# Primary Pulmonary Synovial Sarcoma: A Case Report

*Hsin-Hung Chen,[1] Wan-Ting Huang,[1] Wan-Yi Kang,[1,2] Hsuan-Ying Huang,[3] and Chee-Yin Chai[1,2]*
[1]Department of Pathology, Kaohsiung Medical University Hospital, [2]Department of Pathology, Faculty of Medicine, Kaohsiung Medical University, and [3]Department of Pathology, Chang Gung Memorial Hospital, Kaohsiung, Taiwan.

We report a rare case of primary synovial sarcoma of the lung. A 57-year-old man had a well-defined tumor in the right middle lobe seen on chest computed tomography, and underwent lobectomy. Grossly, the nonencapsulated tumor measured 4.5 cm in greatest diameter, with a solid and tan-white cut surface. Histologically, the tumor was mainly composed of a dense proliferation of spindle cells. Immunohistochemical studies were focally positive for epithelial membrane antigen, and diffusely positive for CD99 and Bcl-2. Cytokeratin, S-100 protein, desmin, smooth muscle actin, and CD34 were absent. *SYT-SSX1* gene fusion transcript was detected by reverse transcription–polymerase chain reaction, which is diagnostic of primary synovial sarcoma of the lung. We also review the literature with regard to the clinicopathologic, immunohistochemical, and molecular studies of primary pulmonary synovial sarcoma.

**Key Words:** pulmonary synovial sarcoma, synovial sarcoma, *SYT-SSX* fusion gene transcripts
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Synovial sarcoma is a mesenchymal spindle cell tumor with variable epithelial differentiation. Synovial sarcoma, which accounts for 5–10% of soft tissue sarcomas, occurs most commonly in the para-articular tissues of the extremities. Approximately 90% of cases occur before 50 years of age (most occur between 15 and 30 years), but the tumor may occur in elderly patients [1]. However, synovial sarcoma may arise in various sites, including the head and neck, mediastinum, heart, kidney, prostate, esophagus, and vulva [2]. Histologically, synovial sarcoma is generally classified into four subtypes: (1) biphasic type, with distinct epithelial and spindle cell components in varying proportions; (2) monophasic fibrous type; (3) rare monophasic epithelial type; (4) poorly differentiated (round cell) type [3].

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Address correspondence and reprint requests to: Dr Chee-Yin Chai, Department of Pathology, Kaohsiung Medical University, 100 Shih-Chuan 1st Road, Kaohsiung 807, Taiwan.
E-mail: cychai@kmu.edu.tw

Primary sarcomas of the lung are rare, accounting for less than 0.5% of primary lung cancers, and the majority of malignant mesenchymal tumors of the lung are metastases of a primary tumor elsewhere. Primary pulmonary synovial sarcomas are extremely rare and the diagnosis is made only after clinical and imaging investigation to exclude alternative primary sources [4].

We describe a case of synovial sarcoma arising from the lung, presenting as an asymptomatic lung tumor and treated surgically by lobectomy of the lung; the diagnosis was proven by *SYT–SSX1* fusion gene transcripts using reverse transcription–polymerase chain reaction (RT–PCR). We also review the relevant English literature.

## Case Presentation

A 57-year-old man had a past medical history of ischemic heart disease and diabetes under medical control, as well as a history of operation for oral tumor 15 years previously. A mass in the right lower lobe of

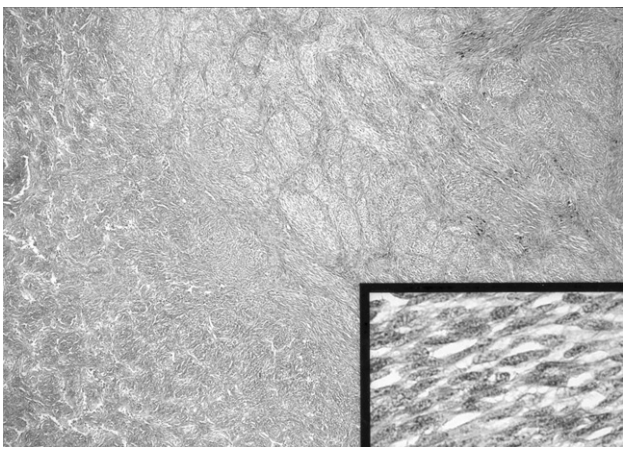

**Figure 1.** *Tumor shows interweaving fascicular spindle cell neoplasm with focal areas of dense hyaline fibrosis. Hemangiopericytoma-like pattern is also noted (left) (hematoxylin & eosin, H&E; original magnification, 40×). Tumor cells are rather uniform with ovoid, pale staining nuclei and inconspicuous nucleoli. The cytoplasm is sparse and the cell borders are indistinct. (Inset: H&E; original magnification, 400×.)*

the lung was found incidentally on routine chest X-ray, and subsequent chest computed tomography revealed a 4-cm well-defined mass occupying the right middle lobe. Since a primary pulmonary tumor was clinically suspected, right middle lobectomy with lymph node dissection was performed.

Grossly, the tumor was relatively well circumscribed and nonencapsulated, measuring 4.5 × 3.2 × 1.7 cm in size, and the cut surface was solid, whitish in color and firm in consistency. Neither necrosis nor hemorrhage was found. Histologically, the tumor showed interweaving fascicular spindle cell neoplasm with focal areas of dense hyaline fibrosis. A hemangiopericytoma-like pattern was also noted. The tumor cells were rather uniform with ovoid, pale staining nuclei, and inconspicuous nucleoli. The cytoplasm was sparse and the cell borders were indistinct (Figure 1). On immunohistochemistry, tumor cells were negative for cytokeratin (DAKO, Copenhagen, Denmark), but focally positive for epithelial membrane antigen (DAKO). Vimentin (Biogenex, San Ramon, CA, USA), CD99 (DAKO) and Bcl-2 (DAKO) were diffusely

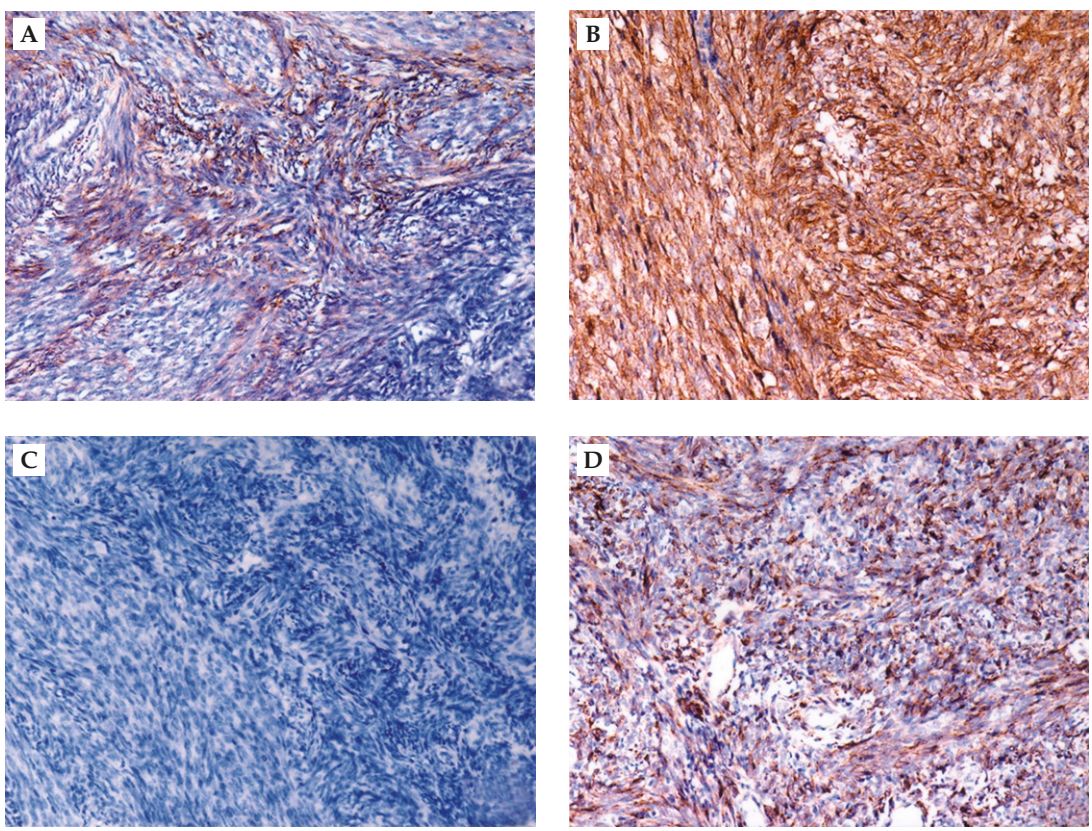


**Figure 2.** *Tumor cells were: (A) focally positive (brown color) for epithelial membrane antigen; (B) diffusely positive for CD99; (C) negative for cytokeratin; (D) diffusely positive for Bcl-2.*

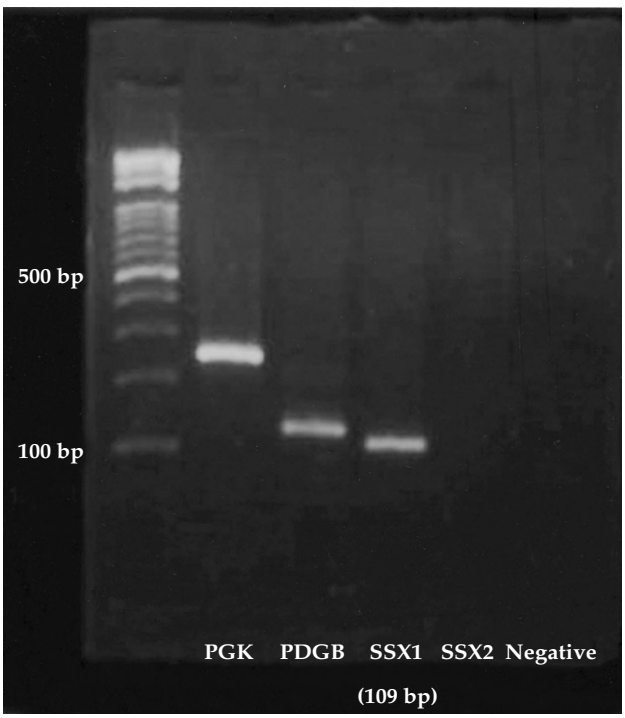


**Figure 3.** *Reverse transcription–polymerase chain reaction demonstrates SYT-SSX1 fusion gene transcripts (forward primer 5′AGACCAACACAGCCTGGACCAC3′ for SSX1).*

positive (Figure 2). However, S-100 protein (DAKO), desmin (Biogenex), smooth muscle actin (Biogenex), and CD34 (DAKO) were all negative. Histologic features and immunohistochemical results were consistent with the characteristics of synovial sarcoma of monophasic type.

To detect characteristic chimeric fusion gene, *SYT-SSX*, RT–PCR assays were performed on RNA, and demonstrated *SYT-SSX1* fusion gene transcripts (Figure 3) resulting from chromosomal translocation t(X;18)(p11,q11) of typical synovial sarcoma.

Although no adjuvant treatment was given, there was no recurrence during 6 months of postoperative follow-up in the outpatient department.

## Discussion

Synovial sarcoma, which accounts for 5–10% of soft tissue sarcomas, is not related to synovium. The tumor is a mesenchymal spindle cell tumor with variable epithelial differentiation. Although more than 80% of synovial sarcomas arise in the deep soft tissues of the extremities [3], it may also arise in other sites, including the head and neck, mediastinum, heart, kidney, prostate, esophagus, and vulva [2]. By application of immunohistochemical and molecular approaches including detection of tumor-specific fusion genes, unusual sites such as the lung have also been reported. To date, approximately 50 cases of pulmonary synovial sarcoma have been published in the English literature [5].

Pulmonary synovial sarcomas are located in peripheral pulmonary parenchyma; they are well circumscribed but nonencapsulated solid tumors. Occasionally, the tumor may diffusely infiltrate chest wall or mediastinal structures. The size of the tumor ranges from 0.6 to 20 cm and the cut surface of the tumor shows cystic degenerative changes and necrosis [6].

The commonly reported symptoms of primary pulmonary synovial sarcoma are chest pain, cough, shortness of breath, and hemoptysis [7]. Low-grade fever and weight loss are rare [6].

The generally accepted histologic subtypes of synovial sarcoma are biphasic, monophasic fibrous, monophasic epithelial, and poorly differentiated subtypes [3], among which the monophasic neoplasm subtype occurs most often in the lung [8]. The case presented here had a monophasic fibrous subtype composed solely of spindle cell component arranged in interweaving fascicles. Hemangiopericytoma-like pattern and focal hyaline fibrosis were also noted.

The differential diagnoses of pulmonary synovial sarcoma include sarcomatoid carcinoma, sarcomatoid variants of pleural mesothelioma, leiomyosarcoma, hemangiopericytoma, malignant peripheral nerve sheath tumor, fibrosarcoma, and spindle cell thymoma. To exclude metastasis from an undetectable extrapulmonary synovial sarcoma is of great importance [8,9]. No other synovial sarcoma has been detected in extraordinary soft tissue previously.

Immunohistochemical studies often supplement histology, since most synovial sarcomas show immunoreactivity for cytokeratin and/or epithelial membrane antigen. Epithelial membrane antigen tends to be expressed more often and widely than cytokeratin. In monophasic lesions, reactivity may be scanty. Vimentin, Bcl-2 and CD99 are frequently positive, while S-100 protein, desmin, smooth muscle actin and vascular tumor markers are usually negative [6]. In our case, immunohistochemistry results were as stated above except for the negativity of cytokeratin.

Recently, histology and immunohistochemistry have also been supplemented by molecular testing.

Coindre et al concluded that molecular testing is not required if the diagnosis of synovial sarcoma is certain or probable on the basis of clinical, histologic, and immunohistochemical evaluations [10]. While the possibility of a diagnosis of synovial sarcoma is not high, for example a monophasic subtype in uncommon or unexpected sites, Coindre et al also concluded that molecular testing can be very helpful or even necessary [10]. Molecular testing of synovial sarcomas reveals chromosomal translocation t(X;18)(p11,q11). The translocation fuses the *SYT* gene from chromosome 18 to either of two homologous genes at Xp11, *SSX1* or *SSX2*. For diagnosis, the sensitivity of this examination is nearly 100%. Most biphasic tumors are found to have an *SYT-SSX1* fusion gene transcript and most monophasic tumors have an *SYT-SSX2* fusion gene transcript [11]. In our case, detection of *SYT-SSX1* fusion gene transcript confirmed the diagnosis.

Trassard et al showed that synovial sarcoma was a high-grade malignancy with a high metastatic rate, with 5- and 10-year survival rates of 24–76% and 11–56%, respectively. Factors for an unfavorable prognosis were tumor size > 5 cm, male gender, greater age (> 20 years), extensive tumor necrosis, high grade, a large number of mitotic figures (> 10/10 high power fields), neurovascular invasion [12], *SYT-SSX1* variant [13], and inadequate resection margin [14].

Although there is no standard therapy, most authors have recommended extensive surgery in addition to adjunctive radiotherapy with or without adjunctive chemotherapy [3]. Although no adjuvant treatment was given to our patient, there was no recurrence over 6 months of postoperative follow-up in the outpatient department. To our knowledge, this is the first report of primary pulmonary synovial sarcoma in Taiwan.

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# 原發性肺滑液肉瘤 — 病例報告

陳欣宏[1] 黃琬婷[1] 康婉儀[1,2] 黃玄贏[3] 蔡志仁[1,2]

[1]高雄醫學大學附設醫院 病理科

[2]高雄醫學大學 醫學院醫學系 病理學科

[3]高雄長庚紀念醫院 病理科

原發性肺滑液肉瘤是一種相當罕見之肺部腫瘤，迄今，僅有數十例零星發表的個案。本文報告一名 57 歲男性在例行的胸部 X 光檢查在右肺意外地發現一顆約 4.5 公分大的腫瘤。經實行肺右中葉切除手術後，由病理檢查及免疫組織化學染色檢查得知結果為滑液肉瘤，且經過反轉錄酶聚合鏈反應的產物確認結果無誤。本文除病例報告外，同時探討其臨床、組織、免疫組織化學染色及分子檢查的表現。

**關鍵詞**：肺滑液肉瘤，滑液肉瘤， SYT-SSX 融合基因轉錄物

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高雄醫學大學醫學院醫學系病理科

高雄市807三民區十全一路100號