Abstract. Solitary fibrous tumors (SFTs) are composed of spindle cells and collagen fibers, and these form rare mesenchymal tumors. SFTs are most frequently observed in intrathoracic sites; however, they may also occur in extrathoracic sites, such as the liver. Unlike the hepatic SFTs (HSFTs) reported in the literature, the SFT detailed in the present case report was a large tumor that originated from the liver, with a dumbbell-shaped growth through the diaphragm into the right thoracic cavity. This posed substantial challenges in both diagnosis and treatment. Thus, the present report outlines the findings of a multidisciplinary team meeting that was used to discuss and develop an optimal and personalized treatment strategy for the patient. Transhepatic arterial embolization was performed to block the major arterial blood supply to the tumor in order to reduce its size. Subsequently, the tumor was fully resected, following the collaboration of the experienced hepatobiliary and thoracic surgeons. Following surgery, the abdominal distension experienced by the patient ceased, and no tumor recurrence was detected at the 1-year follow-up. In conclusion, due to limited previous reports of HSFT treatment using multidisciplinary collaboration, the present study outlined the treatment used for this specific tumor type, and the corresponding literature was reviewed.

Introduction

Multidisciplinary team meetings (MDTMs) are defined as meetings of a group of medical experts in different fields who gather at a specific time to discuss and determine the most appropriate treatment based on objective evidence (1). At present, MDTMs are widely used in both Europe and the United States of America, and play an increasingly important role in the treatment of cancer and other diseases (1). The present case report highlights the importance of multidisciplinary collaboration in the treatment of complex hepatic solitary fibrous tumors (HSFTs).

Solitary fibrous tumors (SFTs) are also known as hemangiopericytomas (2), which originate from the mesenchymal tissue and feature pericytic, fibroblastic and myofibroblastic differentiation (3). SFTs were initially described by Klemperer and Rabin in 1931 (4). The incidence rate of SFTs remains at 1 case/million individuals/year (5). Notably, the majority of SFTs occur in the thoracic cavity; however, previous studies have demonstrated the occurrence of SFTs throughout extrathoracic sites, such as the retroperitoneal space (6), meninges (7), orbit (8), breast (9), thyroid gland (10), pericardium (11), parotid gland (12), spine (13), pelvic cavity (14), omentum (15), perineum (16), bladder (17), prostate (18), external auditory canal (19), pancreas (20) and, less often, in the liver (21).

Clinical manifestations of SFTs depend on the size and location of the tumor (22). HSFTs are usually asymptomatic; however, they may lead to corresponding non-specific clinical symptoms, such as abdominal pain, bloating, indigestion, weight loss, nausea and vomiting, and these symptoms often occur as the tumor size increases (22). Notably, only a small number of patients develop paraneoplastic syndromes, such as hypertrrophic osteoarthropathy and hypoglycemia (5). Hypertrophic osteoarthropathy is attributed to the overexpression of vascular endothelial growth factor (5), and hypoglycemia is caused by the overexpression of insulin-like growth factor 2 (23). A previous study demonstrated that the vast majority of SFTs are benign, and seldom recur or metastasize (24). Notably, TP53, PDGFRB and TERT promoter regions may be involved in the malignant transformation (25,26).

Imaging is often non-specific, meaning that using radiography to distinguish SFTs from other tumors, such as hepatocellular carcinoma, leiomyoma, sarcoma, sclerosed hemangioma and inflammatory pseudotumors, may be challenging (22). The current diagnosis of SFT is based on the histopathological and immunohistochemical features (27).
Histopathological characteristics of an SFT include spindle cells and collagen fibers (27). Immunohistochemical analysis of an SFT demonstrates the expression of vimentin, CD34, STAT6 and CD99, and in some cases, Bcl-2 and β-catenin (22-24,27-32). In addition, previous studies have demonstrated that STAT6 nuclear protein and the NAB2-STAT6 fusion gene are regarded as more precise tools for SFT diagnosis (5).

At present, the preferred treatment option for SFTs is the complete surgical removal of the tumor (27). However, metastasis and recurrence may still occur, despite the ongoing development of this therapeutic approach (27). To date, the clinical benefits of adjuvant chemotherapy and radiation for the treatment of SFTs remain unclear (33). The present study reports a case in which a multidisciplinary collaboration approach was used for the treatment of an HSFT appearing as a dumbbell-shaped growth through the diaphragm into the right thoracic cavity. The corresponding literature was also reviewed.

Case report

A 59-year-old female patient visited The Second Affiliated Hospital of Zunyi Medical University (Zunyi, China) on June 3, 2020, for abdominal distension that had persisted for 1 month. The patient presented with no prior history of viral hepatitis, chronic alcohol consumption or other chronic liver diseases. A physical examination demonstrated abdominal distension and a solid mass (volume, 5x6 cm) that was palpable in the right upper quadrant. Laboratory examination demonstrated that biochemical indices, including routine blood tests, coagulation tests, and liver function and tumor marker analyses (including carcinoembryonic antigen, cancer antigen 19-9, α-fetoprotein, squamous cell carcinoma antigen, progastrin-releasing peptide, neuron-specific enolase and cytokeratin fragment 19), were within healthy ranges.

Magnetic resonance imaging (MRI; Fig. 1) and computed tomography (CT; Fig. 2) of the chest and upper abdomen demonstrated that the tumor was dumbbell-shaped with clear boundaries; notably, the tumor was mainly located in the right upper lobe of the lung and the remaining section was present in the thoracic cavity. The blood supply to the tumor originated from the hepatic artery. There was a partial defect in the diaphragm and the tumor passed into the thoracic cavity. Additionally, atelectasis in the right lower lobe of the lung was present. It was concluded that the tumor originated from the liver, and was closely associated with the diaphragm and thoracic cavity.

For a definitive diagnosis, a fine-needle biopsy of the tumor was performed. Histopathology (Fig. 3) demonstrated that the tumor cells were spindle-shaped, with scant cytoplasm, and homogeneous staining of the oval nuclei. Moreover, the tumor cells were surrounded by abundant collagen fibers, and neither cellular atypia nor mitotic figures were present. Immunohistochemical analysis (Fig. 3) demonstrated that the tumor cells were positive for vimentin, CD34 and STAT6, and negative for desmin, cytokeratin (CK), smooth muscle actin (SMA), S100, myoblast determination protein 1 (MyoD1), anaplastic lymphoma kinase (ALK), epithelial membrane antigen (EMA), CD31, CD68, hepatocyte paraffin 1 (HepPar1) and CD117. The results of the fine-needle biopsy supported the diagnosis of an HSFT.

Due to the large tumor size and complex anatomy, an MDTM was subsequently performed to discuss the management of the tumor. The meeting members included seven chief physicians from the Departments of Oncology, Interventional Radiology, Thoracic Surgery, Hepatobiliary Surgery, Pathology, Imaging and Anesthesiology (The Second Affiliated Hospital of Zunyi Medical University). In the MDTM, meeting members discussed the requirement for arterial embolization due to the abundant blood supply and large size of the tumor. This can result in the tumor becoming ischemic and necrotic, or the tumor may shrink (34). However, the therapeutic effects of hepatic artery embolization alone remain limited, and tumor cells may produce a variety of vascular growth factors under hypoxia to stimulate angiogenesis (35). Therefore, we hypothesized that hepatic artery embolization combined with radical surgery may be an optimal treatment option.

Moreover, the possibility of metastasis to the diaphragm and the right lower lobe of the lung was discussed. Notably, the primary tumor and metastatic lesions may require resection simultaneously; however, this could not be performed by single-discipline surgeons. Moreover, a broad range of anatomical variations or extensive adhesions of the tumor may be present, which may cause tumor rupture during surgery, as well as tumor dissemination. Therefore, resection following the collaboration of experienced hepatobiliary and thoracic surgeons may improve the safety of the surgery. In addition, the possibility of adjuvant radiotherapy and chemotherapy were rejected in the meeting due to their unclear roles in SFTs (33).

Following the MDTM, a consensus was established and a personalized treatment protocol was developed. This included transhepatic arterial embolization to block the major arterial blood supply, and a full resection of the tumor, using the collaboration of experienced hepatobiliary and thoracic surgeons. The treatment protocol was fully discussed with the patient and written informed consent was obtained. Angiography showed the staining of the tumor with contrast agents, with multiple branches of the hepatic artery participating in the blood supply to the tumor. Subsequently, an interventional radiologist used self-made gelatin sponge particles as embolic agents, to embolize three branches of the hepatic artery. Re-examination of the angiography demonstrated that the staining of the tumor was significantly reduced. There were no complications associated with the hepatic artery embolization.

On day 1 post-hepatic artery embolization, a laparotomy was performed using an anti-L-shaped incision in the epigastrium. Intraoperative abdominal exploration demonstrated that a large tumor of the right liver lobe (volume, 8x7x6 cm), with a hard texture, clear boundaries and an intact envelope, protruded through the surface of the right liver lobe and passed through the diaphragm into the thoracic cavity. Intraoperative thoracic exploration demonstrated that the thoracic tumor (volume, 10x7x7 cm) was intimately connected with the tumor of the right liver lobe and exhibited a strong adhesion to the right lower lobe of the lung, which may have been invaded by the tumor. No metastasis was noted within the remaining thoracic and abdominal cavities.
A self-made red urinary catheter (Fig. 4) was used for the first porta hepatis occlusion, to fully expose the liver and the tumor. Subsequently, a pre-cut liver line (Fig. 4) was marked using an electrocautery knife at a distance of 2 cm from the diaphragm.
Figure 3. Pathological examination of fine-needle biopsy specimen. (A) Histopathology results demonstrating spindle shaped tumor cells with scant cytoplasm, with homogeneous staining of the oval nuclei. The tumor cells are surrounded by abundant collagen fibers, and neither cellular atypia nor mitotic figures are present. Immunohistochemical analysis demonstrating positive staining for (B) vimentin, (C) CD34 and (D) STAT6. Scale bars, 80 µm. H&E, hematoxylin and eosin.

Figure 4. Intraoperative situation. (A) The green arrow indicates the tumor of the thoracic cavity, the purple arrow indicates the tumor boundary of the liver, the blue arrow indicates the self-made red urinary catheter and the yellow arrow indicates the black sutures. The black sutures were used to locate and tract the tumor, which helped remove it. (B) The white arrow indicates the electrocauterized pre-cut liver line. (C) The red arrow indicates the liver section following tumor resection.
The tumor was fully resected. Meanwhile, resection and repair of the diaphragm, and wedge resection of the right lower lobe of the lung were performed. During surgery, the first porta hepatis was intermittently occluded three times. The first time was for 10 min, the second time was for 15 min and the third time was for 5 min. Notably, the intraoperative hemorrhage volume was ~200 ml, and no blood transfusion was performed.

The gross specimen of the tumor (Fig. 5A) demonstrated a dumbbell shape (volume, 14x8x7 cm) with an intact envelope. The cut surface of the tumor (Fig. 5B) demonstrated a grey-white fibrous appearance, with a hard texture and clear boundaries.

Postoperative histopathological analysis demonstrated a negative resection margin (Fig. 6), and the remaining histopathological features were the same as those observed following fine-needle biopsy. In addition, no tumor invasion was observed in the resected lung tissues or diaphragm. Postoperative immunohistochemical analysis (Fig. 6) demonstrated that the tumor cells were positive for vimentin, CD34, and STAT6, and also for CD99, Bcl2 and β-catenin. The remaining immunohistochemical features were the same as those observed following fine-needle biopsy of the tumor.

In the course of the histopathological examinations, the tissue sections were stained with hematoxylin and eosin for 6 min at room temperature. In the process of the immunohistochemical examinations, the tumor tissues were fixed in 10% neutral buffered formalin for 24 h at room temperature. Paraffin sections (slice thickness, 4 µm) were produced using paraffin-embedded tissues. Antigen repair was performed using a pressure cooker to heat tissue sections in ethylene diamine tetraacetic acid buffer (pH 9.0) for 20 min. Endogenous peroxidase was blocked using incubation with 3% H2O2 for 15 min at room temperature. Sections were incubated overnight with primary antibodies at 4˚C. Following primary incubation, the sections were incubated with secondary antibodies for 30 min at room temperature. The nuclei were stained using hematoxylin for 6 min at room temperature. The stained sections were analyzed using an Olympus BX46 light microscope (Olympus Corporation, Tokyo, Japan). Immunohistochemical analysis was performed using Image J (version 1.46a; National Institutes of Health).

The postoperative course was uneventful and no abdominal distention occurred. However, the nutritional status of the patient was poor, and recovery time was prolonged. Subsequently, the patient was discharged from the hospital 12 days after the surgery. The patient had not received any postoperative adjuvant chemotherapy. Following discharge, patient follow-up was performed at 1, 2, 3, 6 and 12 months. Examinations during follow-up consultations included MRI and CT scans of the chest and upper abdomen, and tumor marker analysis. At the end of the 1-year follow-up, the patient remained healthy and demonstrated no signs of recurrence.

Discussion
An SFT is a rare tumor of mesenchymal origin, with prominent histological characteristics of a hemangiopericytoma-like tumor.
branching vascular pattern (2). The prevalence of SFTs does not differ between men and women (2), and the age of onset is 20-70 years (5).

The majority of patients with SFTs are clinically asymptomatic; however, the current study presented the case of a patient with abdominal distension that had persisted for 1 month due to the tumor oppressing neighboring anatomical structures.

SFTs often present with typical features during imaging, including single, clear boundaries, inhomogeneous enhancement and high vascularization (36). The results of a previous study demonstrated inhomogeneous enhancement, which may
have been due to the differential enhancement of the admixed cellular and collagenous components (26). However, not all SFT imaging is typical (37). Imaging examinations, including MRI, CT and abdominal ultrasound scans, may be used to reveal liver tumors. Among them, MRI is considered the gold-standard imaging modality for SFTs (38). The results of a previous study demonstrated masses of predominantly low or intermediate signal intensities on both T1 and T2-weighted images, which may reflect the high content of fibrous collagenous tissue, hypocellularity and the relatively small number of mobile protons (37). Moreover, hyperintensity on T2-weighted images may be associated with necrosis, cystic or myxoid degeneration, prominent vascular structures and hypercellular areas (37).

Laboratory examination results often present within healthy ranges; however, a few patients have presented with liver dysfunction or increased levels of thrombocyte or C-reactive protein, which were not specific and did not directly correspond to the diagnosis of an SFT (39,40). In the current case, the patient presented with no abnormalities.

The diagnosis of an SFT depends on the pathological examination, due to inaccuracies in laboratory and imaging examinations. Therefore, a fine-needle biopsy was performed in the present study in order to obtain pathological results and a definitive diagnosis, and this provided a basis for determining whether adjuvant therapy was required. However, the use of a fine-needle biopsy for diagnosis remains controversial. On one hand, previous research has demonstrated that a fine-needle biopsy may help obtain tumor tissues, and that these may be useful for the pathological and differential diagnosis of the tumor (21). On the other hand, research has demonstrated that the results of fine-needle biopsy may cause tumor dissemination, or at the least may be misleading or unclear. This is due to the fact that benign and malignant tumors may exist in the same lesion at the same time, and the punctured tissue may not contain malignant components (22,28).

Common histological and immunohistochemical features are useful to determine a definitive diagnosis. In the present case, pathological examinations of fine-needle biopsy and surgery specimens supported the diagnosis of an HSFT. The histopathology results demonstrated a diffuse proliferation of spindle cells surrounded by collagen fibers. Tissue sections were stained with H&E for pathological examination, and the results demonstrated no malignant transformation. Immunohistochemical analysis demonstrated that the tumor cells were positive for vimentin, CD34, STAT6, CD99, Bcl2 and β-catenin; however, they were negative for desmin, CK, SMA, S100, MyoD1, ALK, EMA, CD31, CD68, HepPar1 and CD117 which is indicative of an HSFT (24,33,39).

The majority of SFTs are benign, but malignant features must be considered when the following evidence is presented: Infiltrative margins, high cellularity, prominent cellular atypia, tumor necrosis and increased mitotic activity (>4 mitoses/10 high-power fields) (3). In the present case, the tumor originated from the liver and grew through the diaphragm into the right thoracic cavity. Thus, this was considered as possessing malignant characteristics. However, it was morphologically benign (no infiltrative margin, low cellularity, no cellular atypia, no significant tumor necrosis and a low mitotic rate). In addition, no tumor invasion was observed in the resected lung tissues and diaphragm. The aforementioned results indicated that there was no specific association between the behavioral and morphological features, and this is comparable to the results of previous studies (2,24).

Radical surgery is the preferred treatment for an HSFT. The resection margin must be at least 1 cm away from the tumor to avoid tumor residue. Intraoperative frozen sections must also be routinely performed. Notably, if infiltrative margins are found, further resection must be considered (41). To date, the treatment methods of HSFTs are increasingly diversified and complicated, and knowledge of a single discipline is insufficient to deal with complex cases. MDTMs are interdisciplinarily, centralized, individualized and precise, and play an important role in the treatment of complex tumors (42).

In the present case, surgery was the most optimal treatment method for the tumor. However, the tumor involved multiple organs and the surgical risk was high; therefore, removal of the tumor was determined to be difficult for doctors of a single discipline. Based on the aforementioned assessment, MDTMs were organized to develop a personalized treatment strategy from a multidisciplinary perspective, in order to successfully treat the tumor according to the specific situation of the patient.

In the present case, the etiology of the diaphragm defect may have been either congenital or acquired. A congenital diaphragm defect may be caused by dysplasia of the diaphragm. The potential mechanism underlying an acquired diaphragm defect is as follows: As the tumor volume increases, the abdominal pressure increases, leading to an increase in the pressure difference between the thoracic cavity and the abdominal cavity. This ultimately causes the tumor to break through the weak area of the diaphragm. In addition, the results of the present case report demonstrated no association between the diaphragm defect and tumor aggressiveness, and this may be due to a clear boundary, the intact envelope of the tumor and a lack of tumor invasion of the diaphragm. To the best of our knowledge, an HSFT exhibiting a dumbbell-shaped appearance has not been previously reported. The dumbbell-shaped appearance of the tumor may be caused by the growth of the tumor through the narrow diaphragm defect. Moreover, the atelectasis in the right lower lobe may have been caused by intrathoracic tumor compression.

Transarterial chemoembolization (TACE) is an important yet variably effective treatment for the management of hepatic malignancies. The arterial blood supply is blocked by chemical embolization, which may result in ischemic necrosis of the tumor (33). In the literature, only three previous cases involving the treatment of an HSFT using TACE have been previously reported (33,43,44). The results of one of these cases demonstrated that the tumor was located in the center of the liver, and invaded the left and right lobes. This was therefore unresectable and TACE was performed on the patient three times (33). The second case investigated a tumor that was located in the right lobe of the liver with right parietal metastasis; notably, TACE was performed, followed by subtotal resection of the right liver and craniectomy in the patient (43). The final study demonstrated that the tumor was located in hepatic segments IV, V, VI and VIII. Subsequently, a right portal vein embolization was performed followed by TACE,
and a right hepatectomy was also performed (44). In the present case, transhepatic arterial embolization was performed before surgery. Following transhepatic arterial embolization, the tumor blood supply was significantly reduced, which greatly decreased the difficulty of the surgery.

The MDTM held during the present study included discussions of serious complications that may occur following hepatic artery embolization, and debate over whether adjuvant chemotherapy and radiation should be performed.

Results of a previous study revealed that few patients suffered from ectopic embolism-related complications, such as tumor rupture, cholecystitis, splenic infarction, liver abscesses, and cerebral and pulmonary embolism (45). These complications were rare (45), and were associated with non-selective embolization, the number of procedures and the volume of embolic material (46). Results of previous studies also demonstrated that the large tumor size may impact the risk of rupture (47) and liver failure (48).

To avoid the occurrence of serious complications, selective catheterization and slow infusion of the embolic material were performed in the present case. In addition, the results of a previous study demonstrated that post-embolization syndrome is closely associated with the side effects of chemotherapy drugs (49). Thus, self-made gelatin sponges were used in the present study to replace the chemotherapy drugs and result in fewer side effects.

Adjuvant therapy is not always necessary and is reserved for when a resection is incomplete, or when pathological examination reveals the features of malignancy or postoperative recurrence with metastasis (25). The role of chemotherapy and radiotherapy in the aforementioned tumor types is ambiguous (33). Doxorubicin has been used as a first-line therapy in advanced soft-tissue sarcoma for >40 years (5). The mechanism of action of doxorubicin involves the insertion of DNA, which disrupts DNA damage repair through topoisomerase II, thus generating free radicals and leading to ulterior cell membrane damage (5). As previously reported, de-differentiated SFT (DD-SFT) with a high malignancy (significant genomic instability, and substantial cytogenetic losses and gains) is the subtype of SFT with the fastest growth (5). Therefore, doxorubicin may be a valuable option for patients suffering from DD-SFT (5). However, doxorubicin administration in patients with non-DD-SFT may be detrimental, adding genomic instability through its direct genotoxic action, or by doxorubicin-mediated oxidative stress production (5). In the present case, histopathology and immunohistochemistry revealed a well-differentiated tumor. Thus, it was determined that doxorubicin was not suitable for chemotherapy. In addition, the use of gemcitabine, as a pyrimidine antitumor agent, has only been reported sporadically in cases of SFT and exhibits poor treatment effectiveness (50,51).

A small retrospective study involving 14 patients with recurrent intracranial SFT demonstrated that the use of external radiation therapy extended overall survival time compared with surgery alone (10.3 vs. 5.3 years) (38). However, a large retrospective study consisting of 549 cases of SFT, 428 (78%) of which underwent surgery and 121 (22%) of which underwent surgery plus postoperative radiotherapy, demonstrated that there was no significant difference in patient overall survival time between the two groups (52). Therefore, radiotherapy was determined to be unsuitable for the present case.

The prognosis of SFTs is often associated with resectability (28). The results of a previous study demonstrated that the 5-year survival rate of patients who underwent curative resection was significantly increased compared with that of patients who underwent non-curative resection [partial excision (79%) or biopsy (50%)] (53). Results of a previous study demonstrated that the 5-year survival rate of patients who underwent curative resection was 100% (54). Similarly, 10-year survival rates of 54% have been observed when complete curative resection is an option (53). It has also been suggested that patients with malignant histological features are more susceptible to recurrence and metastasis (27).

In conclusion, although the majority of HSFTs are benign, they exhibit the potential for malignant transformation. Thus, patients require long-term follow-up. HSFT is a rare mesenchymal tumor, and there is limited previous evidence detailing the diagnosis and treatment of this tumor type. Treatment options require multidisciplinary collaboration when complex tumor structures arise.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

JL conceived and designed the present case report. JL and JW collected the clinical data and conducted the follow-up visit. ZC performed the histopathological analysis and provided the associated images. SH and JW performed the imaging analysis and provided the imaging data. JL wrote the initial draft of the report. The present article has been revised by SH, JW and ZC. ZC performed the surgery and provided care for the patient. JL and ZC confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Competing interests

The authors declare that they have no competing interests.
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