Case Report

Primary monophasic synovial sarcoma lung with brain metastasis diagnosed on transthoracic FNAC: Report of a case with literature review

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ABSTRACT

Synovial sarcoma is highly malignant tumor of soft tissues, occurring chiefly in the extremities and limb girdle with a propensity for local recurrence and sometimes metastases to the lungs. Primary synovial sarcoma arising in the lungs is rare and brain metastasis as presentation is further uncommon. We report a case of primary monophasic synovial sarcoma lung presenting with brain metastasis in a 35-year-old male patient. The diagnosis was made on percutaneous transthoracic needle aspiration from left-sided pulmonary mass and later confirmed by immunohistochemistry. The utility of preoperative diagnosis by percutaneous aspiration cytology is also stressed.

KEY WORDS: Brain metastasis, fine needle aspiration cytology, monophasic synovial sarcoma lung

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INTRODUCTION

Synovial sarcomas are uncommon tumors that occur predominantly in the extremities, where they tend to arise in the vicinity of large joints, especially the knee region.[1] Primary synovial sarcoma arising in the lung is very rare compared to metastatic sarcoma and sarcomatoid carcinoma, accounting for less than 0.5%.[2] In most reports on primary synovial sarcoma lung, the diagnosis was made postoperatively following resection of the tumor mass.[3,4] There are only few cytological studies available on synovial sarcoma of soft tissues.[5] Fine needle aspiration (FNA) diagnosis of synovial sarcoma lung is further rare to find in literature[6,7] and, to the best of authors' knowledge, not reported from India. Brain metastasis in monophasic synovial sarcoma lung is a very rare and late manifestation. Present report describes a case of primary monophasic synovial sarcoma presenting with brain metastasis and diagnosed on transthoracic FNA. The importance of preoperative diagnosis by transthoracic FNA in such tumors is stressed.

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CASE REPORT

A 35-year-old male patient presented to us for left-sided chest pain for 1 month. There was no associated cough or fever. His past history revealed surgical removal of a left parieto-occipital brain mass with histological diagnosis of grade II astrocytoma at a private hospital, 3 months back. At that time there were no respiratory symptoms.

On examination, patient was healthy male with no abnormality on physical examination. Chest examination revealed a dull percussion note and decreased breath sounds at left upper lung fields. X-ray chest revealed a mass lesion at left upper zone with shift of mediastinum to the right side [Figure 1]. Routine investigations of blood and urine and other biochemical tests were normal. Computed tomography (CT) scan chest revealed a lobulated, soft tissue mass at left upper lobe, measuring $12.7 \times 11.3 \times 17$ cm and extending toward the mediastinum. The density of mass was heterogeneous with clear, dark, and gray areas representing necrosis and hemorrhage in the tumor [Figure 2]. The radiological features were highly suggestive of a malignant neoplastic lesion.

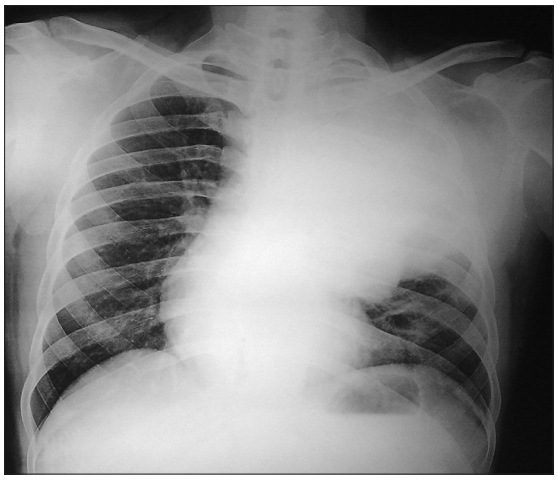

Figure 1: X-ray chest PA view showing left upper lobe mass lesion

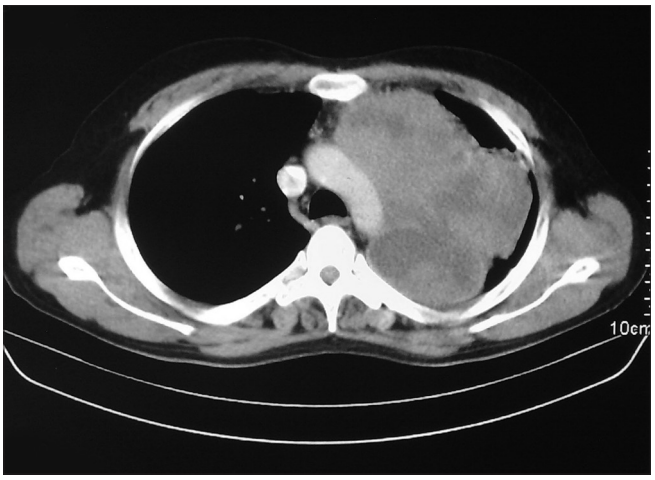

Figure 2: CT scan chest showing a large, soft tissue density mass at left upper lobe lung with central necrotic areas

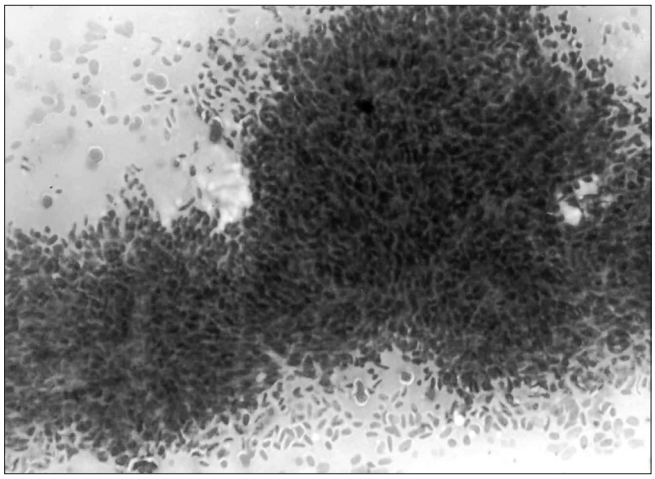

Figure 3: Photomicrograph of fine needle aspirate from lung lesion showing pleomorphic bipolar spindle cells with oval to spindled nuclei (H and E, ×200)

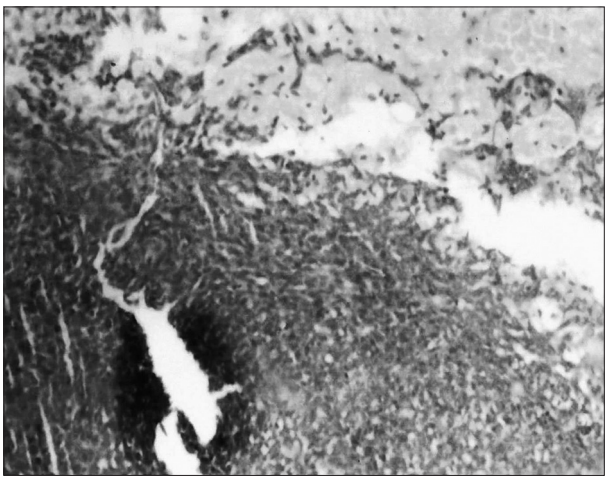

Figure 4: Photomicrograph of histological sections of brain mass tissue showing typical features of metastatic monophasic synovial carcinoma (H and E, ×200)

A percutaneous transthoracic FNA was done from left suprascapular region. The smears were highly cellular with irregular branching tissue fragments containing moderate pleomorphic, bipolar spindle cells showing small to medium-sized ovoid to spindled nuclei having evenly distributed bland chromatin, inconspicuous nucleoli, and occasional mitotic figure. The cytoplasm was scanty and delicate. Some bare nuclei were also seen [Figure 3]. The cytological diagnosis of smears was reported as malignant spindle cell tumor with strong possibility of monophasic synovial sarcoma or fibrosarcoma lung. The tissue blocks of brain mass reported as astrocytoma from the private hospital were asked for and reviewed by the authors. Review of the histopathologic sections of brain tissue mass revealed histological appearance suggestive of monophasic synovial sarcoma [Figure 4]. To further confirm the diagnosis, tissue blocks and FNA smears were subjected to immune histochemistry (IHC) that showed positive reaction for cytokeratin, vimentin, bcl-2 protein, calponin, and epithelial membrane antigen (EMA). The S-100 protein, glial fibrillary acidic protein (GFAP), synaptophysin, and chromogranin-A markers were negative on IHC. A thorough search was done to rule out any primary site. A final diagnosis of primary monophasic synovial sarcoma lung with brain metastasis was made as there was no evidence of any tumor in the vicinity of bones, joints, or soft tissue. Patient was referred to radiation oncology department where he received concomitant chemotherapy with temozolamide and radiotherapy to the skull. Patient survived 6 months after initial diagnosis with pleural effusion, ascites, and anasarca as a terminal event.

DISCUSSION

Synovial sarcoma is a well-defined clinical and morphological entity that was originally described by Simon in 1865 and was so named in 1934 by Sabrazes[8] because of its resemblance to developing synovial tissue under light microscope. The term "synovial sarcoma" is however a misnomer as the tumor cells do not share the

same immune histochemical and ultrastructural features of the normal synovium. The cellular origin of this tumor is probably considered as neural crest derived cells.[9]

Synovial sarcoma is a highly malignant tumor that occurs mainly in adolescents and young adults between 15 and 30 years of age, and is usually seen in the extremities in the vicinity of joints, most commonly the knee and lower thigh region. The tumor is intimately related to tendon, tendon sheath, and bursal structures, usually just beyond the confines of the joint capsule. This tumor accounts for 5–10% of the soft tissue sarcomas.[1] Primary synovial sarcoma arising in the lung is very rarely seen in clinical practice.[4,9] Review of the literature yields few reports of such tumors, with only isolated cases or small series that often include different types of tumors of this lineage.[7,10-14] Only 60 cases of synovial sarcoma at pleuropulmonary region were reported in English literature till 2005.[13] The largest reported series of primary pulmonary synovial sarcoma comprised 25 cases, where 7 had chest pain, 9 had hemoptysis, shortness of breath, cough, or fever, and 9 were asymptomatic.[14] In an analysis of 104 cases of synovial sarcoma at Royal Marsden Hospital, London, between 1978 and 2003, only 10 were having primary location at the chest trunk.[15] Kottu *et al*.[5] in their series of 12 cases of synovial sarcoma over a period of more than 10 years could not found a single primary tumor at the lungs. Ewing *et al*.[6] find only two primary cases at the lungs among the 17 synovial sarcomas detected between 1993 and 2002. There are only few published Indian reports on synovial sarcoma arising at lung, pleura, and pleuropulmonary region, where pleural effusion was seen at presentation in most of them.[4,16-18] There is also one report describing primary monophasic synovial sarcoma arising in the mediastinum along with mediastinal lymphadenopathy.[19] Application of molecular techniques in the diagnosis has recently increased the number of published reports of synovial sarcomas at unusual sites such as pleural, prostate, peritoneum, and lungs.[4]

Pulmonary sarcomas are rare accounting for less than 0.5% of lung cancers. Most of these tumors are secondary to the primary site elsewhere in the body and their diagnosis is established only after clinical and imaging investigations to exclude the alternative primary site.[20] Primary pulmonary synovial sarcoma represents a small subset of pulmonary sarcomas that shares similar histomorphologic and chromosomal translocations as their soft tissue counterparts.[2,14] Diagnosis of primary pulmonary synovial sarcoma is often a diagnostic challenge as the tumor is often misdiagnosed as primary pulmonary spindle cell sarcoma/carcinoma or metastatic sarcoma.[14] An accurate specific diagnosis requires further workup including IHC, polymerase chain reaction, and fluorescent *in situ* hybridization (FISH). The utility of molecular techniques to demonstrate the specific chromosomal translocation, i.e. t(x;18)(p11.2;q11.2), has greatly increased the sensitivity and specificity of diagnosing synovial sarcoma, especially at unusual locations like the lung.[21] This translocation consists of fusion of the *SYT* gene from chromosome number 18 to the genes *SSX1* and *SSX2* in the region Xp11, thus forming an *SYT–SSX1* or *SYT–SSX2* fusion transcript that alters the cellular transcription. The biphasic type tumor usually expresses the *SYT–SSX1* gene fusion, while the monophasic type may express both.[22] Molecular studies are useful when primary location of synovial sarcoma is unusual. Molecular testing may not be necessary despite having high sensitivity, when the diagnosis is certain or probable based on combined clinical, histopathologic, and immunohistochemical findings.[23] Unfortunately, this genetic molecular workup in our case could not be performed due to financial and infrastructural constraint.

There are four subtypes of synovial sarcoma – biphasic tumors, monophasic tumors, monophasic epithelial tumors, and poorly differentiated (round cell) tumors. The biphasic type is easily diagnosed based on the presence of both epithelial and spindle cell component where sharply segregated epithelial cells form gland-like areas.[6,9] Primary pulmonary monophasic synovial sarcoma is mainly of monophasic subtype which is difficult to diagnose due to uniform spindle cell pattern, and therefore needs to be differentiated from other tumors, i.e. sarcomatoid carcinoma, sarcomatoid variant of mesothelioma, malignant peripheral nerve sheath tumor, fibrosarcoma, leiomyosarcoma, Ewing's sarcoma, hemangiopericytoma, spindle cell thymoma, desmoplastic small round cell tumor, solitary fibrous tumor, as well as metastatic sarcomas.[2,21,24]

The cytological feature of monophasic variant of synovial sarcoma includes tissue fragments and single cells containing scanty granular cytoplasm, medium-sized nuclei, and coarse chromatin. A monotonous spindle pattern with comma-shaped or oval and spindled or round nuclei is commonly seen.[6] Densely packed tri-dimensional groups and singly scattered round to oval cells with cellular monomorphism and vascular channels within the cell groups are other remarkable findings on aspiration cytology. Bcl-2, cytokeratin, EMA, and CD99 positivity are seen on IHC staining. The bcl-2 protein expression is seen in about 79% of synovial sarcoma and is useful to differentiate other spindle cell sarcomas including leiomyosarcoma, malignant peripheral nerve sheath tumor, and fibrosarcoma, where it is negative.[25] The IHC features of primary pulmonary synovial sarcoma resemble those of soft tissue synovial sarcomas. Although the cytomorphologic features of synovial sarcoma are characteristic enough to permit its recognition, clinical correlation is also necessary for accurate diagnosis.[5] In our case, the diagnosis of primary synovial sarcoma lung was based on absence of the tumor at any other known primary site. Brain metastasis is very rare in soft tissue synovial sarcomas,[26] and was reported in only three cases previously.[27] Only a single report mentions brain metastasis as a terminal event in primary pulmonary synovial sarcoma.[28] To the best of our knowledge, this

has not been reported previously in primary pulmonary synovial sarcoma at presentation, as observed in our case.

Most of the reported cases of primary pulmonary synovial sarcoma are centrally located and present with symptoms of post-obstructive pneumonia (cough, dyspnea, fever) and hemoptysis. Bronchoscopy may reveal endobronchial polypoidal growth in some cases.[4] Peripheral tumors are less common and initially asymptomatic, but may infiltrate adjacent tissues, i.e. pleura, thoracic wall, and mediastinum, or give rise to distant metastases.[12]

Surgery is the mainstay of therapy and free surgical margins are critical in prevention of local recurrence. However, these tumors are highly aggressive with late presentation, large size, and difficulty in achieving free surgical margins. The adjuvant chemotherapy may increase disease-free survival. The overall prognosis is poor in primary pulmonary synovial sarcoma.[29] The prognosis of pulmonary synovial sarcoma does not differ from sarcomas of other location. The overall 5-year survival rate is 50%, and poor prognostic risk factors include an age of more than 20 years, female sex, incomplete resection, tumor size greater than 5 cm, extensive tumor necrosis, high number of mitoses (>10 per 10 high power fields), neurovascular invasion, and recently, *SYT–SSX1* variant.[30]

CONCLUSION

In conclusion, primary pulmonary synovial sarcoma is a rare and highly aggressive tumor in young adults that may present with brain metastasis. Transthoracic FNA of pulmonary lesions provides early preoperative diagnosis with ample time to decide about most appropriate management in individual cases.

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