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Case Series

A small case series of primary synovial sarcoma of lung

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ABSTRACT

Primary synovial sarcoma of lung (PSSL) is extremely rare accounting for <0.5% of all lung tumors. Less than hundred cases of primary synovial sarcoma of the lung (PSS) have been reported. Thus, very limited medical literature is available regarding the clinical presentation and treatment outcomes of PSSL. Here we highlight the clinico-pathological features, immunohistochemistry, and treatment outcomes of a series of three PSSL cases. The mean age was 70 years and male to female ratio was 2: 1. Chest pain was the most common presenting complaint. Tumor size was more than 5 cm in all the cases. The characteristic biopsy finding was round and short spindled cells. IHC was strong positive for TLE 1 with final diagnosis being biphasic synovial sarcoma for all the three cases. Surgery was offered to all cases but only one was deemed fit for surgery. One received ifosfamide/epirubicin based chemotherapy while the third patient expired after one month of pazopanib. In few recent series, PSSL is being reported as the most common subtype of primary lung sarcoma comprising 14.7% to 18% of all primary lung sarcomas, due to wider utilization of immunohistochemical and cytogenetic analysis. The diagnosis requires clinico-pathologic and immunohistochemical investigations to exclude other primary and metastatic lung sarcoma. Thus, it merits to be in one of the differentials of primary lung masses not categorised as lung carcinomas.

Keywords: Synovial sarcoma, Lung tumor, Pulmonary sarcoma

INTRODUCTION

Synovial sarcoma (SS) is a malignant soft tissue tumor that affects mostly young adults and can arise at any anatomic site. It accounts for 5 - 10% of all soft tissue sarcomas and lung being the most common site of metastasis in SS. Although many SS originate close to joints, the name synovial sarcoma is a misnomer as these lesions do not originate from intra-articular synovium, but from primitive mesenchymal cells.[1,2] Primary intrathoracic SS is extremely rare accounting for <0.5% of all lung tumors. Most commonly, it arises from the lung parenchyma followed by pleura and mediastinum.[2,3] Very limited medical literature is available regarding the clinical presentation and treatment outcomes of Primary synovial sarcoma of the lung (PSSL). Here we describe a series of three PSSL cases who presented to our medical oncology department from February 2024 to April 2024 and confirmed by histopathology, immunohistochemistry with details of the clinical, pathological features and treatment outcomes.

CASE SERIES

Case 1

73-year male who is a chronic smoker (25 pack years), hypertensive and farmer by occupation, presented to hospital with chronic cough. No h/o fever, hemoptysis, chest pain or breathlessness. No weight loss or loss of

appetite. No abdominal pain, vomiting or diarrhea. No comorbidities other than hypertension. No past history of tuberculosis/pneumonia/COVID-19. No history of any major surgeries. No history of any major illness running in the family.

On General examination he was conscious and oriented with no pallor, icterus, clubbing, cyanosis or lymphadenopathy. His Eastern Cooperative Oncology Group (ECOG) performance was 2. His pulse was 102 per minute, respiration rate of 20 per minute, blood pressure of 100/60 and a saturation of 96% in room air. Examination of the respiratory system revealed reduced breath sounds over the right infra-axillary and infra capsular region. Examination of cardiovascular and gastrointestinal system did not reveal any abnormality. Chest X ray showed a well-defined radio-dense opacity in right lung measuring 51×49 mm in the lower zone of right lung field. No calcifications/air bronchograms within. Rest of the lung fields were clear.

PETCT thorax showed a 5×4.3 cm lesion in right lung lower lobe, superior segment with no mediastinal nodes or any distant metastasis (Figure 1). Haemoglobin/total count/platelet count were 10.8/9.66/4.45 lakh. Serum electrolytes, creatinine and Liver function tests were within normal range. HIV/Anti HCV/HBsAg were negative. 2 D echocardiography showed no regional wall motion abnormalities and Ejection Fraction of 60%. Ct guided lung biopsy on microscopy showed multiple cores of tissue bits, composed of highly atypical cells in nests, sheets and vague rosette like pattern. Cell is round to oval with minimal cytoplasm, medium sized, with fine chromatin and area of necrosis and apoptotic bodies noted (Figure 1).

IHC was positive for CK 7 (focal) and TLE 1 (strong positive); negative for CD 56, TTF 1, Synaptophysin and Chromogranin; Ki 67 of 40%. IHC features was suggestive of biphasic synovial sarcoma. Suggested SS18-SSX translocation study for further confirmation but owing to financial constraints it was not done. Surgical oncology opinion was sought but surgery deferred as the patient had very poor effort tolerance on pulmonary function test. Patient was started on chemotherapy with ifosfamide and epirubicin in reduced dosing, but due to poor tolerance patient could not receive any further treatment after the first cycle. He is currently on best supportive care.

Case 2

66-year-old female, diabetic and hypertensive admitted in CTVS department with complaints of chest pain since, 6 months, intermittent in nature, moderate to severe in intensity, aggravated on coughing and deep breathing. Pain non-radiating and not associated with sweating or palpitations. No history of fever or any trauma to the chest. History of total abdominal hysterectomy with bilateral salpingo-oophorectomy in 2015. On general physical examination elderly female patient, moderately built and nourished, conscious, cooperative, well oriented to time place and person. No pallor, icterus, cyanosis, clubbing, generalized lymphadenopathy or oedema. Pulse-118 bpm, bp-148/82 mm of Hg, SpO2-94 % in room air. ECOG of 2. On systemic examination left side reduced air entry was noted. Examination of cardiovascular and gastrointestinal system did not reveal any abnormality. No focal neurological deficits noted on central nervous system examination.

HRCT thorax showed a large heterogeneous soft tissue density lesion in the left hemithorax predominantly in the upper lobe of left lung measuring 11×5.5×5 cm. The patient then underwent left thoracotomy and left upper lobectomy under the CTVS department. The postoperative biopsy showed cells were round to oval, short spindled with scant cytoplasm and hyperchromatic nuclei. 0-1 mitosis/HPF. Impression being poorly differentiated malignancy (Figure 2).

IHC positive for PAN CK (focal), TLE 1, vimentin, CD99 (focal) BCL2 and negative for CD 45, synaptophysin, chromogranin and CD1 a. The Ki 67 being 15 %. Features are suggestive of Biphasic Synovial sarcoma of left lung, FNCLCC Grade 3. The patient was then referred to medical oncology for further management. A whole-body PET CT was done for staging and metastatic workup, which showed no other extra thoracic lesion with a single 2 cm lesion in the cerebellum detected incidentally. The patient was offered further treatment with radiation therapy or surgical excision of the brain lesion but the patient and relatives denied any further treatment. Currently the patient is doing well with no apparent symptoms.

Case 3

73-year-old gentleman with diabetes and coronary artery disease presented with complaints of change in voice quality since, 4 months and pain in right side of chest since, 1 month, associated with occasional cough, weight loss and loss of appetite. No history of fever, respiratory distress, palpitations or hemoptysis. Past history of diabetes mellitus since, 15 years, CAD and post PTCA 7 years back, currently on antidiabetic medications and dual anti-platelets. On examination there was no pallor, icterus, clubbing, cyanosis or lymphadenopathy. ECOG of 2. On systemic examination right side reduced air entry was noted.

Cardiovascular and gastrointestinal system did not reveal any abnormality. No focal neurological deficits were found on central nervous system examination. On evaluation ECG was within normal limits. Echocardiography showed–LV regional wall motion abnormality, concentric LVH, normal RV function and EF of 48%. Doppler carotid showed eccentric hypoechoic plaque in the right carotid bulb extending into proximal ICA region, causing 15-20% stenosis with no significant

hemodynamic changes. CT thorax showed a large well defined round soft density lesion measuring 11×8×9.5 cm in right upper lobe with subtle calcifications within it associated with destruction/involvement of posterior aspect of right 3rd rib likely neoplastic etiology, with mediastinal lymphadenopathy. Patient was incidentally also detected to be HCV (Hepatitis C virus) positive, for which medical gastroenterology opinion was taken. HCV viral load was below detection level in HCV Quantitative Real time PCR. Patient then underwent CT guided lung biopsy.

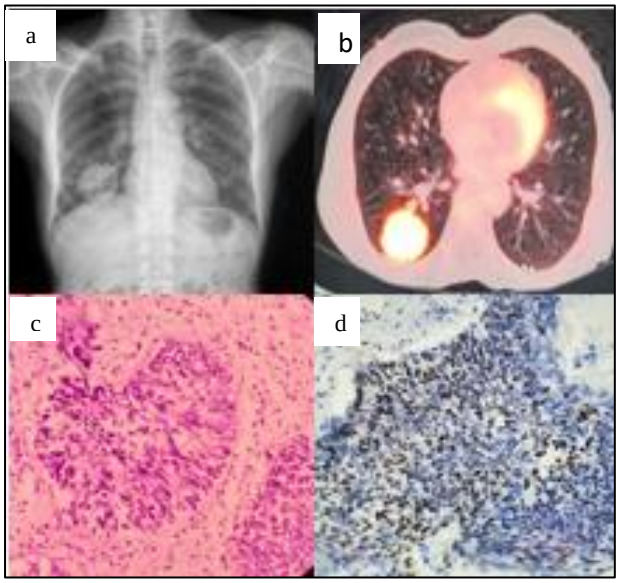

Figure 1: (a) CXR (PA) showing right lung mass. (b) PET CT showing right lung lesion with increased uptake. (c) Biopsy (H&E) show atypical cells in nests. (d) IHC-strong TLE 1 positive.

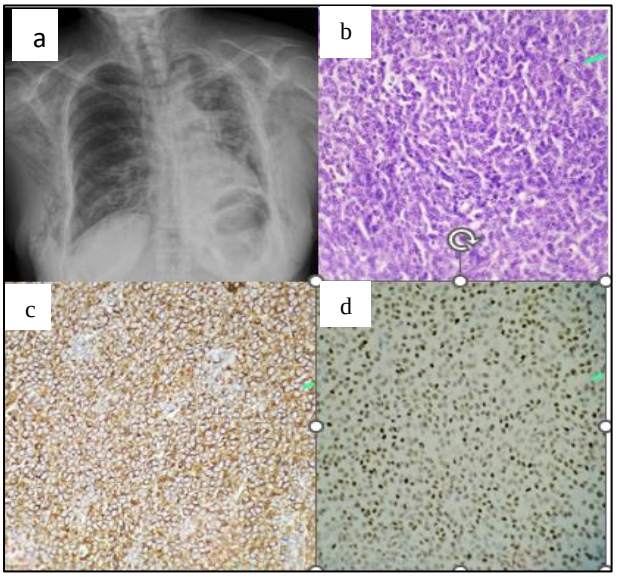

Figure 2: (a) CXR (PA) showing left lung mass. (b) BIOPSY-H&E 40x, round to short spindled cells. (c) IHC-Vimentin positive. (d) IHC TLE 1 strong nuclear positive.

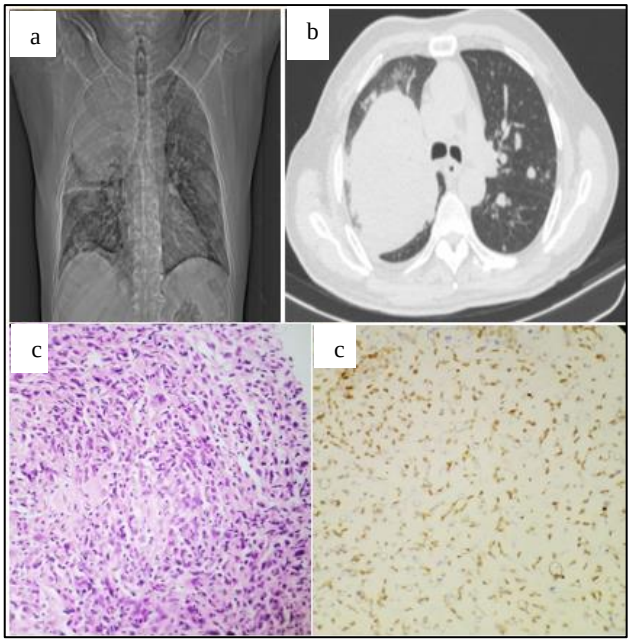

Figure 3: (a) CXR(PA) shows right lung mass. (b) CECT thorax show a large right upper lobe mass. (c) Biopsy: H&E show round and spindle cells. (d) IHC-strong TLE 1 positive.

DISCUSSION

The mean age of presentation in our study was 70 years and male to female ratio was 2:1. Chest pain was the most common presenting complaint. All the three had an ECOG of 2. Tumor size was more than 5 cm in all the cases. The characteristic biopsy finding was round to oval and short spindled cells. IHC was strong positive for TLE 1 in all the three cases. A final diagnosis of biphasic synovial sarcoma was made in all the three cases. Surgery was offered to all the three cases but only one was deemed fit and underwent surgery. One patient received ifosfamide/epirubicin based chemotherapy and one received oral tyrosine kinase inhibitor (tab pazopanib) owing to elderly age and multiple comorbidities.

Historically the commoner types of primary pulmonary sarcomas are leiomyosarcoma, undifferentiated pleomorphic sarcoma, fibrosarcoma, and synovial sarcoma.[4-6] Of late PPSS is being increasingly diagnosed as a distinct clinical entity due to wider utilization of immunohistochemical staining and cytogenetic analysis. In few recent series, PSSL is even reported as the most common subtype of primary lung sarcoma comprising 14.7% to 18% of all primary lung sarcomas.[7,8]

It was first described in 1995 by Zeren and colleagues as a distinctive primary lung sarcoma.[9] The subtypes of primary pulmonary synovial sarcomas are monophasic fibrous (spindle), monophasic epithelial, biphasic, and poorly differentiated. The commoner subtypes are biphasic and monophasic spindle cell type. Rarer subtypes are the monophasic epithelial, poorly

differentiated (round cell).[10,11] The diagnosis of PSS is made by clinic radiological, pathological, and immunohistochemical testing and ruling out metastatic or other primary lung tumors. The basic histological feature of biphasic synovial sarcoma has two components, the spindle cells and gland-like epithelial cells. The epithelial component has moderate, distinct amphophilic cytoplasm with round to ovoid nuclei. Poorly differentiated variety are highly cellular with round cells, hyperchromatic nuclei and frequent mitotic activity with necrosis.

Table 1: Clinical characteristics.

S. no.		Case 1	Case 2	Case 3
Age at diagnosis		73	66	73
Sex		Male	Female	Male
Presenting complaint		Chronic cough	Chest pain	change in voice quality chest pain
Smoker		Chronic smoker	Non smoker	Non smoker
Comorbidity		Hypertensive	Hypertensive, diabetic	Diabetic, coronary artery disease
ECOG		2	2	2
Primary site		Right lung-lower lobe, superior segment	Left lung-upper lobe	Right lung-upper lobe
Tumor size (max. Dimension in cm)		5	11	11
Grade		3	3	3
Ki 67 %		40	15	80
IHC	PAN CK		Positive	Positive
	CK 7	Positive		
	BCL2		Positive	Positive
	CD 99		Positive	Positive
	TLE	Positive (strong)	Positive (strong)	Positive (strong)
	WT1			Negative
	Vimentin		Positive	
	CD 99		Positive	
	Synaptophysin	Negative	Negative	
	Chromogranin	Negative	Negative	
	CD 56	Negative		
	TTF1	Negative		
	CD 45		Negative	
Final diagnosis		Biphasic synovial sarcoma	Biphasic synovial sarcoma	Biphasic synovial sarcoma
Treatment		Systemic chemotherapy	Surgery	Oral TKI (pazopanib)
Current status		Alive	Alive	Dead
T(x;18)				5% of tumor cell

Typically, immunohistochemistry is positive for cytokeratin (90%), EMA, Bcl2 (79-100%), TLE1 (80-90%), and vimentin and negative for S100, desmin, smooth muscle actin, and vascular tumor markers. Molecular/cytogenetics characteristics include t (X;18) (p11.2; q11): SYT-SSX1 fusion in 90% of cases, can be detected via RT-PCR.[12] The differential diagnosis of biphasic synovial sarcoma in the lung primarily includes adenocarcinoma which lack spindle cell areas and are typically TLE1 negative, biphasic mesothelioma which can show sarcomatoid features and cytokeratin, WT1 positivity but lacks the SSX translocation. Very rarely, nerve sheath tumors like malignant peripheral nerve sheath tumor and schwannoma can show similar histological features.[10] Radiological feature includes mostly as well-circumscribed pulmonary lesions of considerable size, without involvement of nodal stations. Extrathoracic primary sarcoma should also be excluded by thorough head to toe clinical examination, whole body CT and cranial MRI.[13] If the tumors do not bear an SS18-SSX fusion gene but have the morphological and clinical features of synovial sarcoma, it cannot be entirely excluded from the differential. In rare instances (<5% cases), synovial sarcomas do not carry the characteristic SS18-SSX transcripts, where these tumors may arise from alternative gene fusions (such as SS18L1/SSX1) or cryptic rearrangements.[15] There are no standard recommendations for the treatment of PSSL. The usual therapy of choice is surgical resection of the tumor with the aim to achieve negative resection margins. Chemotherapy or radiotherapy may be required in some

cases apart from surgery. The overall prognosis for primary pulmonary sarcomas is poor.[14]

CONCLUSION

Primary synovial sarcoma of lung is increasingly being diagnosed as a distinct clinical entity. In few recent series, PSSL is even reported as the most common subtype of primary lung sarcoma comprising 14.7% to 18% of all primary lung sarcomas, thus it merits to be in one of the differentials of primary lung masses not categorized as lung carcinomas. The diagnosis requires a detailed clinical, radiological, histopathological and immunohistochemistry investigations to exclude any other primary lung or metastatic sarcoma. Surgical excision with negative margins whenever feasible, with or without chemotherapy is the most appropriate treatment but with guarded prognosis.

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