and they also recommended applying risk grade instead of the definitive diagnosis of benignity or malignancy, due to the limited number of cases which is insufficient to draw conclusive criteria. In this case, the external phase, histological morphology, and invasiveness resulted in the diagnosis of a malignant entity.

Immunohistochemical staining is another useful method for establishing diagnosis. SFT is generally positive for CD34, bcl2, STAT6, CD99, and vimentin^[17]. Among these markers, CD34 and bcl2 are more frequently used. It is reported that 82%-95% and 88%-100% of SFTs are positive for CD34 and bcl2, respectively. However, the markers seem ineffective in predicting tumor behavior. The resected specimen from this patient was positive for vimentin and weakly positive for bcl2, CD99, and DOG-1.



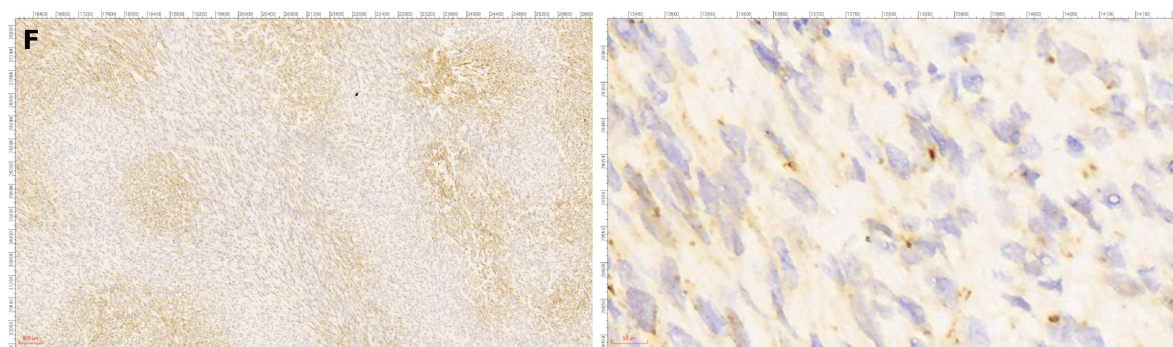


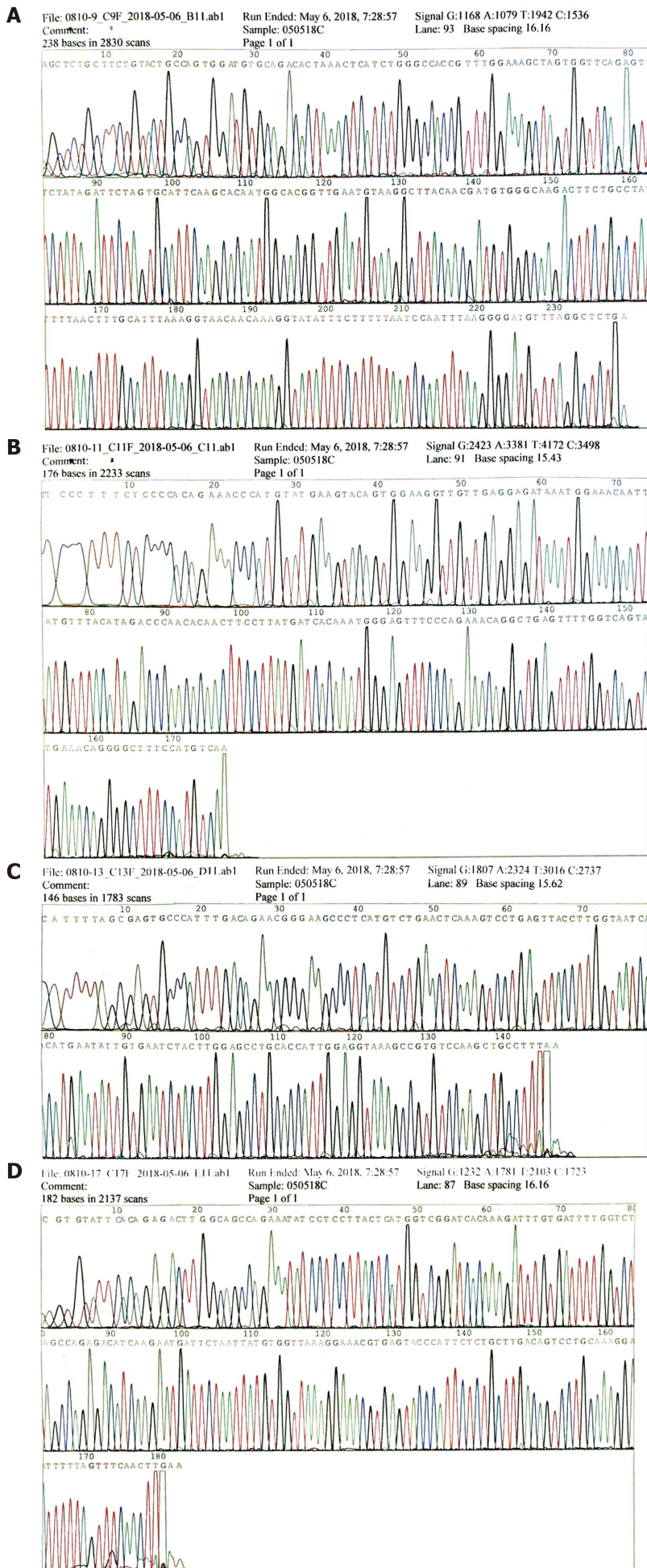
Figure 3 Pathological examination of the tumor. A: The gross morphology of the resected tumor specimen was huge (27 cm × 21 cm × 9 cm) with necrosis and hemorrhage on the surface; B: Pathological examination showed hypercellularity with spindle cells, and a high mitotic activity with a rate of 30/10 high power field (HPF); C and D: On immunohistochemistry staining, BCL-2 and DOG-1 were weakly positive; E and F: CD34 and STAT6 were negative.

Remarkably, it was negative for CD34 and STAT6, which made it difficult to differentiate between SFTs and stromal tumors such as GISTs. Approximately 94%-98% of GISTs are positive for CD117, which is rarely expressed in other abdominal tumors. In addition, oncogenic mutation in c-KIT can occur in 80%-85% of GISTs. In this case, the patient was CD117-negative and had no c-KIT gene mutation. Therefore, malignant SFT was the more probable diagnosis^[27]. This is the first reported case of a malignant SFT of the greater omentum, diagnosed by a combination of immunohistochemical staining and DNA sequencing, based on the negativity of the typical markers, CD34 and STAT6. Along with the comprehensive knowledge of genetic information acquired by clinicians, more genetic loci could be discovered as significant markers of diagnosis and prognosis of SFTs. Moreover, genetic targets of SFTs might be identified, which would alter the current treatment strategy. Therefore, gene sequencing might be more practical, helpful, and frequently used in the future.

Metastasis and recurrence are both typical features of malignant SFT. It mainly metastasizes *via* hematogenous and lymphogenous routes^[13]. In 2009, Prakash *et al*^[15] first reported peritoneal carcinomatosis caused by SFT tumor implants at the time of presentation, which is a rare metastasis route and is mostly observed in recurrent SFTs^[13,25]. Several extra-pleural SFT cases with metastases after surgical excision in the greater omentum have been reported; 8 of the 14 cases reported in the literature involved metastasis or recurrence, and recurrence was observed even as long as 18 years after remission, or several times after resection^[13,16]. Hence, long-term follow-up is necessary for patients who have SFT with malignant potential. Patients affected by recurrence within 2 years had a poor prognosis, and three-quarters of the cases died 2-15 mo after diagnosis of recurrence. In our case, omental and mesentery implants were confirmed during surgery. Such extensive metastases are extremely rare in SFT and indicate aggressive malignancy, which led to recurrence and death after 18 mo. As a result, close follow-up is required for the remainder of the patient's life.

Surgical excision is the only definite treatment for SFT^[17]. Despite complete resections, local recurrences of SFT have been reported^[13]. Considering the malignant and recurring potential of SFT, mass excision with a tumor-negative margin is recommended^[28]. The greater omentum is a supportive vascular fatty fold, which protects against tumor growth and infection^[6], and the decision to perform omentectomy with tumor resection is debatable. In reported omental malignant SFT cases, 8 patients underwent total or partial omentectomy. Of these 8 patients, 6 had recurrence. The high recurrence rate among the patients who underwent omentectomy explains why surgeons such as Shiba *et al*^[3] questioned the significance of omental resection. Post-operative systematic treatment, adjuvant chemotherapy and radiotherapy were performed in several malignant cases^[29]. However, routine usage of adjuvant therapies is questioned by clinicians due to little evidence supporting improvement in aggressive tumors with adjuvant chemotherapy^[17,30]. Only 3 patients received adjuvant chemotherapy; all 3 patients had poor outcomes caused by recurrence and metastasis (Table 1). Moreover, the Tumor-Node-Metastasis staging system is not applicable to SFT, resulting in the lack of a standard guidance for the systematic treatment of malignant SFTs. Gene sequencing might be a potential solution for the current dilemma. It may provide evidence in order to decide which chemotherapy approach is more beneficial.

In managing this patient, our main limitation was the unavailability of sufficient knowledge on pre-operative diagnosis and post-operative treatment. In the treatment



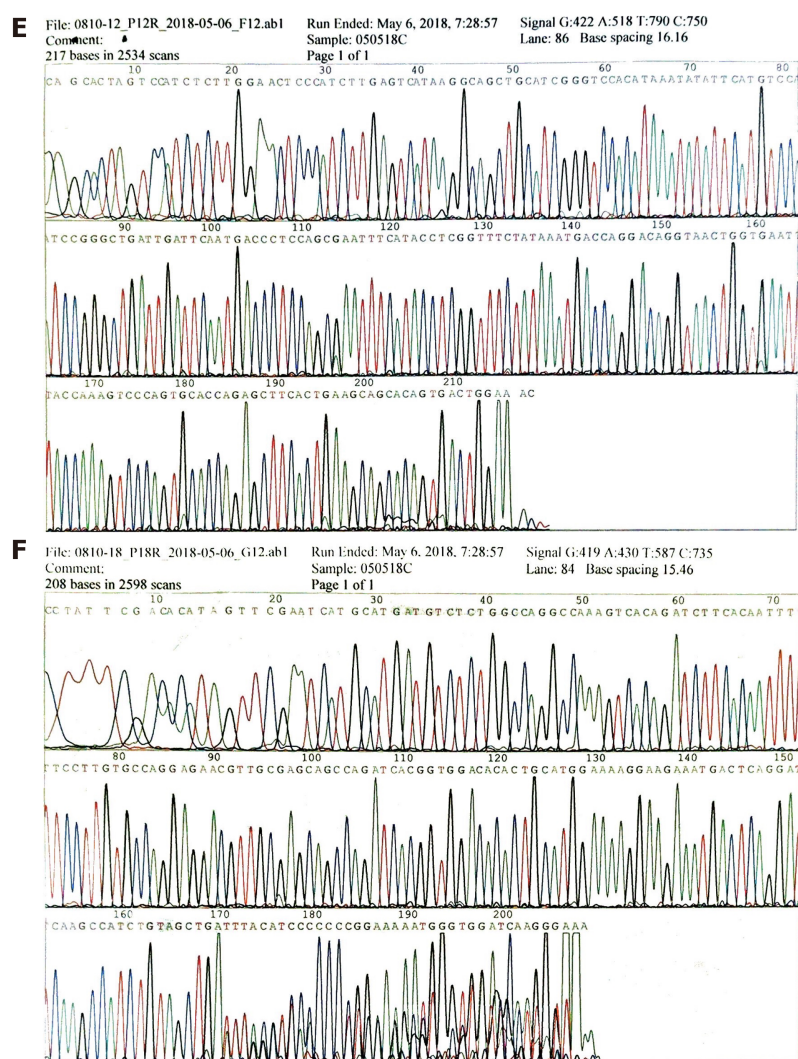


Figure 4 Gene sequencing was performed using the paraffin-embedded tumor section. A-F: Four exons of c-KIT including 9 (A), 11 (B), 13 (C), and 17 (D); and 2 exons of PDGFRA including 12 (E) and 18 (F) were sequenced using the Sanger method. The results revealed negative gene mutation in all the exons.

of our patient, omentectomy and tumorectomy with nodule clearance were provisional intraoperative treatment decisions due to the diffuse tumor implants. The limited knowledge on the pathology, origin, and metastasis status impeded the surgical plan, which resulted in an exploratory surgery instead of a specific procedure; therefore, there is an urgent requirement for accurate specific diagnostic work-up. In addition, the present systemic therapy lacks convincing clinical evidence and requires further confirmation before application in SFT patients with metastasis. Lastly, as a rare disease with a consistently low number of reports, cases of malignant SFTs of the greater omentum were not documented in a consistent manner; instead, there were a lot of variations in the completeness of the information contained in the reports. Such inconsistency does not allow a better understanding of the disease. For improvement, the records may be taken into a database of a centralized tumor registry, which is able to provide more comprehensive and consistent data for further research.

CONCLUSION

In this study, we report a rare case of a malignant SFT of the greater omentum, which was diagnosed *via* immunohistochemical staining and gene sequencing. Although the patient underwent tumorectomy and clearance, the patient died due to recurrence after 18 mo. In this case, gene sequencing was used to diagnose the SFT when the results of immunohistochemical staining were not able to distinguish between an SFT and GIST. In addition, more comprehensive records are necessary when reporting such a rare malignancy, which is able to stimulate the establishment of more effective

management guidelines for omental malignant SFT cases and improve outcomes.

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