

PLEUROPULMONARY SARCOMA-A CASE REPORT

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ABSTRACT

A 42-year-old female presented with hemoptysis, chest pain and a pleural-based mass, and was found to have primary sarcoma of the lung. Primary pulmonary sarcomas comprise <1% of all primary lung malignancies. They present clinically in young adults with cough, chest pain, shortness of breath, or hemoptysis, with a mass on x-ray and computerized tomography scan. Diagnosis is made by histology and immunohistochemistry. Histologic diagnosis has recently been supplemented by cytogenetic analysis, which offers important prognostic information. The mainstay of treatment remains complete surgical excision. Prognosis is poor, with an overall 5-year survival rate of 50%.

KEYWORDS: Primary Pulmonary Sarcoma, Lung malignancy.

INTRODUCTION

Pulmonary sarcomas constitute only 0.1%–0.5% of all primary lung malignancies. The most frequently reported subtypes of sarcomas in the lung are leiomyosarcoma, malignant fibrous histiocytoma, fibrosarcoma and more recently, synovial sarcoma.^[1] The term *synovial sarcoma* first appeared in the German surgical literature in 1865, where it was used to describe a complex multinodular lesion apparently arising from synovial tissue in the knee of an adult patient.^[2] Fifty years later, in 1910, French authors Lejars and Rubens-Duvall published a description of the classic pathologic features.^[3] In 1947, the Armed Forces Institute of Pathology (AFIP) presented the first notable series of synovial sarcoma cases, a group of 32 lesions that were termed “synoviomata.” Currently, synovial sarcoma accounts for 7%–10% of all soft-tissue sarcomas. The most common sites of origin are the thigh, knee, ankle, foot and upper extremity.^[4,5] In unusual cases, synovial sarcoma may arise within the chest wall, mediastinum, heart, lung, or pleura.^[4,6–11] Increasingly sophisticated diagnostic techniques in immunohistochemistry, electron microscopy and cytogenetic analysis have led to more frequent recognition of PPSS as a distinct histologic subtype of sarcoma in the lung.^[1,5,12] Diagnosis is established by immunohistochemistry and molecular analysis. Primary modality of treatment is surgery followed by chemotherapy. Even with adequate surgical resection and postoperative treatment, recurrence of the disease and metastases are common

CASE

A 40-year-old female nonsmoker resident of Akola with 2 issues, with no background or family history of cancer

or respiratory illness presented with 2 weeks history of breathlessness and nonproductive cough and a single episode of hemoptysis. she also had right sided chest pain. She had history of right sided tubercular pleural effusion 10 years back, had taken AKT for the same. This time prior to admission, thoracentesis was done at private hospital she was started on 5 drug AKT (injection streptomycin, rifampicin, isoniazid, ethambutol, pyrazinamide). In view of persistence of symptoms, Intercostal chest drain was inserted and she was referred to our hospital for further management. She had no history of co morbidities like diabetes mellitus or hypertension. Her menstrual history was insignificant.

On respiratory sytem examination, there was ICD in situ in right 6 th intercostals space in anterior axillary line with decreased movements over right hemithorax with decreased vocal resonace and breath sounds over the right hemithorax.

Her investigations were as follows-

Hb 10.2.

Total leucocyte count 7200.

Renal functions and Liver functions were within normal limits.

Viral markers were negative (HIV and HBs Ag).

Sputum for AFB done by ZN stain was negative.

Sputum Culture no pathogen was grown.

USG Thorax- Minimal pleural collection in Right pleural space with consolidation with tip of ICD noted within consolidation.

Evaluation with contrast-enhanced computed tomography (CECT) chest was suggestive of airspace

opacification in right middle and lower lobes. right mild pleural effusion with enhancement of pleura. Intercostal tube was seen passing through 6th intercostals space with its tip in right middle lobe.

Biopsy of the lesion was suggestive of synovial sarcoma.

Immunohistochemistry: Bcl-2-strongly positive Mic 2 weakly positive.

AE1/AE3 focally positive. Tdt and chromogranin were negative.

Her ICD tube was removed. It was planned to give her neoadjuvant chemotherapy with ifosfamide- and doxorubicin-based chemotherapy and assess response after 2-3 cycles for surgery. The patient tolerated chemotherapy well. After two cycles of chemotherapy patient declined further chemotherapy and surgery. She was subsequently lost to follow up.

DISCUSSION

Synovial sarcoma accounts for 10% of all soft tissue tumors.^[13,14] It presents in adolescents and young adults affecting the pararticular locations of the extremities, neck, lung, heart, and rarely mediastinum and abdominal wall. Extremities account for 70% of the cases followed by neck and chest involvement accounting for 7% each. Pulmonary synovial sarcoma (PPSS) is a rare variant of synovial sarcoma accounting for 0.5% of all primary lung malignancies.^[15] It was described as a distinct anatomic subset in 2002 by Essary *et al.*,^[16] having similar pathologic features to soft tissue sarcoma. It can arise in the lung, pleura, chest wall, heart and mediastinum. A strong correlation to cigarette smoking has been postulated.^[17] The median age of presentation is 25 years. There is no predilection to either sex. Both our cases were males, aged 37 and 47 years, respectively. Presentation was with pleural-based mass lesions.

Patients present clinically with chest pain (24-80%), breathlessness (8-36%), cough (8-33%), and hemoptysis (20-25%). Symptoms usually are of a few months duration. Occasionally, patients may present acutely with a rapidly enlarging tumor or pneumothorax. PPSS may be detected incidentally on a routine radiograph in at least 40% patients.^[18] One of our cases presented with chest pain and the other with breathlessness and nonproductive cough. In a recent review, most of the cases of PPSS were centrally located and associated with postobstructive pneumonia.^[19] Peripheral tumors were uncommon and usually slow growing and asymptomatic. Both our patients had peripheral location of tumor. Differential diagnosis includes bronchogenic carcinoma, lung metastases, mesothelioma, lymphoma, abscess, histoplasmosis, coccidiomycosis, fibro sarcoma, and leiomyosarcoma. PPSS may metastasize to bone, liver, skin, brain and breast tissue.^[20] None of our patients had metastases at presentation.

On chest X ray, it appears as a homogenous opacity in the lung, often accompanied by ipsilateral pleural effusion. It may appear as a consolidation or a complete opacification of the hemithorax or as a pleural thickening.^{[21],[22]} Rarer presentations may include pneumothorax. Significant mediastinal adenopathy is usually not seen in PPSS and argues more in favor of bronchogenic carcinoma. Other mimics could include metastases to lungs, fibro sarcoma, hemangiopericytoma, mesothelioma and leiomyosarcoma. On CT scan, it appears as a well-defined heterogeneously enhancing mass lesion with areas of fluid indicating necrosis or hemorrhage. Both the cases in this report appeared as large masses with nonhomogenous enhancement. There was no evidence of pleural effusion. Soft tissue sarcomas arising in the chest wall display cortical bone destruction, tumor calcification and invasion. One differentiating feature between PPSS and soft tissue sarcoma is the presence of triple sign (bright, dark and gray) representing tumor, hemorrhage and necrosis on magnetic resonance imaging (MRI). MRI aids in more accurate localization and is useful to know the extent of tumor invasion.^[23] It was, however, not done in our cases.

Pathologic examination reveals the presence of fascicles of spindle cells with a high-mitotic rate. PPSS is believed to originate from multipotential mesenchymal cells with synovial differentiation, hence, the term synovial sarcoma. The histological subtypes of PPSS are biphasic, monophasic spindle cell, monophasic epithelial and poorly differentiated types.^[24] The monophasic variant is more commonly seen. It is composed of uniform spindle cells with elongated nuclei, basophilic cytoplasm and indistinct cell borders. The monophasic type poses certain diagnostic difficulties due to the uniform spindle cell pattern. It may be confused with fibrosarcoma, hemangiopericytoma, leiomyosarcoma and carcinosarcoma. These tumors are immunoreactive for cytokeratin and EMA. They also show variable positivity to S-100 (30%), CD 99 (70%) and Bcl-2 (75-100%).^[25] Both cases were positive for vimentin and Bcl-2, while one case was positive for CD99. Our cases were of the monophasic fibrous variety.

Nearly all synovial sarcomas have a specific chromosomal translocation t (X; 18) (p11.2; q11.2). This results in the fusion of the SYT gene on chromosome 18 with the SSX1 or the SSX2 on chromosome X.²⁶ SYT-SSX1 and SYT-SSX2 are believed to function as aberrant transcription regulators. Hartel *et al.*,^[27] reported that 92% patients with PPSS and mediastinal sarcoma were positive for t (X;18). SYT-SSX1 is present in majority of the biphasic tumors, while in the monophasic tumors there is an equal frequency of both translocations. There seem to be certain prognostic implications associated with the specific translocations, with SYT-SSX1 common in younger adults and having a poorer prognosis as compared to SYT-SSX2. In one study patients with SYT-SSX1 type had a poorer 5-year

survival rate. In another study by Mirzoyan *et al.*,^[28] patients with SYT-SSX1 were younger, had similar mean tumor size and had lesser grade 3 tumors. Translocation studies were not done in our subjects.

Owing to the rarity of the tumor, there are no guidelines on the optimal treatment of PPSS. Surgery followed by radiation or chemotherapy is the current standard. Wide excision followed by radiation therapy is used in high-grade (G2-3), deep and >5 cm lesions. Radiation is given at doses of 50-60 Gy, with fractions of 1.8-2 Gy. It is also applicable in cases where R0 resections have not been achieved. Radiotherapy was not administered in our patient as he did not consent for the same.

Ifosfamide-and doxorubicin-based regimen is commonly employed with an ORR of 24%. Adjuvant chemotherapy improves the time to local recurrence with a trend toward better overall survival. In a large series of 80 patients by Spillane *et al.*,^[29] chemotherapy was given in the neoadjuvant and adjuvant setting with ifosfamide and doxorubicin. The combination of these two drugs produced a 58% objective decrease in tumor size when compared to 36% when used singly. Median survival for the combination arm was 15 months.^[30] In another study of 25 patients, follow-up of 18 patients confirmed that 55% had died within 7 years of diagnosis, 22% were alive with recurrent or metastatic disease and 22% were disease-free 20 years after diagnosis.

Failure to achieve a complete resection, large tumor size (>5 cm), male gender, older age (>20 years) high-grade tumor, presence of necrosis, neurovascular invasion, high mitotic rate (>10 per 10 high power fields) and SYT-SSX1 variant portend a poor prognosis.^[31] The overall 5-year survival rate varies between 36% and 76%. Future therapeutic targets could include the SYT-SSX protein, EGFR, HER2/neu and Bcl-2.

REFERENCES

- Keel SB, Bacha E, Mark EJ, Nielsen GP, Rosenberg AE. Primary pulmonary sarcoma: a clinicopathologic study of 26 cases. *Mod Pathol*, 1999; 12(12): 1124-1131.
- Cadman NL, Soule EH, Kelly PJ. Synovial sarcoma: an analysis of 34 tumors. *Cancer*, 1965; 18: 613-627.
- Fisher C. Synovial sarcoma. *Ann Diagn Pathol*, 1998; 2: 401-421.
- Miettinen M. Soft tissue tumors with epithelial differentiation. In: Miettinen M, ed. *Diagnostic soft tissue pathology*. Philadelphia, Pa: Churchill Livingstone, 2003; 463-468.
- Raney RB. Synovial sarcoma in young people: background, prognostic factors, and therapeutic questions. *J Pediatr Hematol Oncol*, 2005; 27(4): 207-211.
- Kaplan MA, Goodman MD, Satish J, Bhagavan BS, Travis WD. Primary pulmonary sarcoma with morphologic features of monophasic synovial sarcoma and chromosome translocation t(X; 18). *Am J Clin Pathol*, 1996; 105(2): 195-199.
- Gaertner E, Zeren EH, Fleming MV, Colby TV, Travis WD. Biphasic synovial sarcomas arising in the pleural cavity: a clinicopathologic study of five cases. *Am J Surg Pathol*, 1996; 20(1): 36-45.
- Zeren H, Moran CA, Suster S, Fishback NF, Koss MN. Primary pulmonary sarcomas with features of monophasic synovial sarcoma: a clinicopathological, immunohistochemical and ultrastructural study of 25 cases. *Hum Pathol*, 1995; 26(5): 474-480.
- Suster S, Moran CA. Primary synovial sarcomas of the mediastinum: a clinicopathologic, immunohistochemical, and ultrastructural study of 15 cases. *Am J Surg Pathol*, 2005; 29(5): 569-578.
- Perlmutter AE, Saunders SE, Zaslau S, Chang WW, Farivar-Mohseni H. Primary synovial sarcoma of the kidney. *Int J Urol*, 2005; 12(8): 760-762.
- Srivastava A, Nielsen PG, Dal Cin P, Rosenberg AE. Monophasic synovial sarcoma of the liver. *Arch Pathol Lab Med.*, 2005; 129(8): 1047-1049.
- Roberts CA, Seemayer TA, Neff JR, Alonso A, Nelson M, Bridge JA. Translocation (X;18) in primary synovial sarcoma of the lung. *Cancer Genet Cytogenet*, 1996; 88(1): 49-52.
- Mankin HJ, Hornicek FJ. Diagnosis, classification, and management of soft tissue sarcomas. *Cancer Control*, 2005; 12: 5-21.
- Weiss SW, Goldblum JR. From malignant soft tissue tumors of uncertain type. In: Weiss SW, Goldblum JR, editors. *Enzinger and Weiss's Soft Tissue Tumors*, 4th ed. St. Louis: Mosby, 2001; 1483-571.
- Etienne-Mastroianni B, Falchero L, Chalabreysse L, Loire R, Ranchère D, Souquet PJ, et al. Primary sarcomas of the lung: A clinicopathologic study of 12 cases. *Lung Cancer*, 2002; 38: 283-9.
- Essary LR, Vargas SO, Fletcher CD. Primary pleuropulmonary synovial sarcoma: Reappraisal of a recently described anatomic subset. *Cancer*, 2002; 94: 459-69.
- Nappi O, Wick MR. Sarcomatoid neoplasms of the respiratory tract. *Semin Diagn Pathol*, 1993; 10: 137-47.
- Zeren H, Moran CA, Suster S, Fishback NF, Koss MN. Primary pulmonary sarcomas with features of monophasic synovial sarcoma: A clinicopathological, immunohistochemical and ultrastructural study of 25 cases. *Hum Pathol*, 1995; 26: 474-80.
- Zamarrón C, Abdulkader I, Alvarez UC, Barón FJ, Prim JM, Ledo RL, et al. Primary synovial sarcoma of the lung. *Intern Med.*, 2006; 45: 679-83.
- Banerjee D, Gorse SJ, Cotter M, Johnson RC. Sonographic and pathologic features of metastatic synovial sarcoma of the lung presenting as a breast neoplasm. *Breast J.*, 2004; 10: 372.
- Gaertner E, Zeren EH, Fleming MV, Colby TV, Travis WD. Biphasic synovial sarcomas arising in

- the pleural cavity. A clinicopathologic study of five cases. *Am J Surg Pathol*, 1996; 20: 36-45.
22. Aubry MC, Bridge JA, Wickert R, Tazelaar HD. Primary monophasic synovial sarcoma of the pleura: Five cases confirmed by the presence of SYT-SSX fusion transcript. *Am J Surg Pathol*, 2001; 25: 776-81.
 23. Fujimoto K, Hashimoto S, Abe T, Meno S, Terasaki H, Nishimura H, et al. Synovial sarcoma arising from the chest wall: MR imaging findings. *Radiat Med.*, 1997; 15: 411-4.
 24. Okamoto S, Hisaoka M, Daa T, Hatakeyama K, Iwamasa T, Hashimoto H. Primary pulmonary synovial sarcoma: A clinicopathologic, immunohistochemical and molecular study of 11 cases. *Hum Pathol*, 2004; 35: 850-6.
 25. Miettinen M, Limon J, Niezabitowski A, Lasota J. Calretinin and other mesothelioma markers in synovial sarcoma: Analysis of antigenic similarities and differences with malignant mesothelioma. *Am J Surg Pathol*, 2001; 25: 610-7.
 26. Nagao K, Ito H, Yoshida H. Chromosomal translocation t (X,18) in human synovial sarcomas analyzed by FISH using paraffin-embedded tissue. *Am J Pathol*, 1996; 148: 601-9.
 27. Hartel PH, Fanburg-Smith JC, Frazier AA, Galvin JR, Lichy JH, Shilo K, et al. Primary pulmonary and mediastinal synovial sarcoma: A clinicopathologic study of 60 cases and comparison with five prior series. *Mod Pathol*, 2007; 20: 760-9.
 28. Mirzoyan M, Muslimani A, Setrakian S, Swedeh M, Daw HA. Primary pleuropulmonary synovial sarcoma. *Clin Lung Cancer*, 2008; 9: 257-61.
 29. Spillane AJ, A'Hern R, Judson IR, Fisher C, Thomas JM. Synovial sarcoma: A clinicopathologic, staging and prognostic assessment. *J Clin Oncol*, 2000; 18: 3794-803.
 30. Trassard M, Le Doussal V, Hacene K, Terrier P, Ranchère D, Guillou L, et al. Prognostic factors in localized primary synovial sarcoma: A multicenter study of 128 adult patients. *J Clin Oncol*, 2001; 19: 525-34.
 31. Albritton KH, Randall RL. Prospects for targeted therapy of synovial sarcoma. *J Pediatr Hematol Oncol*, 2005; 27: 219-22.