Primary pulmonary synovial sarcoma: Diagnosis on squash smears

ABSTRACT
Synovial sarcomas are rare tumors accounting for approximately 5-10% of soft tissue sarcomas. They occur predominantly in the extremities, followed by head and neck. Primary pulmonary sarcomas are very rare and comprise only 0.5% of all primary lung malignancies. The diagnosis is established only after sarcomas like primary lung malignancies, and metastatic sarcomas have been excluded. For synovial sarcomas that arise at unusual locations, a definitive diagnosis is challenging and requires the use of ancillary diagnostic procedures such as immunohistochemistry (IHC) and molecular genetic techniques for confirmation of diagnosis. We report a case of 29-year-old male who had right lower lobe lung mass. He underwent right lower lobectomy. Intraoperative squash smears revealed spindle cell sarcoma. Subsequent histopathology and IHC confirmed the diagnosis as synovial sarcoma. We report this case on account of its rarity and to emphasize the utility of intraoperative squash smears in the diagnosis of such cases, which has been under-utilized in clinical practice.

Key words: Histopathology; primary pulmonary synovial sarcoma; squash smears

Introduction
Primary pulmonary sarcoma is rare and accounts for <0.5% of all malignant tumors of the lung.[1] Three most common sarcomas include the leiomyosarcoma, malignant fibrous histiocytoma and synovial sarcoma.[2] Synovial sarcoma is a mesenchymal spindle cell tumor, which is unrelated to synovium and can occur at any site.[3] It is classified into three major histological subtypes: Monophasic (epithelial and fibrous type), biphasic and poorly differentiated type.[3-5] As metastatic sarcomas are more common, proper evaluation of the patient should be done before giving a diagnosis of primary pulmonary sarcoma. Definitive diagnosis requires a detailed immunohistochemistry (IHC) and imaging investigations to exclude primary source. Most synovial sarcomas show immunoreactivity for cytokeratin (CK), epithelial membrane antigen (EMA), CD99, bcl-2, S-100 and other markers.[2,3] Synovial sarcoma has a consistent chromosomal translocation t(x:18)(p11;q11) and this translocation fuses SYT gene with either of the two homologous genes SXX1 OR SXX2.[6-7]

The present treatment includes resection followed by adjunctive chemotherapy or radiotherapy.[8] We report this case on account of its rarity and to emphasize the utility of intraoperative squash smears in the diagnosis of such cases, which has been under-utilized in clinical practice.

Case Report
A 29-year-old Kashmiri male presented with cough and blood tinged sputum of 1-month duration. Patient was a nonsmoker and had no significant history. General physical examination was unremarkable. Examination of the respiratory system revealed a dull percussion note over right lower chest. Hemogram, serum blood chemistry, electrocardiography and ultrasound abdomen were normal. Chest radiograph showed right lower lobe opacity. Pulmonary function test showed an obstructive pattern. Sputum for acid fast bacilli and malignant cells was negative. Contrast enhanced computed
tomography chest revealed well defined right lower lobe homogenous nonenhancing lesion of soft tissue, in relation to superior basal segments. It measured 6 cm × 5 cm. No pleural effusion or lymphadenopathy was observed. Trachea was central, and no intraluminal mass density was seen in trachea or bronchi. On bronchoscopy, no endobronchial lesion was seen.

Subsequently right posterolateral thoracotomy was done. Per operatively a solid firm well circumscribed yellowish white mass was seen in the right lower lobe of the lung. Some tissue was sent to the pathology department for a quick preoperative diagnosis. As the tissue was soft and easily crushable, imprint as well as squash smears was made.

Microscopy of these smears reveals high cellularity with spindle to epithelioid cells present in fragments as well as scattered singly. These cells had a unipolar or bipolar moderate cytoplasm. Nuclei were spindle to oval with granular chromatin and prominent nucleoli. Frequent mitotic figures along with small foci of calcification were seen [Figure 1b]. Based on these observations preliminary diagnosis of spindle cell sarcoma was given. Subsequently right lower lobectomy was done. Gross examination of the specimen showed right lobe of the lung with a 7.5 cm × 6.5 cm cavity from which the tumorous mass had been enucleated. The separate mass was firm globular greyish white, unencapsulated measuring 6 cm × 5 cm × 4 cm. On cut section, it was nodular greyish white with focal tiny cystic and hemorrhagic spots. No necrotic areas were seen.

Histopathological examination of the soft tissue mass revealed a highly cellular tumor comprising of spindle cells arranged in a fascicular and herring bone pattern [Figure 1a]. Focal hemangiopericytomatous areas were also seen. There were some alternating hypercellular and hypocellular areas as well. Some cells showed epithelioid differentiation. The clusters of epithelioid cells were outlined by reticulin stains. Some small cystic spaces filled with PAS positive eosinophilic material were seen. Cellular areas showed brisk mitosis and atypia. No necrosis was observed. On IHC the tumor cells were positive for bcl-2 [Figure 2], MIC-2 and EMA. CK-19 and CK highlighted the native epithelium. The tumor cells were negative for CD-34.

Thus, final diagnosis was that of synovial sarcoma lung, based on histopathological features and confirmed on IHC. Patient was evaluated for a primary lesion elsewhere. However, no lesion was found.

**Discussion**

Synovial sarcoma is a rare mesenchymal tumor accounting for 5-10% of all soft tissue sarcomas. On an average 85-95% occurs predominantly in the vicinity of large joints. However, synovial sarcoma has been described at every virtual anatomic site.[9] Primary pulmonary sarcomas are rare with only a few case reports in the literature. The diagnosis can be established only after clinical and imaging investigations to exclude primary sources.[10]

It is most prevalent in adolescents and young adults with a slight male predilection.[9] 2/3 of reported cases were centrally located and associated with cough, dyspnea, fever and hemoptysis. Peripheral tumors are less common and usually asymptomatic but may infiltrate into adjacent tissues and give rise to distant metastasis. Bronchoscopy is diagnostic in 40-60% of cases.[1,4] Radiological investigations are helpful to characterize the tumor and to rule out any primary source.
Multiple spotty radioopacities caused by focal calcifications are seen on radiography.\textsuperscript{[9]}

Grossly tumor maybe completely or partially encapsulated, firm yellowish to greyish white. Cystic formation is maybe prominent.\textsuperscript{[8,9]} Microscopically tumor can be broadly classified into four types biphasic, monophasic fibrous, monophasic epithelial and poorly differentiated.\textsuperscript{[1,2,8,9]} Biphasic lesions are composed of sharply segregated epithelial and sarcomatous components.\textsuperscript{[8]} Monophasic type is composed of only one of the two components. It is usually of fibrous type composed of spindle cells arranged in fascicles and hemangiopericytomatosus like areas.\textsuperscript{[10]} A poorly differentiated form is being increasingly recognized by increased degree of cellularity, necrosis, atypia and mitotic activity. Cells may be spindle, small or large and clear.\textsuperscript{[8,9]}

The case reported here was a fibrous monophasic type with densely packed spindle and epitheloid cells in fascicles with brisk mitosis. The case was initially diagnosed on intra-operative crush smear. We could not come across any literature describing crush smears in synovial sarcomas. However, cytological features have been described on fine needle aspiration cytology.\textsuperscript{[11,12]} In monophasic synovial sarcoma, fine-needle aspiration biopsy consists of a monotonous population of short spindle cells arranged in fragments and single cells containing scant granular cytoplasm and coarse chromatin with comma shaped nuclei. Biphasic synovial sarcoma contains small acinar like structures composed of round cells with prominent nucleoli in addition to spindle cells. Features of monophasic synovial sarcoma were noted on crush smears in our case, and a diagnosis of spindle cell sarcoma with features favoring synovial sarcoma were given.

Differential diagnosis of monophasic synovial sarcoma includes fibrosarcoma, hemagiopericytoma, leiomyosarcoma, spindle cell variant of squamous cell carcinoma. IHC is mandatory for confirmation. Synovial sarcomas are positive for vimentin CK, EMA, CD-99, bcl-2, and negative for CD34 and S-100. All morphological types are characterized by specific chromosomal alteration t(x;18)(p11;q11).\textsuperscript{[4,7,9]}

Owing to its rarity and paucity of data regarding its natural history, there are no guidelines for optimal treatment. Therefore, current treatment includes complete surgical resection (lobectomy or pneumonectomy), followed by adjuvant chemotherapy and radiotherapy.\textsuperscript{[2-6]} Our patient underwent lobectomy with adjuvant chemotherapy. One year after surgery he is currently on follow up and remains asymptomatic.

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