# Primary synovial sarcoma of the pleura in an 18-year-old male patient: A case report

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**Abstract.** Primary synovial sarcoma of the pleura (PSSP) is a rare disease. The present study reported the case of a patient (male; age, 18 years) with two tumors (7.8x2.8 cm and 6.5x5.8 cm) treated with surgery and chemotherapy. To the best of our knowledge, this is the first reported case of two tumors diagnosed as PSSP, which was confirmed by immunohistochemical staining. After six months of follow-up, the symptoms of dry cough and wheezing disappeared and all of the laboratory results were within normal limits. PSSP requires clinical suspicion combined with strategic diagnostic evaluation to confirm the diagnosis and a comprehensive treatment program based on surgery and assisted by chemotherapy.

## Introduction

Synovial sarcoma (SS) is a relatively common high-grade sarcoma, accounting for 5-10% of all soft tissue sarcomas, most commonly occurring in the juxta-articular location (1). SS located in the pleura are rare and rarely reported in the literature, with the majority of cases reported (2). Nearly 40 cases of primary SS of the pleura (PSSP) have been reported since Gaertner *et al* (3) published the first case in 1996. It has been reported in all age groups. Since most of the published papers are case reports, there is no clear prognosis or recurrence rate reported in the literature. It is frequently misdiagnosed as lung cancer or other pleural tumors before surgery due to the lack of clinical and imaging specificity. SS has a comparatively poorer prognosis and higher recurrence rate. To date, <50 cases have been published in the English language. The present study reported a rare case of two simultaneous PSSP in an adolescent.

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## Case report

An 18-year-old male patient presented with a 1-month history of repeated sporadic dry cough and wheezing admitted to the The Second People's Hospital of Liaocheng (Linqing, China). The patient had no history of smoking or asbestos exposure. The cough worsened after exercise and in the lateral decubitus position accompanied by general fatigue, no fever, no blood in sputum and no hemoptysis. The patient's laboratory results were as follows: Erythrocyte sedimentation rate, 52 mm/h ↑ (normal range, ≤20 mm/h); platelets, $383x10^9$/l ↑ (normal range, $100-300x10^9$/l); C-reactive protein, 98.46 mg/l ↑ (normal range, 0-10 mg/l); prothrombin time, 15.40 sec ↑ (normal range, 9.4-12.5 sec); fibrinogen, 5.8 g/l ↑ (normal range, 2-4 g/l), D-dimer determination, 5.57 mg/l ↑ (normal range, 0-0.5 mg/l). Hydropleural biochemistry was as follows: Hydropleural protein, 51.8 g/l ↑ (normal range, 0-30 g/l); hydropleural lactate dehydrogenase, 1,022 U/l ↑ (normal range, 0-200 U/l); hydropleural cholesterol, 1.62 mmol/l ↑ (normal range, 0-1.60 mmol/l). Computed tomography of the chest revealed two tumors in the left parietal pleura (7.8x2.8 cm; 6.5x5.8 cm), with unclear boundaries with the adjacent chest wall, localized thickening of soft tissue in the left anterior intercostal space at 8 and 9, left pleural effusion (considered hemorrhagic), incomplete expansion of the left upper lobe of the lung and shadow consolidation of the left lower lobe of the lung (Fig. 1). Abdominal and pelvic CT and bone scans were normal without evidence of metastasis. Three pleural effusion cytological examinations (one per day for three consecutive days) showed no tumor cells. The patient refused to undergo preoperative MRI, positron emission tomography-CT and biopsy for financial reasons. The patient underwent a left intrathoracic tumor resection. During the operation, a fifth intercostal incision was performed on the left lateral chest. The exploration revealed pleural adhesion, separation adhesion, blood clots in the chest, the formation of pleural fiberboard in the left lower lobe of the lung, and two lesions in the chest; the larger one was located near the spine at the level of the lower lung ligament, closely related to the descending aorta, and the other one was located in the costophrenic Angle. The hemoaccumulation in the chest was cleared, two lesions were completely resected. During the operation, rapid freeze pathology examination, performed according to standard procedures, was used to confirm that

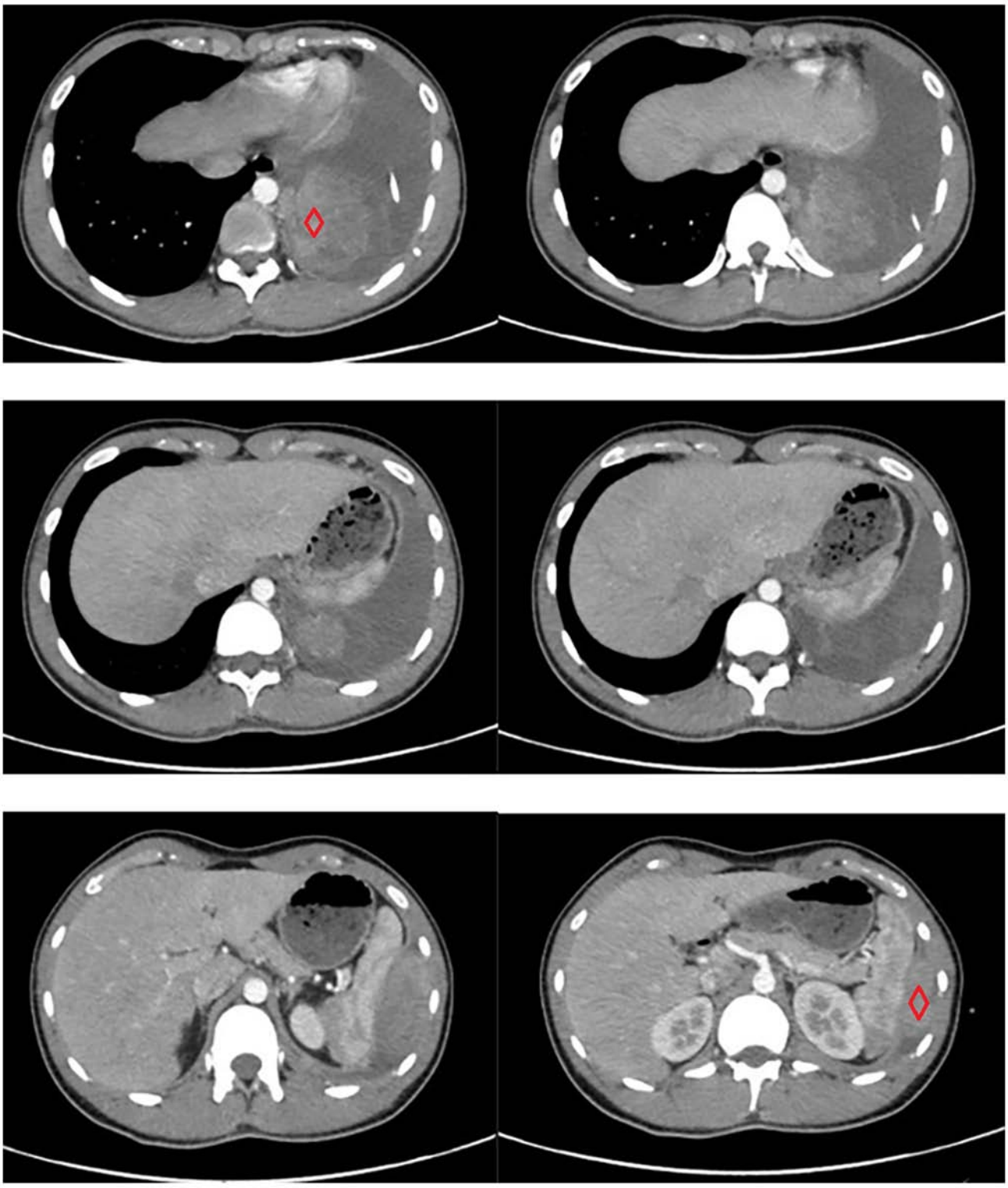

Figure 1. Computed tomography of the chest showed two tumors in the left parietal pleura (7.8x2.8 cm; 6.5x5.8 cm; red squares).

the surgical margin was negative, and the final specimen pathology, performed according to standard procedures, also confirmed that the margin was negative. The operation was deemed successful.

By histopathology with H&E staining (performed according to standard procedures; Fig. 2, bottom), the tumor was confirmed to be a monophasic synovial sarcoma (consisting of spindle-like cells in a perivascularomatous vascular morphology, with mitotic or interwoven bundles of spindle-like cells). Immunohistochemistry performed according to routine procedures was used revealed the following: Cytokeratin (CK) (-), epithelial membrane antigen (EMA) (-), CD99 molecule (CD99/MIC-2) (-), signal transducer and activator of transcription 6 (STAT6) (-), smooth muscle actin (SMA) (-), Desmin (-), receptor tyrosine kinase (CD117) (-), WT1 transcription factor (WT1) (-), RING

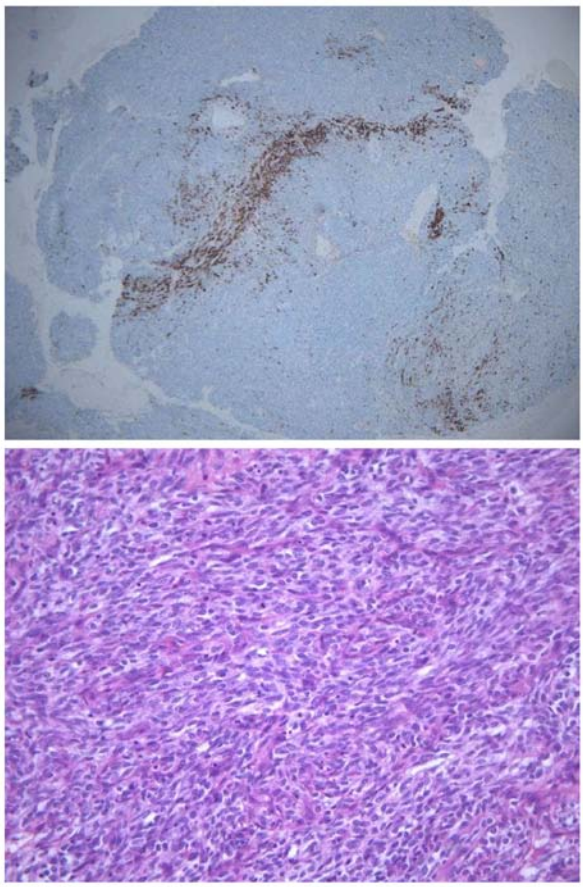

Figure 2. Pathological analysis confirmed the presence of primary synovial sarcoma of the pleura. Bottom: H&E staining; Top: CR (+). The sample was confirmed to be a monophasic synovial sarcoma (consisting of spindle-like cells with a perivascularomatous vascular morphology, with mitotic or interwoven bundles of spindle-like cells. Note the differentiation: A biphasic synovial sarcoma is seen with an epithelioid area and a fissured adenoid space with scattered tubular-papillary differentiation (magnification: Top, x40; bottom, x200).

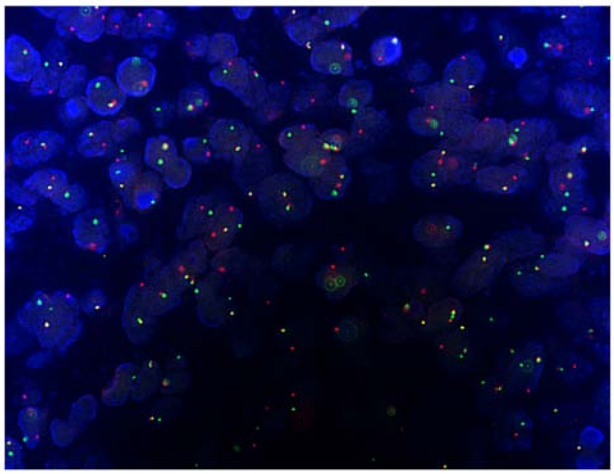

Figure 3: Fluorescence *in situ* hybridization assay of SS18 gene fusion (magnification, x400).

finger-like protein Ini1 (INI-1) (-), premelanosome protein (HMB45) (-), tumor protein p63 (p63) (small amount +), BCL2 apoptosis regulator (Bcl-2) (part +), antigen identified by monoclonal antibody Ki 67 (Ki67) (+ 40%), methylation of histone 3 lysine 27 (H3K27ME3) (+), cyclin D1 (+),CD34 molecule (CD34) (+), calretinin (CR) (+) (Fig. 2, top), podoplanin (D2-40) (part +), transducer-like enhancer split 1 (TLE-1) (+) and SS18 subunit of BAF chromatin remodeling complex SSX family member 2 (SS18-SSX) (+). In brief, consecutive parallel sections were stained with the following antibodies (the dilution was according to the manufacturers' recommendations for immunohistochemistry for each antibody): CK [rabbit anti-human monoclonal antibody (mAb); cat. no. RAB-0050], EMA (rabbit anti-human mAb; cat. no. kit-0011), CD99 (mouse anti-human mAb; cat. no. MAB-0059), STAT6 (rabbit anti-human mAb; cat. no. RMA-0845), SMA (mouse anti-human mAb; cat. no. kit-0006), Desmin (mouse anti-human mAb; cat. no. MAB-0766), CD117 (rabbit anti-human mAb; cat. no. kit-0029), WT1 (rabbit anti-human mAb; cat. no. MAB-0678), INI-1 (mouse anti-human mAb; cat. no. MAB-0696), HMB45 (rabbit anti-human mAb; cat. no. MAB-0098), p63 (mouse anti-human mAb; cat. no. MAB-0694), Bcl-2 (mouse anti-human mAb; cat. no. MAB-0711), Ki67 (mouse anti-human mAb; cat. no. MAB-0672), cyclin D1 (rabbit anti-human mAb; cat. no. RMA-0541), CD34 (mouse anti-human mAb; cat. no. kit-0004), CR (mouse anti-human mAb; cat. no. MAB-0716), D2-40 (mouse anti-human mAb; cat. no. MAB-0567), TLE-1 (mouse anti-human mAb; cat. no. MAB-0686), SS18-SSX (rabbit anti-human mAb; cat. no. RMA-1049; all from Maixin Fuzhou) and H3K27ME3 (mouse anti-human mAb; cat. no. P68431; Absin). The secondary antibodies used were goat anti-mouse IgG-FITC antibody (cat. no. abs20140; Absin) and Elivision™ plus polymer HRP (mouse/rabbit) IHC Kit (cat. no. KIT-9903; Maixin Fuzhou). Genetic testing (fluorescence *in situ* hybridization), performed according to routine procedures (4), indicated SS-18 (+) (Fig. 3).

After surgery, the patient received ifosfamide and doxorubicin combined chemotherapy. He underwent four cycles of chemotherapy (cyclophosphamide 9 g, once a day for 5 days; doxorubicin 150 mg, once a day for 3 days; 21 days as a cycle) and has been well followed up. After six months of follow-up, the symptoms of dry cough and wheezing disappeared. All of the laboratory results were within normal limits and no post-operative complications, tumor recurrence or metastasis occurred.

## Discussion

PSSP is a highly malignant and rare tumor type that is common in adolescents and is not associated with smoking. Typical symptoms include acute chest pain, dyspnea, hemoptysis and hemorrhagic effusion in the ipsopleural cavity (5). Diagnosis of SSP is often difficult owing to its rarity and its similarity (clinically and histologically) to other types of pleural tumor, particularly sarcomatous mesothelioma. The most common presentation is a well-defined mass with effusion on CT (2). On CT of the chest, a synovial sarcoma of the pleura is commonly characterized as a heterogeneously enhanced mass with well-defined margins, cortical bone destruction, tumor calcifications and tumor infiltration of the chest wall musculature (6). Duran-Mendicuti *et al* (7) reported 5 cases of primary pleural synovial sarcoma, showing radiologically uneven enhancement and well-defined

masses without calcification. The pathologic types may be divided into monophasic, biphasic and poorly differentiated types. In monophasic synovial sarcoma, spindle cells may be seen interwoven into bundles. Immunohistochemical examination of synovial sarcoma is characterized by positive staining of cytokeratin and epithelial cell membrane antigen, negative staining of nerve (S100) and smooth muscle markers and uniform staining of epithelial cell marker BerEp4, which facilitates the differentiation from malignant mesothelioma. Most synovial sarcomas exhibit at least an exocentric immune response to cytokeratin and epithelial membrane antigens, which are usually more prominent in epithelial components. CD99 and Bcl-2 were also detected in most cases.

Therefore, the diagnosis of PSSP requires clinical, radiological, pathological and immunohistochemical examination to exclude other primary tumors and metastatic sarcomas.

Although there is no standardized treatment for PSSP, based on the generally effective treatment for soft tissue sarcomas, a multidisciplinary treatment regimen that includes radical excision as the primary means of treatment, combined with chemotherapy (doxorubicin and ifosfamide) and radiotherapy, may be recommended (8). Prior to radical resection, neoadjuvant chemotherapy may be beneficial because it causes tumor volume reduction and has the potential to treat micrometastases, but there is no experience in PSSP. A previous study reported that the disease-free survival of 5 patients after surgical resection of PSSP was 2-14 months (7). Despite aggressive combination therapy, the prognosis is uncertain and long-term follow-up is warranted.

The present study described a case of primary pleural synovial sarcoma, the first published case to date of two simultaneous intrapleural tumors, treated by radical resection plus chemotherapy. Postoperative pathology, immunohistochemistry, genetic testing and radiological examination confirmed malignant tumors. At six months after surgery, the patient is currently in good health with no recurrence or metastasis.

In conclusion, PSSP is a rare and aggressive neoplasm in adolescents; it is difficult to diagnose with imaging alone, especially in the case of two masses in the pleura at the same time and hemorrhagic pleural effusion. Genetic testing may help confirm the diagnosis. Radical surgery is the main treatment in combination, followed by adjuvant chemotherapy. The long-term outcome remains to be seen, as PSSP has a poor prognosis.

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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**

YZ and CM designed the study. YZ was the principal person responsible for the study and wrote the original manuscript. XX provided the surgical details described in the manuscript. YZ, CM and HL performed histological analysis of the specimens and provided all pathological details described in the study. YZ and CM performed analysis and interpretation of CT imaging data. CM, XX and HL performed a critical literature review, contributed to the acquisition, analysis and interpretation of data and contributed to the drafting of the Introduction and Discussion sections. YZ and XX confirm the authenticity of all the raw data. All authors have read and approved the final version of the study.

**Ethics approval and consent to participate**

The study was conducted in accordance with the ethical standards from the 1964 Declaration of Helsinki and its later amendments; local ethical approval was obtained from the Ethics Committee of the Second People's Hospital of Liaocheng (Linqing, China).

**Patient consent for publication**

Written informed consent was obtained from the patient for the case information and images to be published in this case report.

**Competing interests**

All authors declare they have no competing interests.

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