

Recurrence of multiple metastases after surgical removal of a primary malignant solitary fibrous tumor from the main bronchus

A case report

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Abstract

Rationale: Limited knowledge is available regarding solitary fibrous tumors (SFTs), about 15% of which are malignant. In particular, the long-term survival of patients with malignant SFTs (mSFTs), the disease course, and the potential for recurrence of second primary tumors or distant metastases are largely undetermined.

Patient concerns: We report a rare case in which an mSFT was found at the main bronchus of the right lung of a 37-year-old man.

Diagnosis: The tumor cells of mSFT were spindle-shaped and expressed antigen Ki-67, B-cell lymphoma 2, cluster of differentiation 31, and vimentin.

Interventions: A total pneumonectomy was performed.

Outcomes: The patient developed fibrosarcoma of the small intestine at 6 months, as well as extensive pleural and peritoneal metastases at 1 year, after removal of the primary mSFT from the right main bronchus.

Lessons: From these findings, we expect that patients with primary mSFT, especially of the lung, have a high potential to develop second tumors or distant metastases. Close monitoring after surgery is necessary to improve the outcomes of these patients.

Abbreviations: mSFT = malignant SFT, SFTs = solitary fibrous tumors.

Keywords: immunohistochemistry, long-term management, malignant solitary fibrous tumor, multiple metastases

1. Introduction

Solitary fibrous tumor (SFT), also known as localized fibrous tumor, benign mesothelioma, localized fibrous mesothelioma, submesothelial fibroma, or pleural fibroma, refers to a rare mesenchymal tumor originating in the pleura or soft tissue.^[1–6] SFT was first mentioned in the scientific literature by Wagner,^[5] followed by a description of its clinical and pathological properties by Klemperer and Rabin in 1931.^[2] SFT has been defined as a “tumor composed of small cells, individually separated by thin bands of collagen fibers.” Approximately 78% to 88% of SFTs are benign, and 12% to 22% are malignant.^[1–6] About 80% of SFTs originate in the visceral pleura, and 20%

arise from the parietal pleura.^[5,6] Although the tumors are often very large (up to 40 cm in diameter), over half of patients are asymptomatic at diagnosis.^[6,7]

Clinical and pathological features and findings from immunohistochemical analysis are the basis for the diagnosis and differential diagnosis of SFTs.^[1,8–21] The character of SFT includes a branching, hemangiopericytoma-like (staghorn) vasculature with a “patternless” architecture containing hyper- and hypocellular collagenized stroma.^[8–11] The cell of origin of SFT is controversial and has not been clarified. Criteria for malignant SFT (mSFT) are not standardized; however, according to the World Health Organization Classification of Soft Tissue Tumors, the main features include hypercellularity, moderate to significant cellular atypia, tumor necrosis, 4 mitoses among 10 high-power fields, and infiltrative margins.^[1,8] Compared with benign SFTs, malignant tumors are radiographically characterized by larger size, higher likelihood of CD34, and B-cell lymphoma 2 (Bcl-2) expression,^[22,23] clinically symptomatic presentation,^[24–26] higher propensity to recur or metastasize, and poorer survival rates.^[6,14,24,27,28]

Standard treatment for benign or malignant SFT is complete en bloc surgical resection. From a population-based analysis of patients with thoracic mSFTs, stage and cancer-directed surgery had the greatest impact on overall survival and cause-specific survival. Patients treated by surgery showed better survival rates.^[24–26,28,29] The prognosis of benign SFTs treated by surgery is excellent. Only 8% will recur after the first resection, and the recurrence tumor can usually be cured by additional surgery.^[6] However, the prognosis of mSFTs is much poorer, and these

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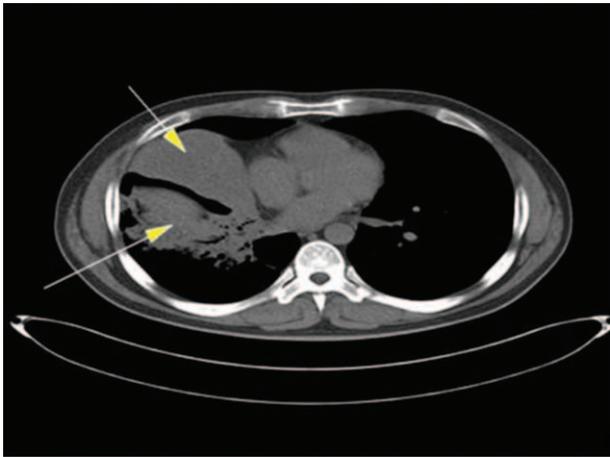


Figure 1. CT scans of the patient's chest (lung window) 10 days before hospitalization, showing lesions in the right lung. CT = computed tomography.

tumors should be managed with caution. Most patients (63%) will have tumor recurrence, and more than half of recurrent patients will succumb to disease progression in 2 years.^[6] Adjuvant chemotherapy and radiotherapy are suggested for mSFTs, but their effectiveness remains controversial.

2. Case presentation

The study was approved by the Research Ethics Committee of the First Hospital of Jilin University. Informed written consent was obtained from the patient for publication of this case report and accompanying images. A 37-year-old man presented to the Thoracic Surgery Department of our hospital with continuous cough for 1 month and increased dyspnea for 1 day (02/2012). The patient was subjected to lung computed tomography (CT) scanning 10 days before admittance to our department. Lesions were found in the right lung (arrowheads in Fig. 1). Bronchoscopy analysis revealed a mass at the right bronchus near the middle of the lung (Fig. 2). The mass was smooth, but spindle cell lesions were evident.

Two-phase enhanced CT was performed to re-examine the patient's chest (Fig. 3). The right main bronchus and bronchial



Figure 2. Bronchoscopy results upon admission to the Thoracic Surgery Department. A tumor blocked the right main bronchus, extended over the carina, and blocked the left main bronchus.

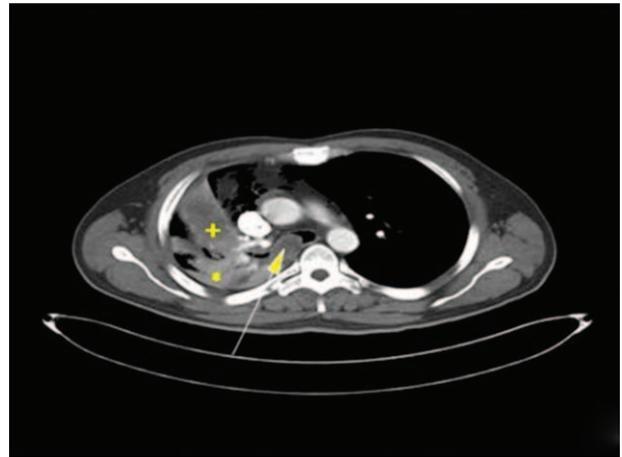


Figure 3. Two-phase enhanced CT was performed to re-examine the patient's chest. The right main bronchus and the bronchial cavities in each lobe of the right lung were filled with a high-density mass (arrows). The lumen was blocked and locally convexed at the tracheal lumen (arrowheads). The volume of the distal lobes of the right lung was reduced, and their density was increased. Most of them were consolidated, and there were some flakes of gaseous lung tissue (asterisks). The intensity of the middle lobe of the right lung was uneven and of low density, with the presence of irregular flakes of tissue (crosses). CT = computed tomography.

cavities in each lobe of the right lung were filled with a high-density mass (arrows in Fig. 3). The lumen was blocked, and there was a convex mass at the tracheal lumen (arrowheads in Fig. 3). The volume of the distal lobes of the right lung was reduced, and their density was increased. Most of these lobes were consolidated, and there were some flakes of gaseous lung tissue (asterisks in Fig. 3). The intensity of the middle lobe of the right lung was uneven and had a low density, with the presence of irregular flakes within the tissues (crosses in Fig. 3).

Diagnostic imaging revealed space-occupying lesions in the right main bronchus and bronchial cavities in each lobe of the



Figure 4. Diagnostic imaging revealed space-occupying lesions in the right main bronchus and bronchial cavities in each lobe of the right lung.

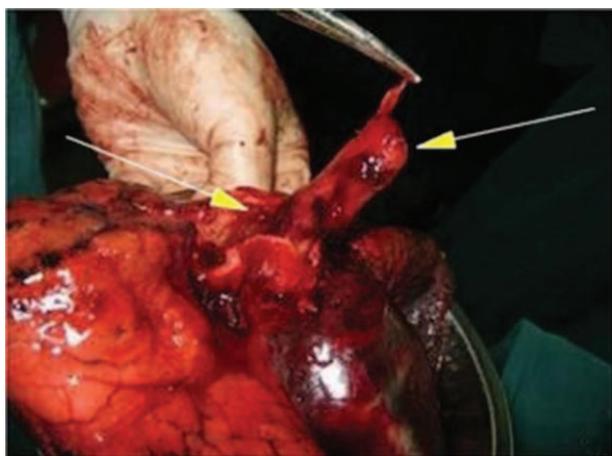


Figure 5. Resected right lung and tumor in right thoracotomy surgery.

right lung (Fig. 4). Bronchoscopy performed under full anesthesia revealed that a tumor blocked the right main bronchus, extended over the carina, and blocked the left main bronchus (arrow in Fig. 5). The patient exhibited dyspnea, hypoxia, and incessant coughing. Blood-gas analysis showed a pH value of 7.44, low oxygen pressure, high carbon dioxide pressure, and a blood oxygen concentration of 78%. Emergency right thoracotomy surgery under full anesthesia was necessary and performed.

During surgery, a tumor was found in the right bronchus esophagus. The tumor had grown along the right main bronchus to the proximal end and was blocking the right main bronchus. It extended over the carina and blocked the left main bronchus and carina without invasion. Resection of the full right lung and part of the carina was performed (Fig. 6). The resected tumor was sent for pathological examination, which revealed positive expression of antigen Ki-67, Bcl-2, cluster of differentiation 31 (CD31), and vimentin, without expression of CD34, cytokeratin (CK), smooth muscle actin (SMA), or actin (Fig. 7). The tumor was confirmed to be an mSFT. The patient did not receive chemotherapy and showed a stable disease course.

After 3 months (May 2012), the patient developed asphalt-like black stool. Normally, the patient had 3 bowel movements per day, with each having a volume of 200 to 300 mL. The patient had pain around the umbilicus, with some pain relief after a bowel movement. The patient did not show mucilage, sepsis, or fever. After eating, the patient sometimes had nonradiating pain of the left upper abdomen, which could last from a few minutes to several hours, with eventual resolution of the pain on its own. One month later (June 2012), the patient reported feeling fatigue, palpitations after moving, and shortness of breath. An abdominal CT image showed limited intestinal bowel changes of the left lower abdomen, including local lesions with intussusception, as well as multiple lesions on the right side of the diaphragm and left abdominal peritoneum. The disease progressed, and blood was identified in the stool 1 month later (July 2012). The patient was admitted for intussusception surgery, and part of the small intestine was removed for pathological analysis. The biopsy

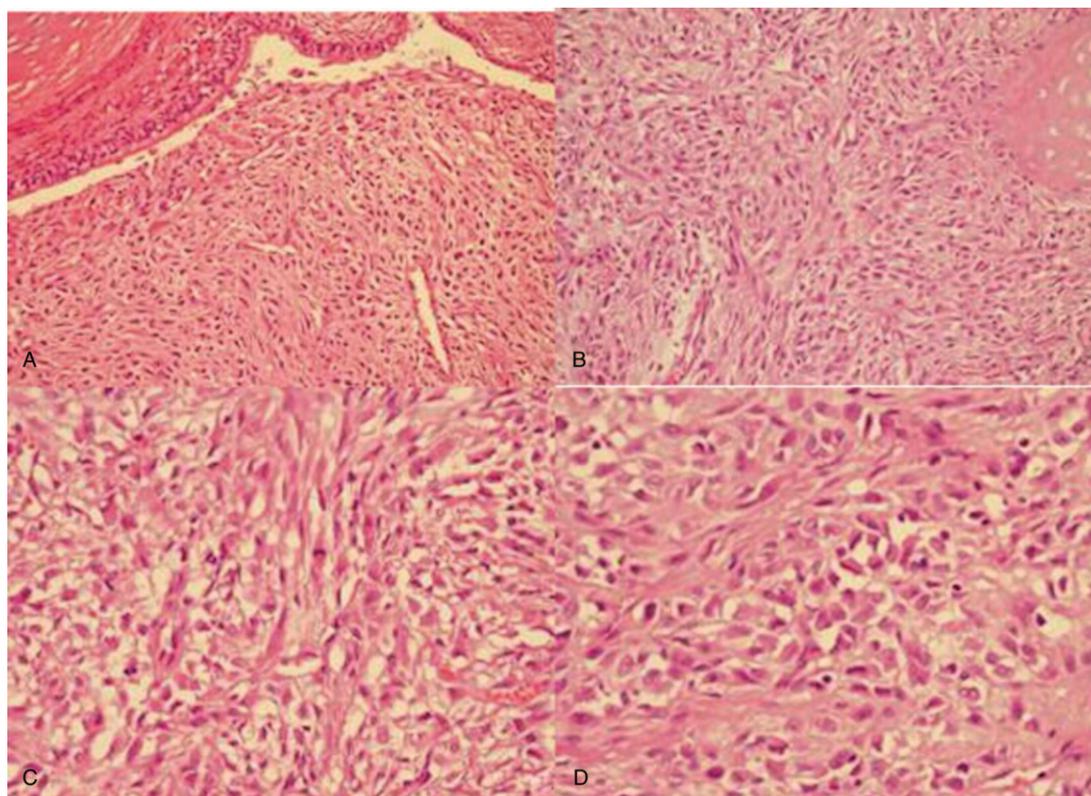


Figure 6. Hematoxylin and eosin (HE) staining of the resected tumor from the endobronchial cavity (mag. 200×).

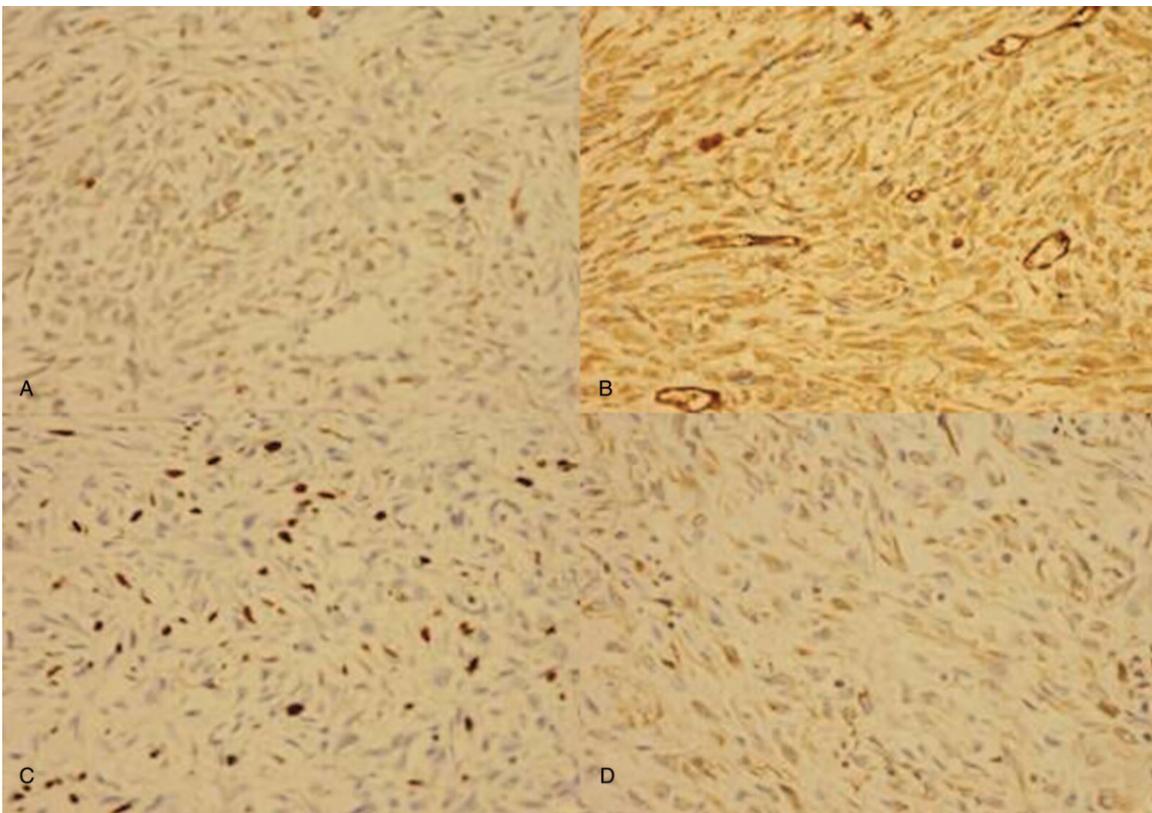


Figure 7. Immunohistochemical analysis of the resected tumor. A. Vimentin staining. B. Antigen Ki-67 staining. C. Cluster of differentiation 31 (CD31) staining. D. B-cell lymphoma 2 staining.

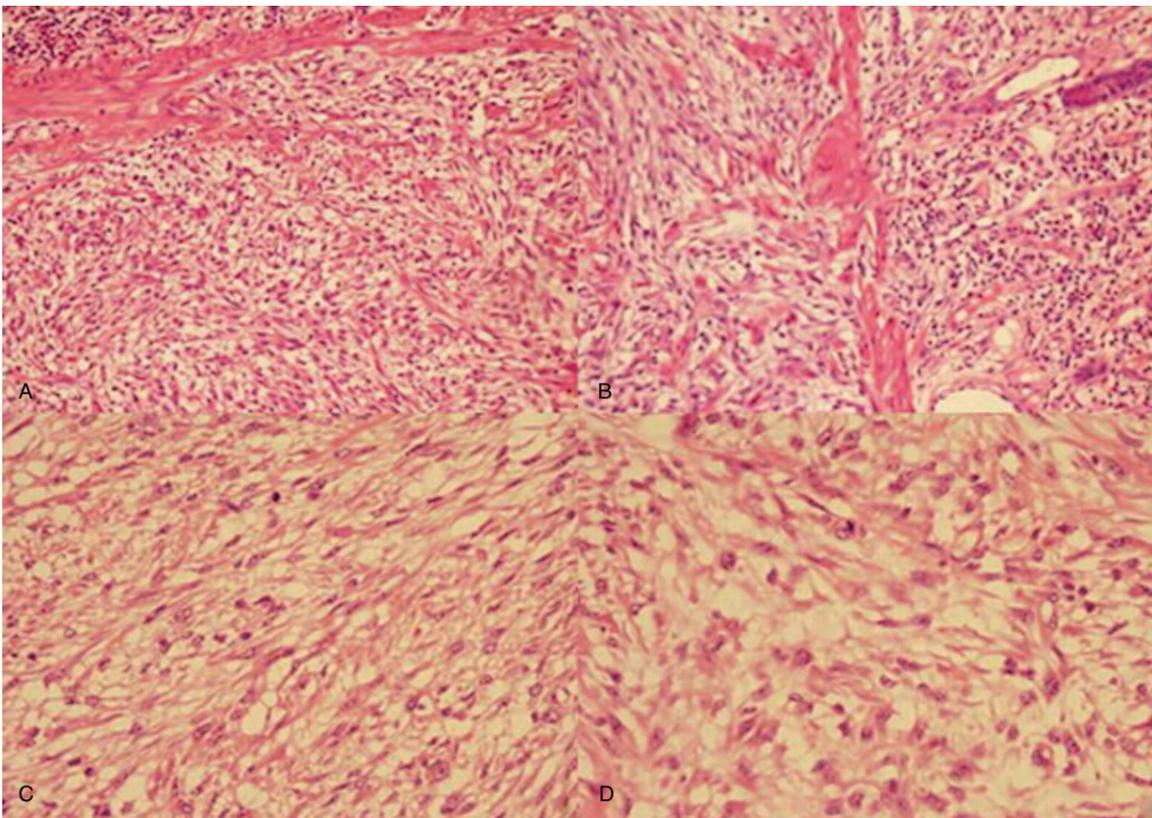


Figure 8. HE staining of the resected intestine (mag. 200 \times).

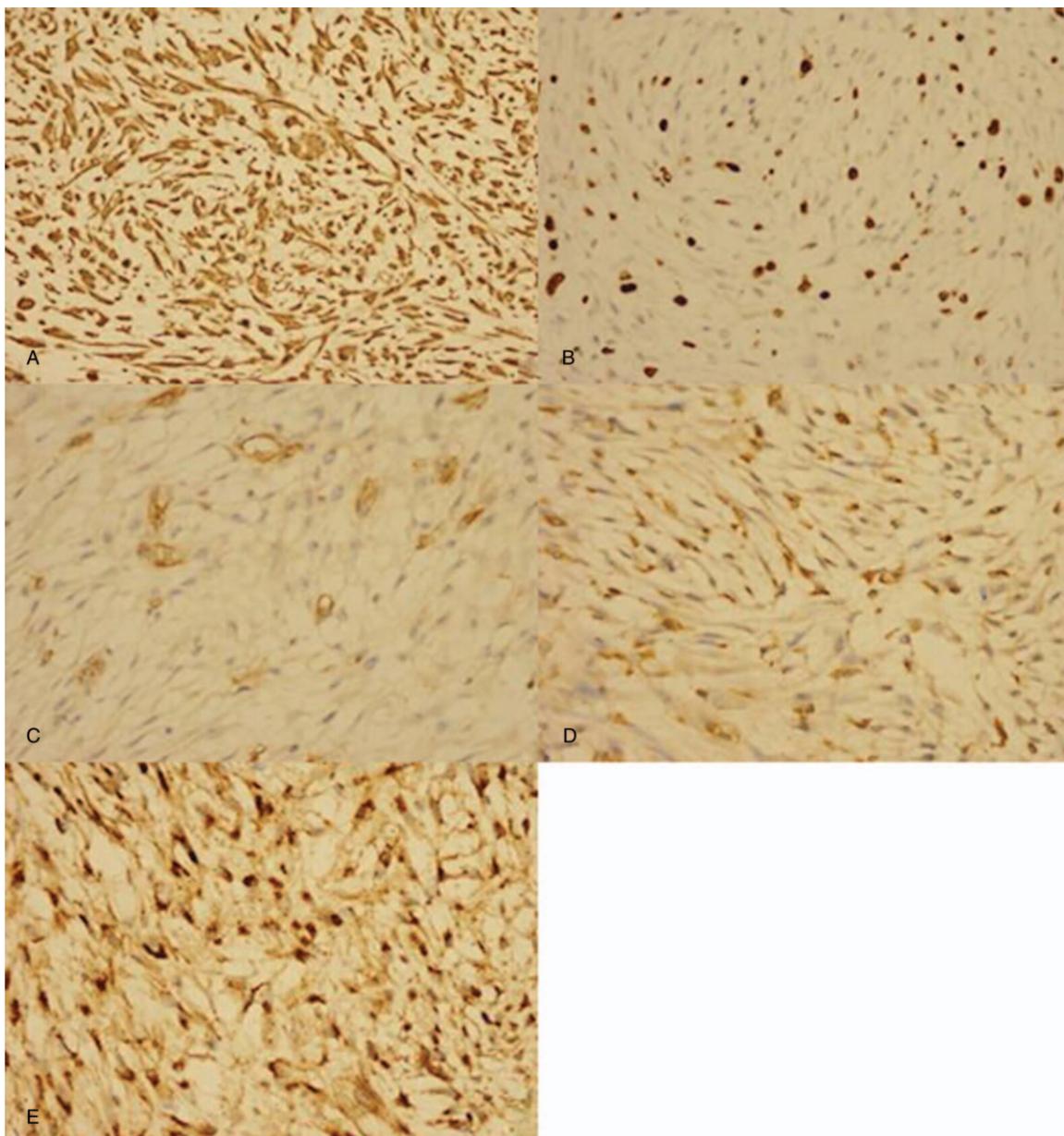


Figure 9. CT scans of the patient's chest (lung window) 1 year after the initial surgery. CT scans showed thoracic and peritoneal metastases. CT=computed tomography.

indicated low-grade fibrosarcoma with mucoid degeneration (Fig. 8).

The patient received 2 courses of MAID (Mesna+Adriamycin +Ifosfamide+Dacarbazine) chemotherapy regimens, but abdominal CT scanning and axillary lymph node color Doppler ultrasound showed disease progression after chemotherapy. The chemotherapy strategy was changed to 4 courses of GP (Gemcitabine+cis-Platinum), which was completed about 1 year after the primary surgery (February 2013). Lung and abdominal CT scans after GP chemotherapy showed a progressive disease, with an enlarged mass under the left costal arch. Subsequently, the patient received 3 courses of DP (Docetaxel+cis-Platinum) chemotherapy. Follow-up analysis showed a stable disease after 2 courses of DP chemotherapy.

About 5 months later (July 2013), the patient showed an enlarged mass at the right axillary and left abdomen. Color Doppler ultrasound showed a progressive disease. The chemotherapy strategy was changed to 3 courses of the IN regimen. Five months later (December 2013), the abdominal mass had continued to enlarge and was considered unsuitable for local radiation. Because of the patient's extensive chemotherapeutic history and poor response, gemcitabine and docetaxel were given. However, the patient developed severe thrombocytopenia and grade IV bone marrow arrest during chemotherapy, and gemcitabine was removed from the regimen on day 8 of chemotherapy course. The patient was in very poor health and unsuitable for further chemotherapy. At the request of the patient and his family, he returned home and could not be followed up.

3. Discussion

The question of whether SFT is derived from mesothelial or mesenchymal cells is controversial. Most investigators accept that mesenchymal tumors arise from dendritic stromal cells expressing the CD34 antigen and can occur in any part of the body.^[2] Consistent with this hypothesis, SFT has been reported to occur in the thyroid gland, salivary glands, upper respiratory tract, liver, kidneys, mediastinum, eyes, extrapleural spinal cord, lungs, and central nervous system. However, SFT originating from the right middle lobe and penetrating into the main bronchus has been seldom reported.^[30] The outcome and disease course of patients with such SFTs have been largely undetermined. Here, we present the detailed treatment course and disease development of a patient with SFT of the right middle lobe and main bronchus. We believe that this information will greatly benefit the future management of patients with lung SFTs, and we suggest close monitoring of patients with mSFTs.

According to the histological findings, the excised tumor consisted of a proliferation of spindle and polygonal cells arranged in a storiform pattern, embedded in a fibrous matrix (Figs. 1–4). The tumor cells were spindle or oval in shape and exhibited an acidophilous cytoplasm. Their nuclei were round or oval with small nucleoli. Fibroblast-filled areas rich or sparse in spindle-shaped cells showed small or large numbers of collagen fibers, respectively, between the tumor cells. Tumor cells were arranged in bundles, and mitotic cells were abundant (Figs. 6–9). These histological features are consistent with SFTs.^[1–6]

Between 90% to 95% of SFTs express CD34, and 90% express Bcl-2.^[22,23] CD34 is recognized as a relatively specific and accurate marker of SFTs.^[4] Generally, the expression of CD34 is higher in morphologically benign regions, and decreases or disappears in regions undergoing deterioration.^[22,23] Antigen Ki-67 or bFGF expression may also indicate the presence of a malignant tumor.^[15] In this case, the tumor cells were positive for antigen Ki-67, Bcl-2, CD31, and vimentin, but not for CD34, CK, SMA, or actin (Figs. 6–9), indicating that the tumor was similar to an SFT.^[19] The disease course clearly demonstrated that the tumor was malignant. Thus, mSFTs from different locations might differ in terms of protein expression. This possibility should be examined further. Moreover, because the tumor was found in the right main bronchus and the carina, we conclude that lung SFT may originate from mesenchymal cells in the lung fissures or from subcutaneous components between the lung parenchyma.^[30]

Clinically, SFT patients do not always show early symptoms. As their slow-growing tumors gradually increase in size, patients will show compression symptoms, such as cough, pain, and breathing difficulties, months or years after the tumor arises. Upon presenting to the hospital with these symptoms, a diagnosis of SFT can be made by imaging.^[30] It is rare for an SFT to exhibit significant changes in only 10 days. It is unknown whether the rapid growth in the present case was stimulated by bronchoscopy, bleeding, change in tumor location, etc., or by its own specificity.

SFTs are less sensitive than other tumors to radiotherapy and chemotherapy,^[24–26] and surgery remains the treatment of choice.^[24–29] Recurrence and metastasis are very common for mSFTs. In this case, the patient developed low-grade intestinal malignant fibrosarcoma 6 months after the initial surgery and extensive pleural and peritoneal metastases 1 year after the surgery. We conclude that long-term follow-up procedures should be performed after surgery in patients with mSFTs.

Author contributions

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Validation: Kaizhong Wang.

Visualization: Kaizhong Wang.

Writing – original draft: Guangchao Lv, Kaizhong Wang.

Writing – review & editing: Guangchao Lv.

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