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Solitary primary pulmonary synovial sarcoma: A case report

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Abstract

BACKGROUND

Synovial sarcoma (SS) is an uncommon and highly malignant soft tissue sarcoma in the clinic, with primary pulmonary SS (PPSS) being extremely rare. Here, we describe the clinical characteristics, diagnosis, and treatment of a solitary PPSS case confirmed *via* surgical resection and fluorescence in situ hybridization (FISH).

CASE SUMMARY

A 33-year-old man was admitted because of intermittent coughing and hemoptysis for one month, with lung shadows observed for two years. Whole-body positron emission tomography-computed tomography (PET-CT) revealed a solitary mass in the upper lobe of the right lung, with uneven radioactivity uptake and a maximum standardized uptake value of 5.6. The greyish-yellow specimen obtained following thoracoscopic resection was covered with small multi-nodulated structures and consisted of soft tissue. Hematoxylin and eosin staining revealed spindle-shaped malignant tumor cells. Immunohistochemistry indicated these tumor cells were CD99 and BCL-2-positive. Furthermore, the FISH test revealed synovial sarcoma translocation genetic reassortment, which confirmed the diagnosis of SS.

CONCLUSION

PPSS is extremely rare and tends to be misdiagnosed as many primary pulmonary diseases. PET-CT, histologic analysis, and FISH tests can be used to differentiate PPSS from other diseases. Surgical resection is regularly recommended for the treatment of solitary PPSS and is helpful for improving the prognosis.

Key Words: Primary pulmonary synovial sarcoma; Spindle cells; Fluorescence in situ hybridization; Synovial sarcoma translocation; Solitary pulmonary nodule; Positron emission tomography-computed tomography; Case report

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Core Tip: Synovial sarcoma (SS) is an uncommon and highly malignant soft tissue sarcoma in the clinic, with primary pulmonary SS (PPSS) being extremely rare. It tends to be misdiagnosed as many primary pulmonary diseases. Here, we described the clinical characteristics, diagnosis, and treatment of a solitary PPSS case. Positron emission tomography-computed tomography, histologic analysis, and fluorescence in situ hybridization tests can be used to differentiate PPSS from other diseases. Surgical resection is regularly recommended for the treatment of solitary PPSS and is helpful for improving the prognosis.

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INTRODUCTION

Synovial sarcoma (SS) is an uncommon and malignant soft tissue tumor that accounts for around 10% of soft tissue sarcomas[1]. Although it often arises in the limbs, particularly near the knee joints, SS has the potential to occur in any part of the body, including the head and neck, lungs, kidneys, prostate, skin, vulva, blood vessels, and nerve tissue[2]. The remarkable genetic feature of SS is the pathognomonic t(X;18)(p11;Q11) translocations, resulting in fusion of the SS18 gene, known as SYT, on chromosome 18 with one of the three highly homologous SSX genes (SSX1, SSX2, or SSX4), which are all on the X-chromosome[3,4].

While most of the synovial sarcoma in the lung is metastatic, primary pulmonary SS (PPSS) is extremely rare, especially solitary PPSS[5]. Because of a lack of specific characteristics, PPSS tends to be confused with other benign or malignant lung lesions, such as teratoma, lymphoma, spherical tuberculosis, and pulmonary cryptococcosis. In this report, we describe a case of solitary PPSS that was confirmed *via* positron emission tomography-computed tomography (PET-CT), histological analysis, immunohistochemistry (IHC), and fluorescence in situ hybridization (FISH) genetic testing. Additionally, we conduct a review of the clinical manifestations, diagnosis, and treatment of this type of disease using pertinent literature.

CASE PRESENTATION

Chief complaints

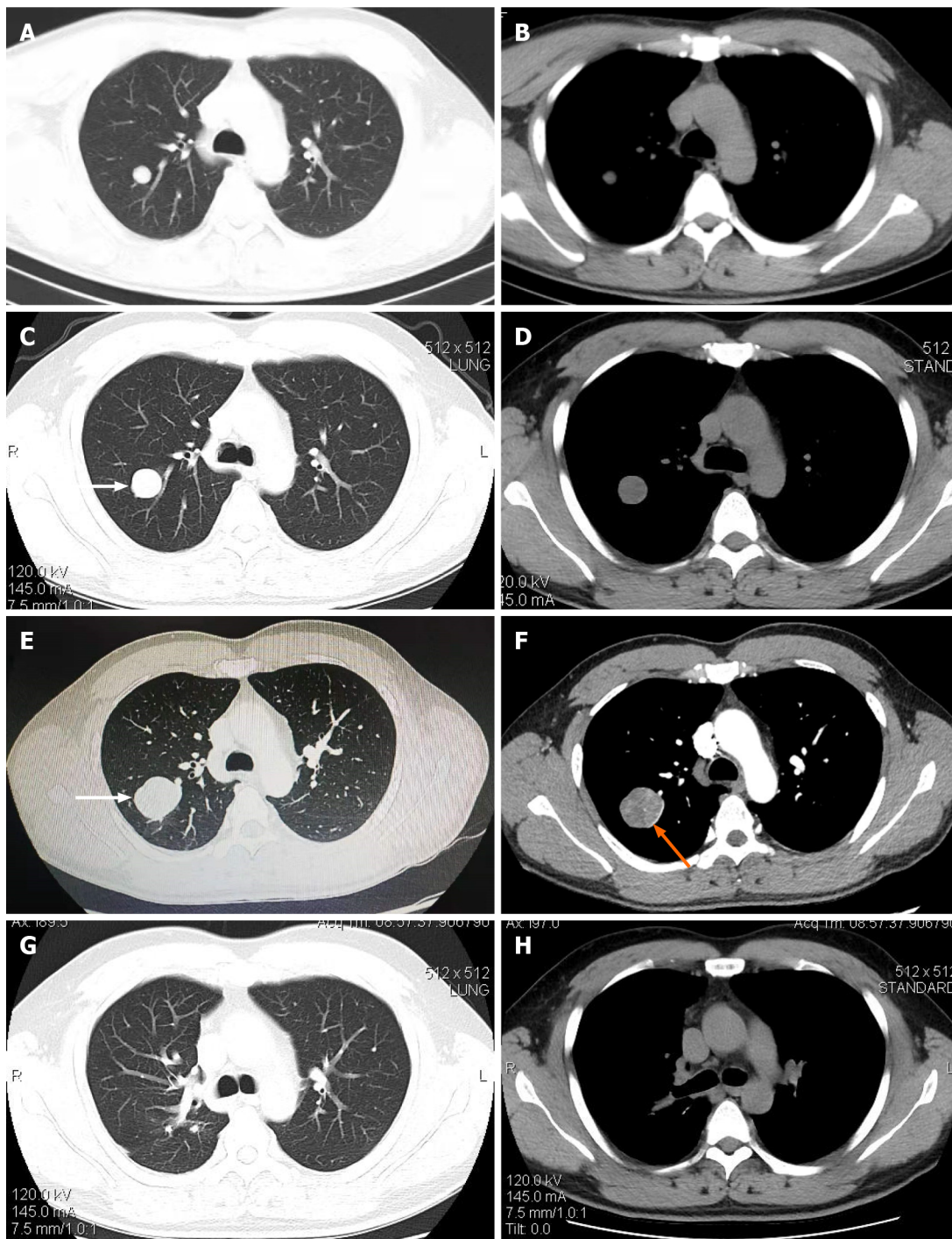
In August 2020, a 33-year-old male was admitted due to two years of discovered lung shadows, and intermittent coughing and hemoptysis for one month.

History of present illness

The patient had undergone a routine chest computed tomography (CT) examination in July 2018 due to trauma, which had shown a solitary roundish nodule with a maximum diameter of approximately 14 mm and smooth edges in the upper lobe of the right lung (Figure 1A and B). The nodule was initially diagnosed as a benign lung tumor and was left untreated. In November 2019, a chest CT re-examination revealed that the lesion had grown bigger significantly, reaching approximately 30 mm in diameter, with a smooth edge and visible shallow lobes. The patient declined the suggestion of a further diagnosis by biopsy (Figure 1C and D). From July 2020, the patient exhibited intermittent coughing with white sputum and hemoptysis. The amount of hemoptysis varied from 50 to 100 mL, without accompanying chills, fever, chest tightness, wheezing, chest pain, weight loss, or night sweats. The hemoptysis became severe two days before admission, occurring dozens of times per day.

History of past illness

The patient had not noticed any remarkable medical conditions in the past.



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Figure 1 Computed tomography scans of the chest. A and B: The shadow of the round nodules in the upper lobe of the right lung was detected in 2018, with a maximum diameter of about 14 mm and smooth edges; C and D: In 2019, the detected lesion had grown significantly larger, reaching a maximum diameter of approximately 30 mm, with smooth edges and shallow lobes (white arrows); E and F: By 2020, the lesion had grown to approximately 20 mm × 34 mm × 42 mm in size, with irregular density, smooth edges spotted with calcifications, slightly shallow lobes (white arrows), an uneven level of enhancement, and a ring-shaped enhanced image around the perimeter (orange arrow); G and H: From postoperative to 2021, no shadows with an abnormally high density were observed.

Personal and family history

The patient has no known family history of genetic diseases.

Physical examination

Upon admission to the hospital, the patient's initial physical examination were all within normal limits.

Laboratory examinations

The patient's major laboratory tests, including hematological test, blood biochemical test, infection

related, tumor biomarker tests and immune related were all within normal limits.

Imaging examinations

The enhanced chest CT revealed a significantly enlarged round mass of approximately 20 mm × 34 mm × 42 mm in the posterior segment of the right upper lobe with uneven density, distinct edge boundary, spot-like calcification, and a slightly shallow profile. Additionally, the enhanced chest CT scan revealed an uneven level of enhancement of the mass, and the mass periphery had an enhanced shadow in the shape of a ring (Figure 1E and F).

Further diagnostic work-up

Later, the bronchoscopy procedure revealed a neoplasm at the posterior opening of the right upper lobe surrounded by purulent secretions and a small amount of bleeding. Clamp biopsy was performed due to the mass completely obstructing the airway and preventing the lens body from passing through (Figure 2E and F). H&E staining of the biopsy showed spindle-shaped malignant tumor cells, and IHC showed CKpan (-), CK8/18 (-), CK7 (-), Syn (-), TTF1 (-), P40 (-), P63 (-), CK5/6 (-), dcsmin (-), SMA (-), S-100 (-), and Ki-67 (30% +). The subsequent PET-CT whole-body scan revealed only a mass in the upper lobe of the right lung, with uneven radioactivity uptake and a standardized uptake value (SUV) max of 5.6 (Figure 2A-D).

Under general anesthesia, the patient underwent surgical thoracoscopic resection of the posterior segment of the right upper lobe of the lung. The specimen was grayish-yellow in color, covered with small multi-nodulated structures, and composed of soft tissue (Figure 2G). H&E staining of the excised specimen showed a large number of spindle-shaped malignant tumor cells (Figure 3A), and IHC indicated CD99 (3+), BCL-2 (2+), EMA (-), CD34 (-), and TLE1 (-) (Figure 3B-F). In addition, the FISH test showed the splitting of SS18, which furthermore confirmed the diagnosis of SS, pathologically classified as monophasic fibrous or spindle-cell type.

FINAL DIAGNOSIS

The final diagnosis of the presented case is PPSS.

TREATMENT

Under general anesthesia, the patient underwent surgical thoracoscopic resection of the posterior segment of the right upper lobe of the lung. After the operation, the patient recovered and was discharged after declining chemotherapy.

OUTCOME AND FOLLOW-UP

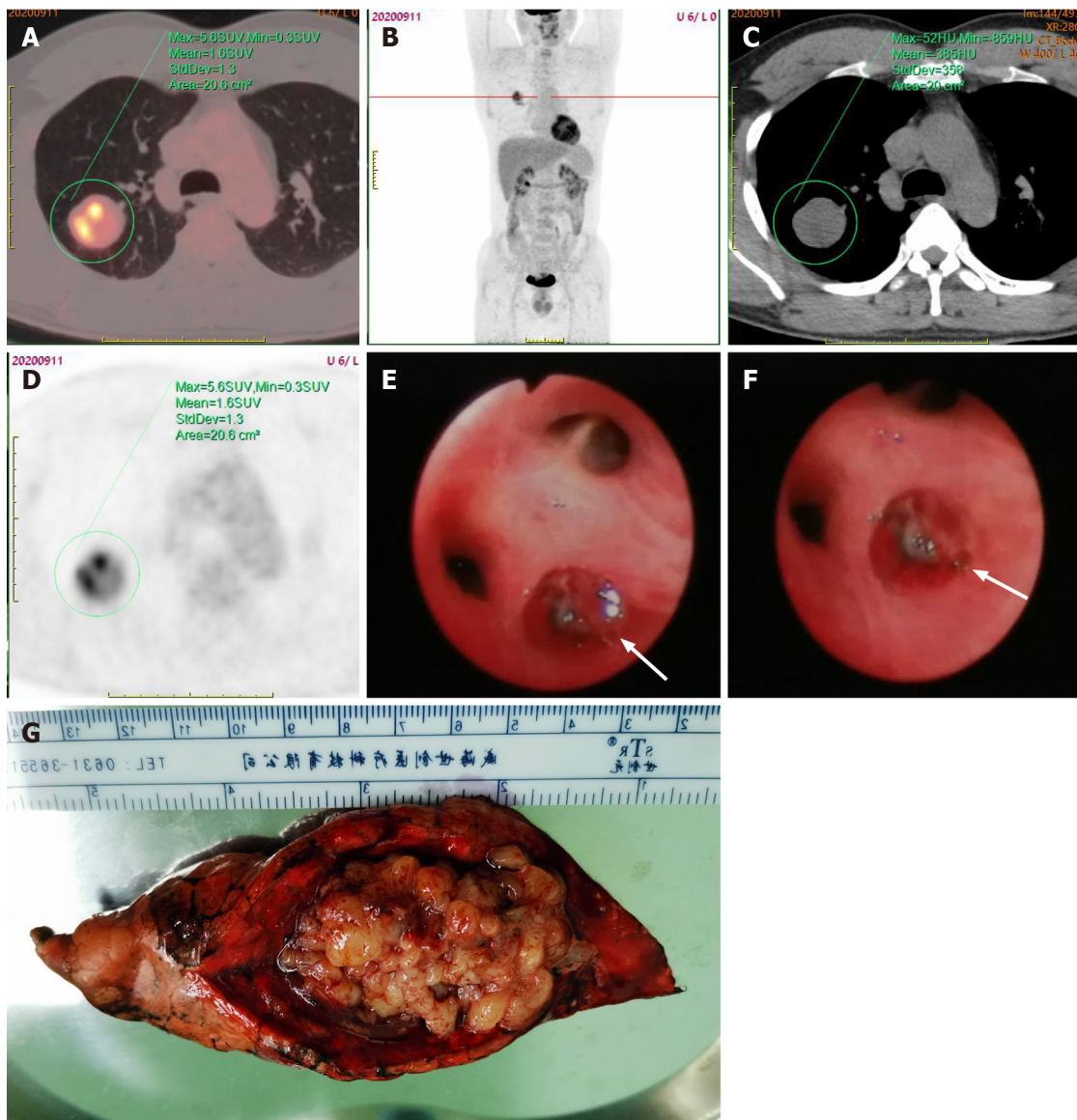
The patient recovered after the operation, and six months after the operation, the follow-up chest CT examination revealed no obvious abnormality (Figure 1G and H).

DISCUSSION

PPSS is more prevalent in young and middle-aged adults, with an average onset age of 36.5-58 years[6-10] and a male-to-female incidence ratio of 2:1[6,11]. Cough, chest pain, dyspnea, and hemoptysis are all common symptoms. In this case, the patient's primary clinical manifestations were intermittent cough and severe hemoptysis. We ruled out the potential of metastatic lesions from an extrapulmonary primary SS using a PET-CT whole-body scan. Additional H&E staining, IHC, and FISH detection of surgically resected specimens confirmed the diagnosis of PPSS.

PPSS is characterized by roundish parenchymal masses with smooth edges and inconspicuous lobes on imaging. The lesions may be accompanied by necrosis, liquefaction, calcification without cavitation, burrs, and bronchial traction. In addition, enhanced CT frequently reveals an uneven enhancement of the mass or a thick-walled ring, often associated with ipsilateral pleural effusion[12]. In this case, the chest enhanced CT revealed typical peripheral pattern changes of PPSS, including smooth edges, uneven lesion density, calcification, and ring enhancement.

Metastatic lesions of primary SS often occur in the lungs and share similar lung imaging characteristics as PPSS. Thus, it is necessary to use an approach capable of distinguishing these two types of lesions for the determination of further treatment[13]. In this case, using the whole body PET-CT scan ruled out the possibility of extrapulmonary primary SS. PET-CT examination frequently reveals a



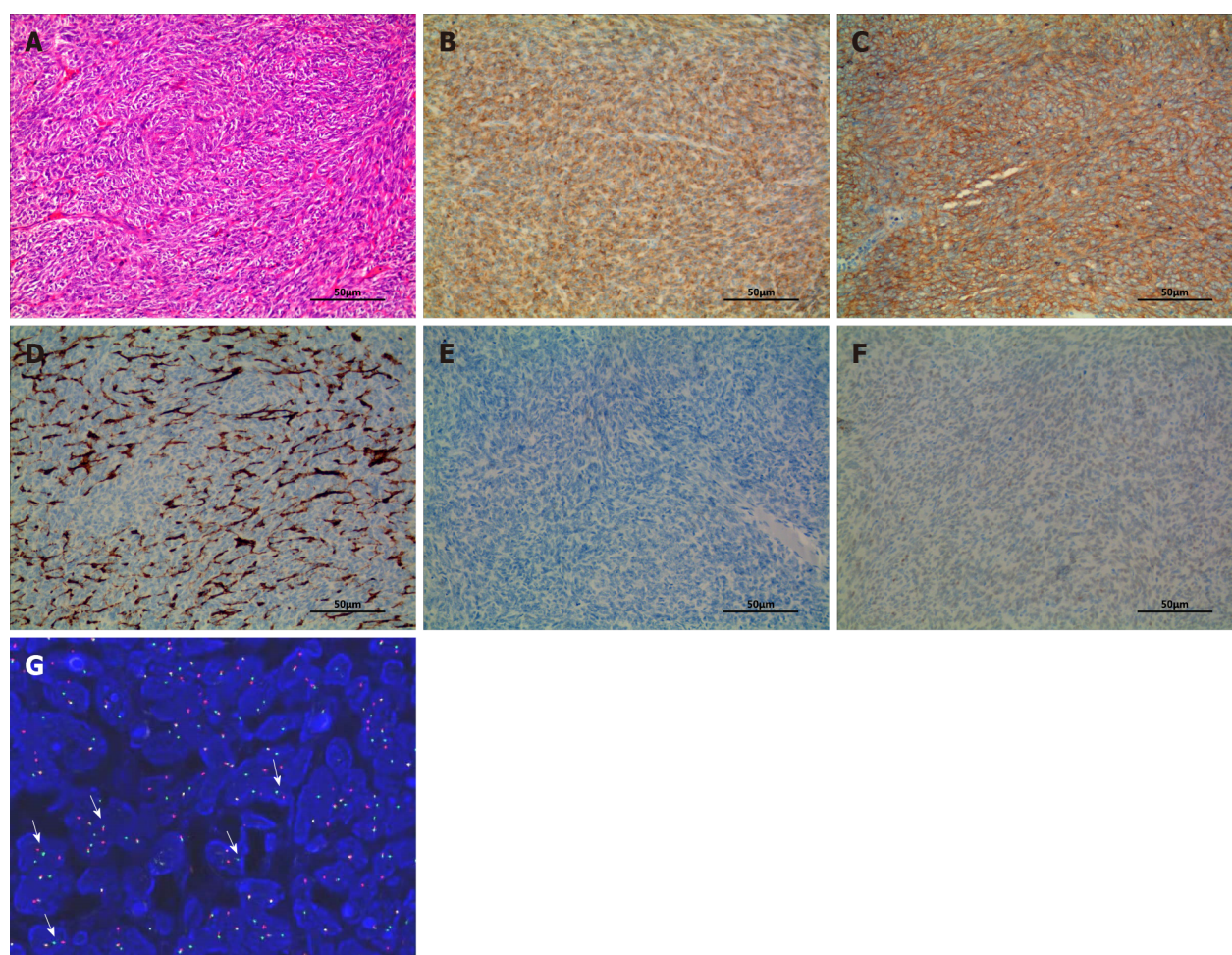
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Figure 2 Positron emission tomography-computed tomography scan. A-D: Showed a solitary round mass in the upper lobe of the right lung, with unevenly increased radioactivity uptake and an SUVmax of 5.6; E and F: Fiberoptic bronchoscopy revealed the presence of new organisms (white arrows) at the posterior opening of the upper right lobe, with a smooth capsule, surrounded by purulent secretions, and oozing a small amount of blood; G: The specimen obtained following the thorascopic resection of the posterior segment of the right upper lobe of the lung was grayish yellow in color, with some small round-like changes and a soft texture.

significant increase in fluorodeoxyglucose (FDG) uptake in lung lesions, with an SUVmax ranging from 2.2 to 17.6[14]. In this case, the SUVmax value of the lesion was 5.6, which indicated that hypermetabolic activity occurred within the tumor cells.

As with SS, PPSS exhibits bidirectional differentiation into mesenchymal and epithelial tissues. Monophasic fibrous and (or) epithelial cells are intertwined under the microscope to form dense tumor cell bundles, some of which are mucous. IHC helps in identifying the pathological type of SS by detecting epithelial and mesenchymal biomarkers. Machen *et al*[15] reported that BCL-2 was expressed diffusely in 98% of SS cases and CD99 was expressed focally or diffusely in approximately 60% of cases. Consistent with these earlier studies, IHC analysis of the PPSS tissue in this case revealed increased expression of BCL-2 and CD99, as well as a significantly increased Ki-67 index of 30%.

FISH using an SS18 break-apart probe is currently the most widely used approach to demonstrate the presumptive presence of one of the SS18-SSX fusions. If the probe breaks, it suggests that the SS18 gene and SSX gene are fused[16]. It has been reported that the sensitivity and specificity of FISH detection using the SS18 two-color fracture separation probe in the diagnosis of synovial sarcoma are 83% and 100%, respectively[17,18]. In this study, SS18 two-color break separation probe FISH technology was used to specifically detect whether the SS18 gene was broken. The use of isolated probes can cover different fusion subtypes and determine the fusion genes more comprehensively. In this case, the breaking apart of the SYT gene was detected by FISH, which confirmed the final diagnosis of SS.



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Figure 3 Hematoxylin and eosin staining. A: Hematoxylin and eosin (H&E) staining of tissue sections of posterior segment of the right lung upper lobe obtained from surgery (H&E 200×). The tumor was composed of spindle cells, which were arranged in dense cellular sheets or vague fascicles, with a herringbone architectural pattern; B-F Immunohistochemistry (IHC) revealed the tumor cells were diffusely positive for BCL-2 (B) and CD99 (C), and negative for CD34 (D), EMA (E) and TLE1 (F). The blood vessels inside the tumor showed positive staining for CD99 (C) (IHC 200×); G: Fluorescence in situ hybridization analyses: Red and green signals show break-apart regions (white arrows), representing the splitting of SS18 (synovial sarcoma translocation, SYT).

PPSS has a poor overall prognosis, with a 5-year survival rate of approximately 50% to 80%. Due to the rarity of PPSS, there are no guidelines for its optimal treatment. Therefore, the treatment recommendations for SS have shifted significantly in recent years toward radical resection in conjunction with radiotherapy and/or chemotherapy[19]. At present, surgical resection remains the first line of treatment for solitary PPSS. Simultaneously, because SS is a chemotherapy-sensitive tumor[20], Adriamycin alone or in combination with Ifosfamide remains the standard chemotherapy regimen for SS. The combined approach achieves a total remission rate of approximately 50%, which is superior to any monotherapy [19]. Regrettably, the patient in this case refused postoperative chemotherapy.

CONCLUSION

PPSS is an extremely rare disease with atypical clinical manifestations and imaging changes, raising the risk of diagnostic confusion with other lung diseases, which should attract attention from clinicians. Here, we excluded the potential of SS lung metastasis through systemic examination and diagnosed this case as solitary PPSS based on pathological classification using IHC measurements and the SYT gene break-apart characteristics determined with a FISH test. Later, the tumor was removed by surgical resection, which will benefit the patient's survival and prognosis.

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FOOTNOTES

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