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Case Report

Primary Pulmonary Poorly Differentiated Synovial Sarcoma: Transducer-Like Enhancer of Split 1 Immunohistochemistry as A Valuable Diagnostic Aid

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ABSTRACT

Poorly differentiated primary pulmonary synovial sarcomas are rare and challenging for a surgical pathologist to diagnose. Although the demonstration of the tumor specific translocation, t (x; 18)(p11.2;q11.2) or the resultant fusion gene (SYT-SSX) is the gold standard for diagnosis, this test is not always accessible. We report the use of immunohistochemistry, including transducer-like enhancer of split-1 in the diagnosis of one such tumor in a young individual.

Key words: Lung, synovial sarcoma, transducer-like enhancer of split-1

INTRODUCTION

Although synovial sarcomas are better known to occur in the soft-tissues, these are now being increasingly recognized in the lungs as well. Primary pulmonary synovial sarcomas; however, are very rare neoplasms in the lung and pleura and have been reported to comprise less than 0.5% of pulmonary neoplasms.[1,2] Histologically these tend to mimic other tumors at this site. The poorly differentiated variant is even more rare with only isolated case reports or small series reported in literature.[3] These are difficult to diagnose solely on the basis of the histology. In such cases, molecular techniques and the recently developed transducer-like enhancer of split 1 (TLE-1) antibody for use with immunohistochemistry (IHC) have both proved useful in arriving at the correct diagnosis.[4,5] We report one such case.

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CASE REPORT

A 26-year old male presented with an increasing breathlessness over the previous 15 days accompanied by an episode of hemoptysis. On examination, he was moderately built, had low grade fever and absent breath sounds in the right lower chest. On investigation, hemoglobin and the blood counts were in normal range. Chest radiograph revealed features suggestive of a mass lesion with well-defined margins within the right lower lobe. This was followed by a high resolution computerized tomogram, which further confirmed the presence of the mass and showed it to be pulmonary and not pleural in nature. A lobectomy resection was carried out as he was determined to have no other primary site of tumor.

Gross examination revealed a heavy boggy right lower lobe with a congested pleural surface. On sectioning, a well-defined fleshy mass (13 × 12 × 5 cm) with areas of necrosis and hemorrhage involving almost the entire lower lobe was present. The mass seemed to involve the medial aspect of the lobe including the hilar area with some residual remnant of parent lung in the periphery [Figure 1].

Microscopy revealed a cellular unencapsulated neoplasm with tumor cells in vague lobulated

sheets with pushing margins [Figure 2a]. The compact spindle cells most characteristic of synovial sarcoma were largely absent. In most areas, the cells appeared small and round with round to ovoid nuclei and a small amount of eosinophilic cytoplasm [Figure 2d]. In only a few areas was their some degree of spindling with cells growing in fascicular arrays [Figure 2c]. In places, the cells were in nests separated by fine branching staghorn or hemangiopericytomatous type blood vessels [Figure 2b]. Mitosis was brisk (10-14 mitosis/10 HPF). Large areas of geographic necrosis were also present. The differential diagnosis considered based on an initial histology included a neuroendocrine tumor, Ewing's sarcoma, peripheral neuroectodermal tumor (PNET), solitary fibrous tumor, and poorly differentiated synovial sarcoma.

Immunoperoxidase studies on paraffin embedded tissue revealed the neoplastic cells to be focally reactive with antibodies to pancytokeratin along with reactivity for epithelial membrane antibody in approximately 25% of the cells. They failed to react with antibodies to thyroid transcription factor 1 (TTF-1), synaptophysin, smooth muscle actin, S_{100} protein, CAM5.2, CD99, chromogranin, CD45 and CD34. With the above IHC findings, a poorly differentiated synovial sarcoma was considered most likely and a TLE-1 stain was carried out, which revealed diffuse nuclear reactivity of the tumor cells [Figure 3]. This stain provided the definitive diagnosis of a synovial sarcoma. The patient was subjected to chemotherapy; however, over the next 4 months, he developed extensive metastatic disease and eventually succumbed to his illness.

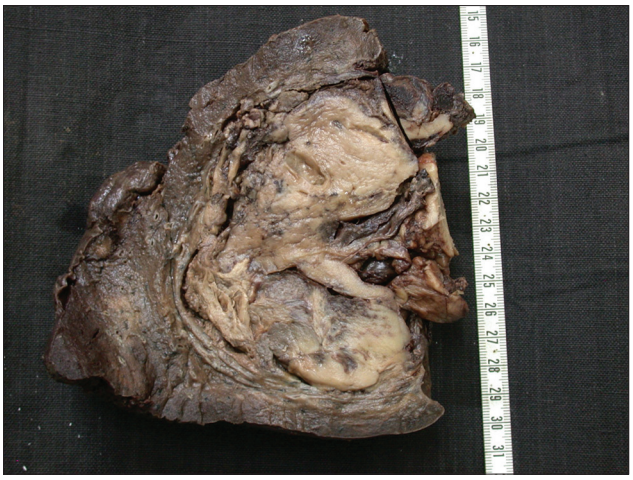

Figure 1: Cut section of the excised tumor reveals a fleshy mass with areas of hemorrhage and necrosis

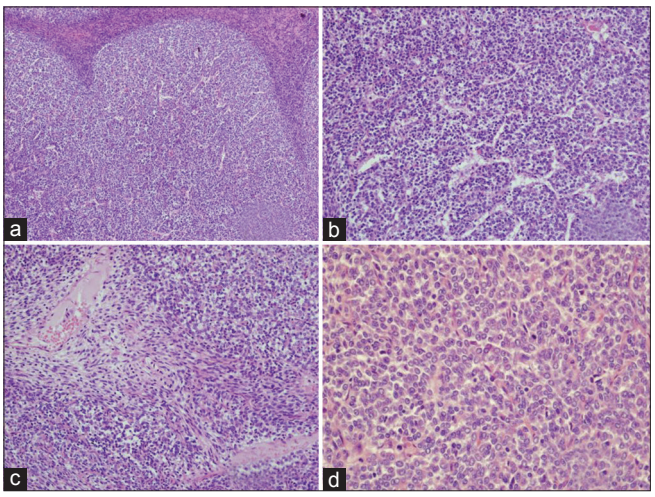

Figure 2: Photomicrographs of the neoplasm showing (a) fairly monomorphic tumor cells in vague lobulated sheets with pushing margins (H and E, ×100), (b) fine branching blood vessels separating the tumor nests (H and E, ×200), (c) areas of spindling and fascicular array (H and E, ×200), (d) monomorphic poorly differentiated round cells in sheets with brisk mitosis (H and E, ×400)

DISCUSSION

A primary pulmonary synovial sarcoma, even if exhibiting its classic biphasic histology, poses diagnostic problems in the lungs because of the possibility of entrapped pulmonary epithelium being misconstrued as epithelial elements of the tumor.[6] Poorly differentiated synovial sarcomas are known to further pose a challenge for definitive diagnosis based on microscopy alone. These tumors mimic round cell tumors on histomorphology. Hence, it becomes imperative to differentiate between the various mimics in this group. Molecular techniques comprising of reverse transcription polymerase chain reaction, *in situ* hybridization for the SYT-SSX fusion gene and karyotyping for t (x; 18) translocation remain the gold standard for diagnosis, but these are expensive, not easily available at most centers and in some laboratories require frozen sections.[7] Lately, there is evidence that TLE-1 immunoreactivity can help resolve the dilemma. This provides a new more specific marker for diagnosis of this rare highly aggressive neoplasm.[8] TLE-1 is a member of the groucho/TLE gene family involved in beta-catenin signaling pathway and encodes a corepressor implicated in neuronal and epithelial differentiation.[9] It has been found to be significantly expressed in synovial sarcomas with a sensitivity of 82% and specificity of 92%.[10] TLE-1 in the same study has also been found to be expressed in 8% of solitary fibrous tumors and in 15% of malignant peripheral nerve sheath tumors. Ewing's sarcoma and primitive neuroectodermal tumors have not been reported to react with TLE-1.

We encountered a primary round cell tumor in the lung that did not resemble a lymphoma on histomorphology. IHC for leukocyte common antigen ascertained the same. The

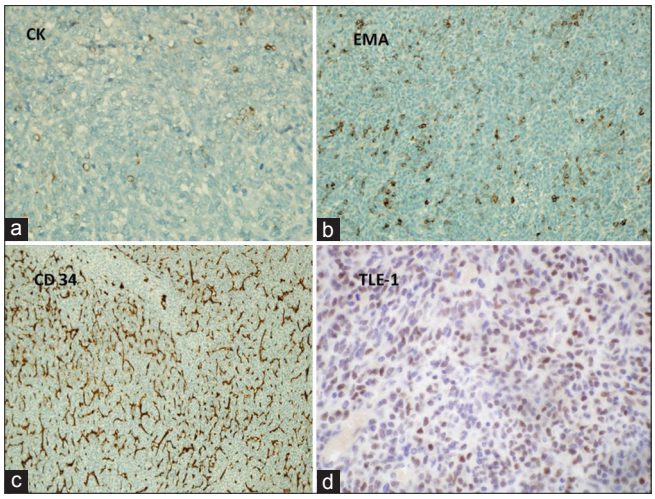

Figure 3: Immunohistochemical profile shows (a) focal positivity for pancytokeratin (b) more reactivity for epithelial membrane antibody (c) CD34 highlights the hemangiopericytomatous pattern of the blood vessels with the negative reaction of the tumor cells. (d) Tumor cells show diffuse nuclear positivity for transducer-like enhancer of split - 1 (DAB, ×200)

differential diagnosis of a Ewing's sarcoma or a PNET, neuroendocrine tumor, and a solitary fibrous tumor were also considered. Immunoperoxidase stains helped negate most of the histologic mimics. TLE-1 was found to be reactive and yielded the final answer. The patient; however, succumbed to the rapidly progressive metastatic disease, he developed thereafter.

This case highlights the utility of TLE-1 in the diagnosis of poorly differentiated synovial sarcomas. We emphasize it as an essential tool in the immunohistochemical laboratory armamentarium especially in centers where molecular techniques are not easily available. These highly aggressive neoplasms when encountered at relatively inaccessible sites like the lungs should be detected at an early stage. A biopsy and further usage of relevant IHC panel inclusive of TLE-1 would be an endeavor to aid diagnosis and perhaps promote further research for yet elusive definitive targeted therapy for these neoplasms.

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