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Case Report

Poorly differentiated primary pulmonary synovial sarcoma confirmed by detection of the SYT-SSX fusion gene: a case report with a literature review

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Abstract: We present a rare case of a poorly differentiated primary synovial lung sarcoma, which infiltrated the pleura with pleural effusion in a 45-year-old man. Chest CT scan showed a well-defined mass in the inferior right pulmonary lobe. The patient underwent a right middle and lower lobectomy, with lymph node dissection. Findings from imaging and histological and immunohistochemical testing led to a diagnosis of poorly differentiated synovial sarcoma, which was confirmed by genetic testing, which detected the *SYT-SSX* gene. We also present a brief review of the literature.

Keywords: Synovial sarcoma, pulmonary neoplasm, pathology, computed tomography

Introduction

Synovial sarcomas (SSs) account for around 5-10% of all primary soft-tissue sarcomas [1, 2]. They usually develop in children and young adults; approximately 95% of SSs occur in the extremities [3], but rarely occur in the mediastinum, lung, or pleural or chest wall. Most studies consider that SS originates not from synovial membrane or synovial differentiation, but from totipotent mesenchymal cells with varied differentiation [4, 5]. Primary poorly differentiated lung SS is rare; few cases have been reported in the literature [6-10]. We report such a case here, of primary poorly differentiated lung SS that infiltrated the pleura with pleural effusion, which was confirmed by detection of a fusion gene.

Case report

A 45-year-old man visited our hospital on 19 November 2015 because of chest tightness and pain of more than 1 month's duration. Physical examination showed normal thoracic symmetry. Breathing in his right lung was low without dry or wet rales or pleural friction sounds. He occasionally coughed and produced small amounts of white sputum, but showed no hemoptysis or shortness of breath. He had a 20-year history of smoking. His laboratory test results included WBC: 15.3 × 10^9/L; CEA: 5.41 ng/mL; NSE: 39.67 ng/mL, but no obvious abnormity in other values.

Computed tomography (CT)

A CT chest scan indicated a well-defined soft-tissue mass measuring 10.2 cm × 11.4 cm × 11.8 cm in his lower-right pulmonary lobe, with uneven density and no calcification. Its average CT value was 40 Hu. Its wide base was connected with the pleura and had displaced adjacent lung tissue and bronchus, resulting in partial atelectasis. A triangular consolidation, with an air bronchogram inside, was noticed in the middle-right lobe (**Figure 1A**, **1B**). A small amount of liquid was perceived on the right side of the pleural cavity. An enhanced CT scan showed a slightly enhanced mass with somewhat heterogeneous density, visible with linear enhancement shadow in the arterial phase (average CT value: 50 HU; **Figure 1C**), and irregular mild continuous enhancement with multiple patchy

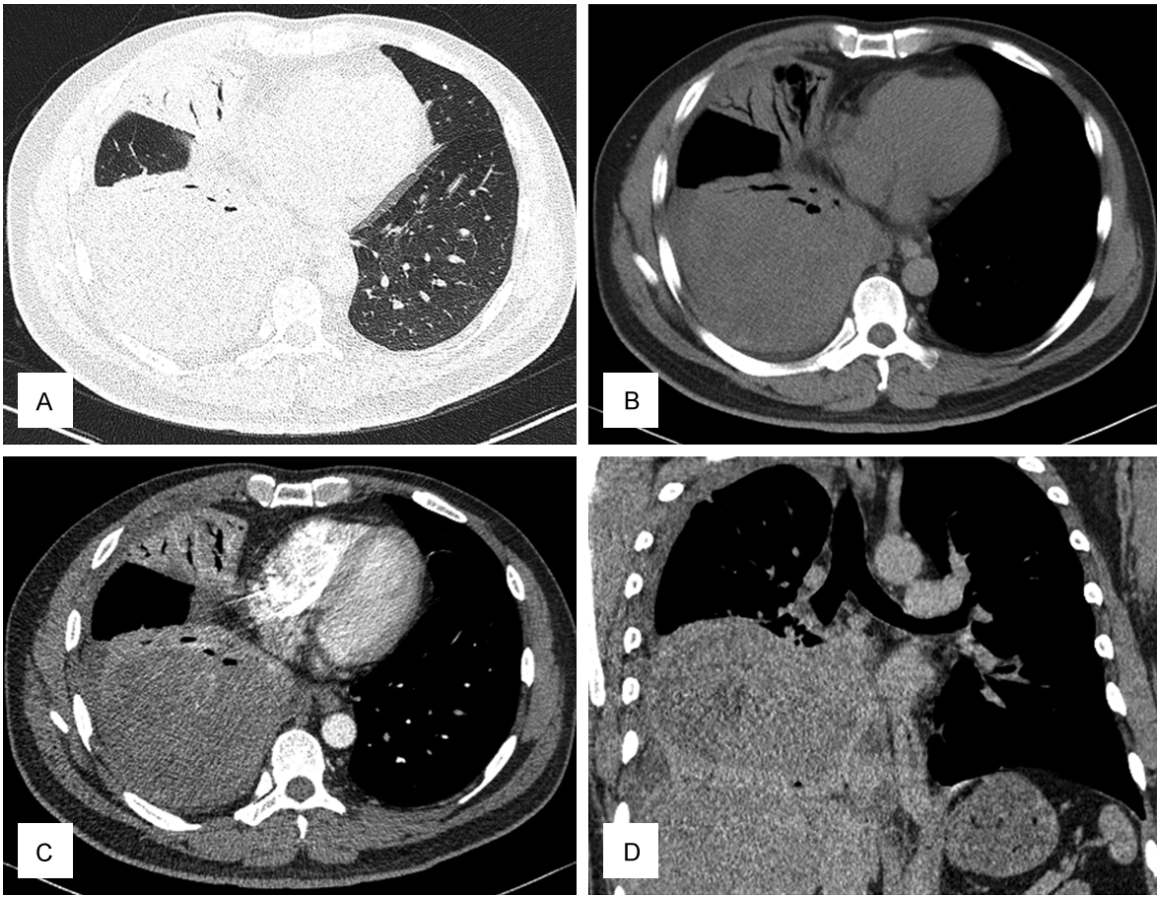

Figure 1. Chest computed tomography scan. (A) Under a noncontrasting enhanced CT scan, a well-defined 10.2 cm × 11.8 cm mass with non-uniform density was observed in the lower-right lung lobe. (B) It was connected to the pleura by a wide base and displaced adjacent lung tissues. Liquid density was seen on the right side of the thoracic cavity. (C, D) Under an enhanced CT scan, the mass presented heterogeneous enhancement with patchy low density in the arterial (C) and delayed phase (D).

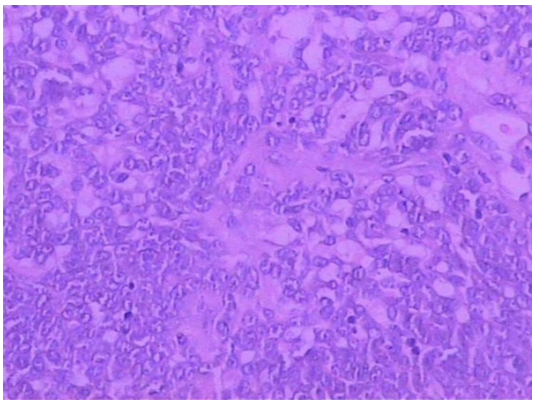

Figure 2. Histopathological examination of the resected specimen revealed the microscopic findings of the neoplasm. Diffuse small round cells and oval cells with clear nucleoli were observed, and nuclear division was spotted frequently (H&E staining, × 200).

weakly enhanced areas in the delayed phase (average CT value: 56 HU; **Figure 1D**). Several lymph node shadows (short diameters: ~1.0 cm) were observed in the mediastinum, but ribs and soft tissue of the chest wall appeared normal. The salient CT findings were (a) enlarged lower-right pulmonary lobe, suggestive of a solitary fibrous tumor of the pleura or pulmonary sarcoma with right pleural effusion; and (b) the lower-right lobe was not full and the middle-right lobe was inflamed.

Pathology findings

The patient's surgery began with a right V-VI intercostal incision under general anesthesia with thoracoscopic assistance, which revealed a tumor of about 18 cm × 20 cm × 20 cm with hard texture at the lower-right lobe that involved

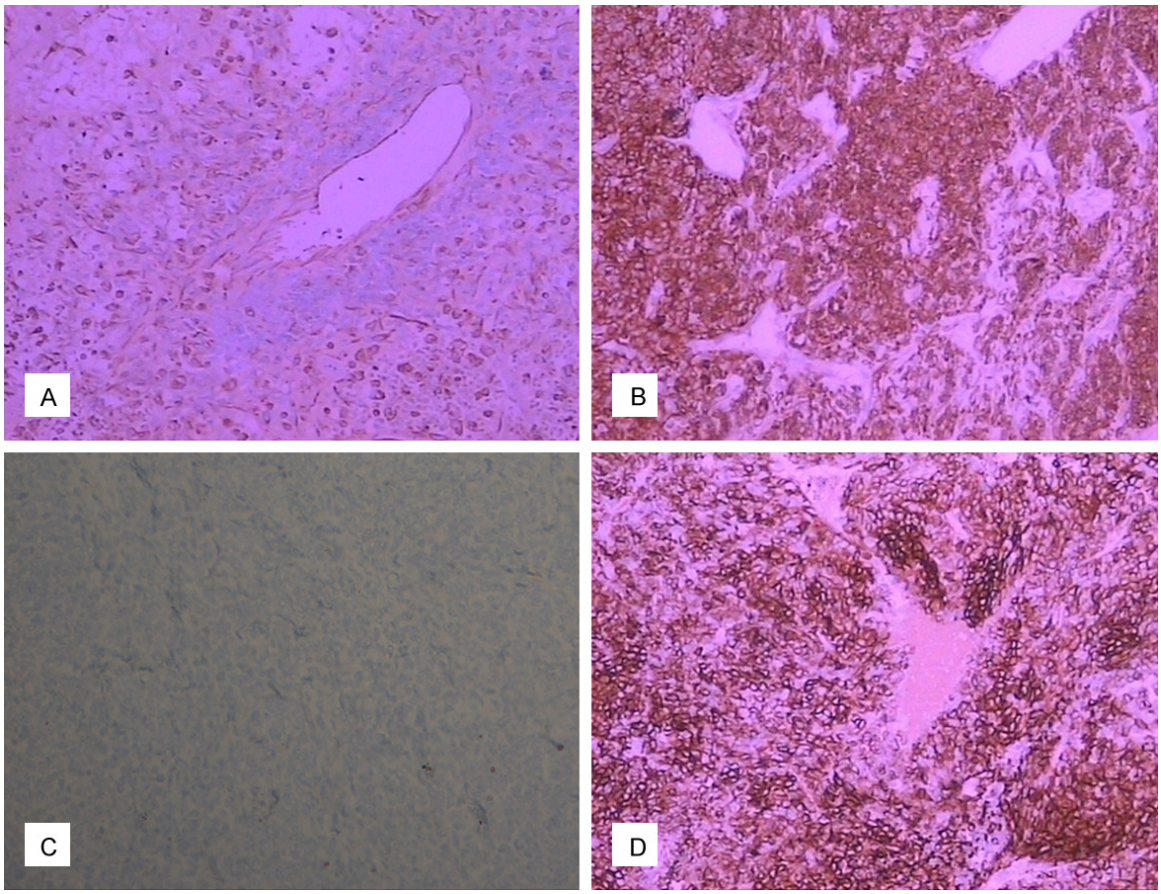

Figure 3. Immunohistochemical examination of the neoplasm. (SP × 100): A. The tumor cells were diffuse positive for vimentin. B. Intense expression of Bcl-2 in tumor cells. C. Negative immunoreactivity with epithelial membrane antigen (EMA). D. CD56 were diffusely positive in tumor cells.

both the visceral pleura and the middle-right lobe. The patient therefore underwent a resection of his middle-right and lower lobes, which also removed enlarged lymph nodes in zones 2, 4, and 7.

Microscopically, the tumor showed small diffuse round or oval cells with distinct nucleoli and frequent nuclear division. Cells around blood vessels were short and spindle-shaped, accompanied by massive hemorrhage and necrosis (**Figure 2**).

Initially, the specimen was differentially diagnosed as a primitive neuroectodermal tumor, mesothelioma or synovial sarcoma. Our immunohistochemical findings were VIM$^+$ (**Figure 3A**), Bcl-2$^+$ (**Figure 3B**), weakly S-100$^+$, EMA$^-$ (**Figure 3C**), CK$^-$, weakly NSE$^+$, CD34$^+$ in vessels, CD56$^+$ (**Figure 3D**), weakly CD99$^+$, weakly P53$^+$, weakly CgA$^+$, and weakly Syn$^+$. Gene testing showed an *SS18* (18q11.2) ectopic chromosome but not a *EWSR1* (22q12) ectopic chromosome. According to the above pathological data, right pulmonary SS was finally diagnosed. The patient subsequently received adjuvant chemoradiotherapy, and is currently surviving.

Discussion

Primary pulmonary synovial sarcoma (PPSS) is a rare disease that accounts for less than 0.5% of all primary lung malignancies [1, 2, 4]. Because PPSS is often located in the periphery of the lung and takes the pleura as the base, its origins can be difficult to identity; therefore, some scholars call it primary pleuropulmonary synovial sarcoma [6, 11]. The most common symptoms of PPSS are dyspnea, cough and chest pain [5, 12]. Etienne-Mastroianni et al described peripheral PPSS as uncommon and usually asymptomatic, but it may infiltrate adjacent pleura, thoracic wall, and mediastinum, or metastasize to hilar or mediastinal lymph

Table 1. Comparison of published cases of PPSS

Author	Age/ Gender	Site	Size (cm)	Clinical symptoms	Shape	Margin	Imaging features	Prognosis
Zhang et al [6]	29/F	Left lower lobe	13 × 16 × 18	No Data (ND)	Rounded	Well-defined	Heterogeneous enhancement with large patchy cystic and necrotic areas	Remission
	54/M	Right upper lobe	12.5 × 13 × 15	ND	Rounded	Well-defined	Heterogeneous enhancement with patchy cystic and necrotic areas	Recurrence
	54/M	Left lower lobe	5 × 6 × 6	ND	Rounded	Well-defined	Heterogeneous enhancement with patchy low density, pneumothorax	Recurrence
	39/M	Right middle lobe	5 × 6.5 × 8	ND	Rounded	Well-defined	Heterogeneous enhancement with patchy low density	Remission
	70/M	Right upper lobe	14 × 15 × 19	ND	Oval	Well-defined	Heterogeneous enhancement with large patchy cystic and necrotic areas	Died
Kamath et al [7]	36/F	Entire right hemi-thorax	ND	Cough and chest pain	Oval	Infiltrating	Heterogeneous enhancement with invasion into the mediastinal structures as well as the chest wall	Recurrence
Morikawa et al [8]	64/M	Left lower lobe	15 × 20	Chest pain	Oval	Well-defined	Heterogeneous enhancement with large patchy cystic and necrotic areas	Recurrence
Sareen et al [9]	40/F	Right lung	6 × 7 × 8	Cough, chest pain and dyspnoea	Rounded	Well-defined	Homogeneous mass extending into pleura with multiple small nodules	ND
Fatimi et al [10]	35/M	Entire left hemi-thorax	ND	Cough and dyspnoea	Oval	Well-defined	Heterogeneous enhancement with large patchy cystic and necrotic areas	Remission
Present case	45/M	Right lower limb	10.2 × 11.4 × 11.8	Chest pain and dyspnoea	Oval	well-defined	Heterogeneous enhancement with patchy low density	Recurrence

F: Female; M: Male.

nodes, adrenal, brain, and spinal cord [13]. In this case, CT displayed a mass with heterogeneous density, a wide pleural base, and well-defined pressure on peripheral pulmonary parenchyma with an ipsilateral right pleural effusion. The enhanced CT scan showed the mass to have uneven, slightly continuous enhancement, which accords with other reports of PPSS [4-6]. We have summarized previous similar cases (see **Table 1**). The larger mediastinal lymph nodes were shown pathologically to have no metastasis. Reportedly, contralateral lungs usually appear normal (as in this case), although mediastinal shift might occur in the presence of a very large mass [7].

According to the World Health Organization's histopathological classification of tumors, PPSS can be classified into four categories: biphasic, monophasic spindle, monophasic epithelial, and poorly differentiated. The former two are the most common types. The typical PPSS immunohistochemistry of PPSS is positive for cytokeratin (CK), epithelial membrane protein (EMA) or vimentin (Vim). In this case, EMA and CK were negative but Vim, Bcl-2 and CD56 were positive, which indicates some limitations in pathological diagnosis. Cytogenetically, PPSS is characterized by the presence of translocation t (x; 18) (p11.2: q11.2) of chromosome 18 and chromosome X, leading to fusion between an *SYT* gene on chromosome 18 and an *SSX*-family gene (*SSX1*, *SSX2*) on the X chromosome, the former is found most frequently in dual-phase type and the latter is seen by most of the single-phase type. Reportedly, *SS18-SSX1*$^+$ cells are more invasive and show poorer prognosis than *SS18-SSX2*$^+$ tumors [14]. Although *SS18-SSX* fusions do not seem to occur in other types of sarcomas [3], more than 90% of PPSS are reported to harbor the *SS18-SSX* translocation, which thus offers high specificity for diagnosing PPSS [4, 8, 9, 11]. Currently, the genetic test for t (X; 18) and fluorescence in situ hybridization (FISH) or the RT-PCR method to detect the *SYT-SSX* fusion gene with its expression products have become the "gold

standard" for diagnosis of SS. In this case, based on the facts from imaging findings, clinical symptoms, pathology of small round cells and oval cells, immunohistochemistry and genetic testing results, the final diagnosis was poorly differentiated PPSS. The presence of poorly differentiated tumor cells within lesions of either subtype is considered indicative of poorer prognosis [7].

This case was initially considered to be a solitary fibrous tumor of the pleura, which shows images similar to those of PPSS. In particular, if the patient had also had symptoms of hypoglycemia or hypertrophic osteoarthropathy, the diagnosis of focal fibrous tumor of the pleura would have been better supported. This case also needed to be distinguished from other diseases including primary lung cancer, pulmonary and pleural metastasis, and malignant pleural mesothelioma. If signs of lung cancer associated with the pulmonary hilus and mediastinal lymph nodes had appeared, we would have diagnosed primary lung cancer. Pulmonary metastases are often multifocal, and are rarely seen in the pleura of a huge isolated mass. Malignant mesothelioma exposes pleural thickening and copious pleural effusion; such patients usually have histories of asbestos exposure and pleural plaques on the sides of lungs.

Because PPSS is so rare, no guidelines are available for its treatment. The main existing treatment includes surgery (pneumonectomy/lobectomy), followed by either radiation, chemotherapy or both when feasible [10], which can prolong survival. Currently, with known genetic alterations in PPSS, new therapies that target DNA or protein are under investigation. Vaccine of the SYT-SSX junction peptide was tested in a pilot study [15], although its therapeutic efficacy remains under evaluation.

In conclusion, although PPSS image findings have certain characteristics, they lack specificity, and may require pathologic, immunohistochemical and genetic testing to confirm a diagnosis-especially the last, when immunohistochemical results are equivocal.

Disclosure of conflict of interest

None.

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References

[1] Falkenstern-Ge RF, Kimmich M, Grabner A, Horn H, Friedel G, Ott G and Kohlhäufl M. Primary pulmonary synovial sarcoma: a rare primary pulmonary tumor. Lung 2014; 192: 211-4.

[2] Khan H, Chaubey S, Edlin J and Wendler O. Primary cardiac synovial sarcoma. A rare tumor with poor prognosis. Asian Cardiovasc Thorac Ann 2014; 22: 835-8.

[3] Xu J, Wang J, Cui L and Wu X. Malignant inguinal monophasic synovial sarcoma: report of a case and review of the literature. World J Surg Oncol 2010; 8: 102.

[4] Frazier AA, Franks TJ, Pugatch RD and Galvin JR. From the archives of the AFIP: pleuropulmonary synovial sarcoma. Radiographics 2006; 29: 923-940.

[5] Bakri A, Shinagare AB, Krajewski KM, Howard SA, Jagannathan JP, Hornick JL and Ramaiya NH. Synovial sarcoma: imaging features of common and uncommon primary sites, metastatic patterns, and treatment response. AJR Am J Roentgenol 2012; 199: 208-215.

[6] Zhang WD, Guan YB, Chen YF and Li CX. CT imaging of primary pleuropulmonary synovial sarcoma. Clin Radiol 2012; 67: 884-8.

[7] Kamath V, Mishra N, Gunabushanam V, Agaba E, Gupta R, Hyman K and Glassman LR. Primary pleuropulmonary synovial sarcoma. Am Surg 2010; 76: E113-4.

[8] Morikawa H, Tanaka T, Hamaji M, Ueno Y, Yasuda S, Kato T, Kohno Y and Toguchida J. A case of primary synovial sarcoma of the thorax with a variant SYT-SSX1 fusion transcript. Ann Thorac Surg 2009; 88: 297-300.

[9] Sareen R and Pandey CL. Rare case: monophasic pleuropulmonary synovial sarcoma. South Asian J Cancer 2013; 2: 120.

[10] Fatimi SH, Anees A, Hanif HM and Muzaffar M. Synovial sarcoma of the lung presenting late with compression of mediastinal structures and its successful resection a case report. Heart Lung Circ 2011; 20: 136-138.

[11] Yao H, Hu Z, Lin H and Shi H. Primary pulmonary synovial sarcoma with multiple pleural metastases: a case report and review of the literature. Chinese-German Journal of Clinical Oncology 2012; 67: 884-8.

[12] Mirzoyan M, Muslimani A, Setrakian S, Swedeh M and Daw HA. Primary pulmonary synovial sarcoma. Clin Lung Cancer 2008; 9: 257-261.

[13] Etienne-Mastroianni B, Falchero L, Chalabreysse L, Loire R, Ranchère D, Souquet PJ and Cordier JF. Primary sarcomas of the lung: A clinicopathologic study of 12 cases. Lung Cancer 2002; 38: 283-9.

[14] Ren T, Lu Q, Guo W, Lou Z, Peng X, Jiao G and Sun Y. The clinical implication of SS18-SSX fusion gene in synovial sarcoma. Br J Cancer 2013; 109: 2279-2285.

[15] Kawaguchi S, Wada T, Ida K, Sato Y, Nagoya S, Tsukahara T, Kimura S, Sahara H, Ikeda H, Shimozawa K, Asanuma H, Torigoe T, Hiraga H, Ishii T, Tatezaki SI, Sato N and Yamashita T. Phase I vaccination trial of SYT-SSX junction peptide in patients with disseminated synovial sarcoma. J Transl Med 2005; 3: 1-9.