Case Series

Immunocytochemistry as an Ancillary Technique in the Cytologic Diagnosis of Synovial Sarcoma: Lock With Cell Block

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Abstract

Introduction: Synovial sarcomas are rare tumors accounting for approximately 5-10% of soft tissue sarcomas. For synovial sarcomas that arise at unusual locations, cytologic diagnosis is challenging despite characteristic cytomorphologic features.

Material and Methods: The use of ancillary diagnostic procedures such as immunocytochemistry (ICC) using cell blocks and molecular genetic techniques using aspirated material help in the confirmation of diagnosis. During the period of 18 months from Nov 16 to Feb 18 we reported three cases of SS that occurred in rare locations with the help of ICC on cell blocks in 2 cases and IHC in the third case.

Results: Cells arranged in bundles, perivascular arrangement, tight clusters, acini & singly. Cells are elongated, oval to spindle, presence of uni or bipolar cytoplasmic processes with mildly pleomorphic , hyperchromatic nuclei & fine granular chromatin. TLE1 was positive in all 3 cases.

Conclusion: TLE1 marker is an extremely useful marker that distinguishes SS from other cytological & histological mimics.

The objective of the present study was to call attention and also highlight the variable cytology of synovial sarcoma arising at rare locations. Furthermore, we discuss use of adjunctive ICC on cell blocks that help to lock the diagnosis.

Keywords:

Cell block, Immunocytochemistry, TLE 1, Synovial sarcoma cytology

Introduction

Fine needle aspiration cytology is the first line diagnostic tool in the evaluation of all palpable tumors. It has a fairly well established role, not only in the diagnosis but also typing of soft tissue tumors when ancillary testing is done on FNA material. FNAC allows retrieval of minor tissue fragments for cell block preparation which helps to further refine cytological diagnosis.[ ] Synovial sarcoma (SS) is one of the greatest mimic in the gamut of malignant mesenchymal tumors and is often overlooked in the initial differentials when it is encountered at rare sites. The cytomorphologic diagnosis of SS is a constant challenge because of its subtypes that have overlapping cytological features with other soft tissue tumors.[ ] This difficulty is compounded by the fact that this tumor is known to arise in unusual locations like the head and neck region.[,] We intend to report and highlight the

common cytologic features as seen in the FNAC smears of 3 cases of SS located at uncommon sites. We will also emphasize the importance of ancillary technique of Immunocytochemistry(ICC) using cell blocks, that helped in reaching the final diagnosis in 2 of 3 cases before surgical tissue was made available.

Material and methods

During the period of 18 months from November 16 to February 18 we diagnosed three cases of SS. Cell blocks were prepared and ICC was done in 2 and IHC was performed on tissue of excised specimen in the third case.

Case 1

A 35-year-old female patient presented with gradually progressive swelling in right axilla for 1 year. Clinical examination revealed a globular, non-mobile, deep seated firm lump of 5×5 cm which was not attached to the overlying skin. Breast examination did not reveal any lump. FNA smears were highly cellular with clusters and dispersed cell population. Cell clusters were showing whorls and micro acini formation. Cells were oval in shape and had uni and bipolar cytoplasmic processes giving them a spindly configuration. Nuclei were round to oval to spindle with hyperchromasia. Chromatin was fine and stippled with inconspicuous nucleoli (Fig-1 & 2). Mitotic figures were frequent. Background showed patchy granular necrotic debris and abundant stripped nuclei. A possibility of small round cell tumor was suggested. Microscopic examination of H and E stained sections from cell block revealed slit like spaces which resembled hemangiopericytoma like arrangement (Fig-3). Immunocytochemistry was performed on cell block. The tumor cells showed strong and diffuse immunopositivity for TLE1, vimentin and CD99 and focal immunoreactivity for CK7 and EMA. The tumor cells were immunonegative for pancytokeratin, CK19 and calretinin. This confirmed the diagnosis of poorly differentiated synovial sarcoma. Follow up was lost as the patient succumbed within a month.

Case 2

A 66-year-old male presented with swelling in neck & difficulty in swallowing since 15 days. CT chest revealed a large, well defined, lobulated, hypodense mildly enhancing lesion in right upper paratracheal region and extending in retro-tracheal region and compressing the esophagus and displacing the right lower (pole of) thyroid. It measured 5.4 x 4.5 x 5.6 cm. Scintigraphy findings were more in favor of extra-thyroidal mass lesion. FNAC smears were highly cellular and showed cells arranged in sheets, clusters and scattered singly. Most clusters showed cells arranged around delicate, branching capillaries. Cells were monotonous, medium size mostly round with few spindle cells, indistinct cellular borders, and uniform round to ovoid nuclei. Nuclear chromatin was finely granular with small, inconspicuous nucleoli (Fig- 4). The cytoplasm was scanty, pale, and fragile. Many naked nuclei were seen in background. Possibility of neuroendocrine neoplasm was suggested & ICC was advised. Cell block showed round to oval cells with scanty eosinophilic cytoplasm & round to spindle nuclei with inconspicuous nucleoli. ICC on cell block confirmed SS with TLE1 and vimentin positivity. The general condition of the patient was low and had undergone tracheostomy on admission. The patient succumbed within 3 days of admission.

Case 3

A 64 years male presented with a recurrent mass in the right parotid region. The primary tumor was 5.4 x 4 cms. Ultrasonography, FNAC and histopathology of the primary tumor (done 5 months back) were reported as myoepithelioma. Cytology smears from the recurrent mass were highly cellular and showed a bimodal cell population comprising of spindle cells & round to oval cells. Spindle cells were arranged in bundles at places. Round cells were arranged in sheets and clusters with acinar arrangement at places. Dispersed single cells showed bipolar cytoplasmic processes & finely granular bland chromatin. Cells were seen attached

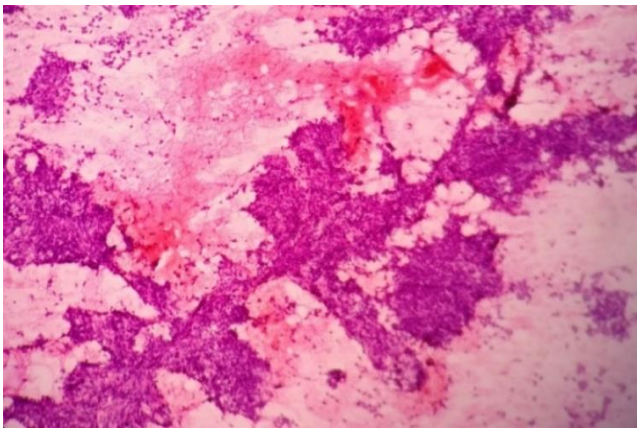

Figure 1 FNAC from axillary swelling (Case-I) Highly cellular smear showing tissue fragments, cell clusters and disperse cell population, Most clusters are seen around delicate, branching capillaries. H and E, 5X.

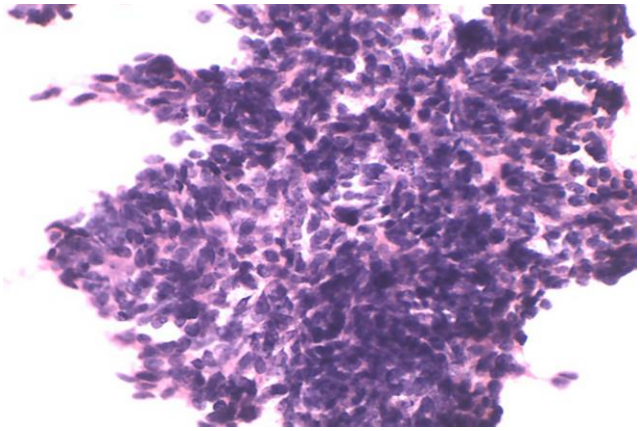

Figure 2 FNAC from axillary swelling (Case-I) shows tissue fragment with monotonous, medium size, mostly oval to spindly cells (upper left corner) having indistinct cellular borders. Nuclei are uniform round to oval & hyperchromatic. H and E, 40X.

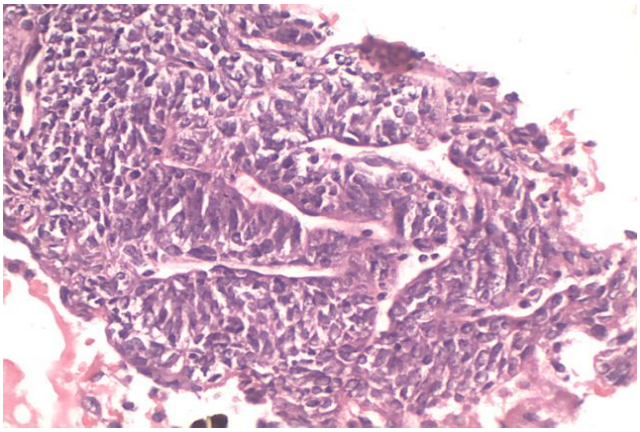

Figure 3 Cell block preparation from axillary swelling (Case-I) showing peritheliomatous arrangement of poorly differentiated cells. H and E, 40X.

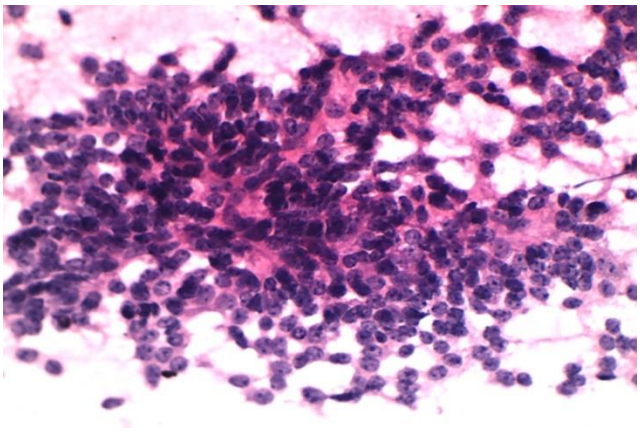

Figure 4 FNAC from parapharygeal mass (case-II) cells are arranged in microacinar pattern, individual cells are mostly round having finely granular stippled chromatin. H and E, 40X.

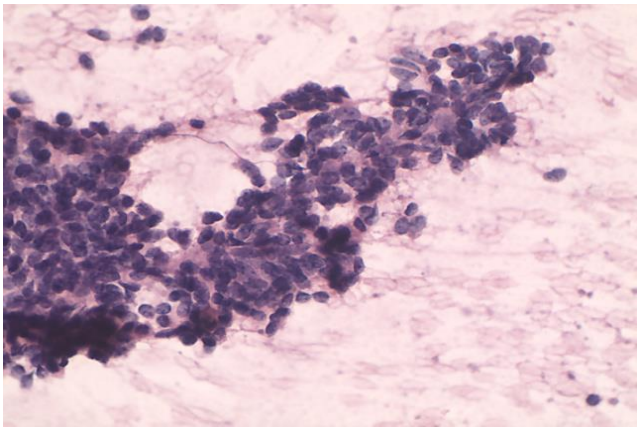

Figure 5 FNAC from parotid mass (Case-III) smears showing medium size cells arrange in acinar pattern, cells are mostly oval spindle with mild nuclear pleomorphism. H and E 40X.

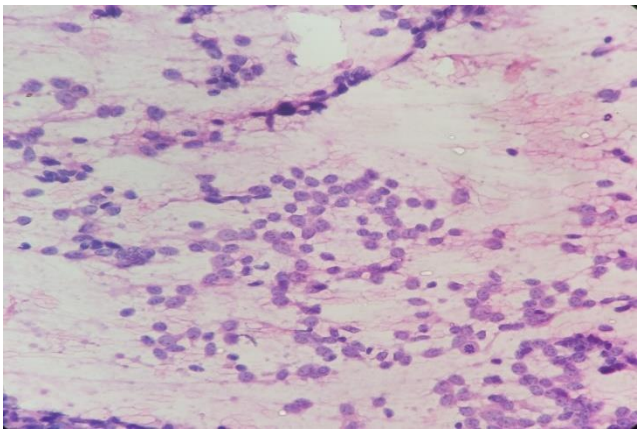

Figure 6 FNAC from parotid mass (Case-III) smear showing disperse population of monotonous cells having oval nuclei, bland chromatin & bipolar cytoplasmic processes. Mitoses seen. H and E, 40X.

to branching capillaries at places. Cytologic findings favored a low grade biphasic tumor with possibility of synovial sarcoma (Fig-5 & 6). Review of histopathology sections of excised tumor mass was also suggestive of a biphasic synovial sarcoma. IHC of these tissue sections showed positivity for TLE1/EMA/CK/CK19/CK14/with focal immune-reactivity for P63 in both the epithelial & stromal elements.

For all the three patients the IHC was performed from an outside institute and we had obtained only IHC reports. We were not able to procure the IHC slides of these patients.

Table 1 Showing comparison of clinico-cytological finding in all 3cases.

	Case 1	**Case 2**	**Case 3**
Age/ Gender	35yrs/Female	66yrs/Male	64yrs/Male
Site	Axillary swelling	Parapharyngeal mass	Parotid gland
Radiology	Soft tissue neoplasm	Laryngeal malignancy	Parotid adenoma
Cell arrangement	Perivascular arrangement, Tight clusters, acini, single cells	 Same Papillary at places	Spindle cells in bundles, sheets, clusters, acini Biphasic pattern
Individual cell	Elongated, oval to spindle, presence of uni or bipolar cytoplasmic process	Mostly round to oval and few spindle cells	Round to oval and spindle cells
Nuclear features	Mildly pleomorphic, hyperchromatic, fine granular chromatin with inconspicuous nucleoli	Mostly monotonous, Fine granular chromatin with +/- inconspicuous nucleoli	Mildly pleomorphic, Bland chromatin.
Background	Hemorrhagic, focal necrosis, stripped nuclei	Stripped nuclei+ No necrosis	Stripped nuclei + No necrosis
Differentials	Ewings / PNET	Epithelial malignancy Neuroendocrine	Possibility of SS
ICC using cell block	TLE1/ vimentin/EMA/CD99	TLE1/ Vimentin	TLE1/EMA/CK/CK19/CK14/P63. (IHC – tissue sections)
Final Diagnosis	PDSS	PDSS	Biphasic SS

Discussion

FNAC plays a major role in distinguishing benign soft tissue tumors from malignant ones and a diagnostic accuracy of 95% has been reported for soft tissue sarcomas.[ ] When additional dedicated passes of fine needle aspirations are made to acquire material for ancillary testing like cell blocks, immunocytochemistry, fluorescence in situ hybridization, cytogenetics and molecular studies, a complete pre-operative diagnosis of SS can be achieved, obviating the need for open biopsy for diagnostic purpose.[2,]

SS is a clinically and morphologically well-defined entity that, despite its name, is extremely uncommon in joint cavities. Literature shows that it can occur in areas with no apparent relation to synovial structures. The most common extra skeletal sites of primary synovial sarcoma are the trunk, retroperitoneal/abdominal region, head and neck.[] Other various rare sites are thymus, kidney, bone, skin, nervous system, liver, pleura, ovary, lung and mediastinum.. Synovial sarcoma in the head and neck region was first reported by Jernstorm in 1954.[ ] In this short case series we came across two elderly patients with parapharyngeal and parotid swellings. Both these are rare sites for SS.[]. Axillary involvement by this sarcoma is also very rare. [ ] One case of ours was found in the axilla of a young female.

The cytomorphologic features of SS are characteristic enough to permit its recognition provided this entity is kept in mind in the

initial differentials when aspiration material is acquired from unusual sites. The cytologic findings in our series of cases are in concert with previous studies as we also found highly cellular smears with clusters and dispersed cells [7,]

A network of branching capillaries along with perivascular arrangement of round to oval cells (Fig-1 & 2) was a common denominator. [ ] Cells arranged in vague glandular or rosette like pattern was another common feature (Table No. 1).[2] These features along with mildly pleomorphic spindle cell component make the cytologic diagnosis of SS relatively easy for biphasic variant. However the subtype of poorly differentiated synovial sarcoma is diagnostically difficult to define.[ ] In these the cells have a primitive mesenchymal look with scant cytoplasm and are not out and out epithelial or polygonal but are small to medium sized round to oval cells.[21, 5] Stroma or mucinous background was not seen in our smears which was an observation in the case series of others.[2, 6] The finely dispersed chromatin, in 2 of our cases, gave an appearance of Ewing's sarcoma or PNET (Fig-4). Locating mast cells in cytology smears has been given importance. We noted them on careful examination only in one case when we revisited the smears. Mast cells were observed retrospectively in the case report of metastasis of SS in the inguinal lymph node by Bose A et al.[ ]

ICC on cell blocks, prepared from repeat FNA from case 1 and 2, defined both these lesions as poorly differentiated SS. TLE1 was positive in all 3 cases. This marker is an extremely useful marker, that distinguishes SS from other cytological & histological mimics specially when CK is negative.[ ] In our case 1, EMA positivity was focal and cytokeratin was negative in neoplastic cells. In case 2, only TLE1 and vimentin was done on cell block as the patient could not afford the cost of the whole panel of markers. Thus, optimization of immuno chemical markers, based on cytomorphological diagnosis helped in reaching a final diagnosis of SS. Over 90% of the SS present translocation between chromosome 18 and X, t(X; 18) (p11; q11) arising from the fusion of gene SYT with the gene SSX1 (biphasic) or SSX2 (monophasic). TLE1 expression also correlates well with t(X;18). Although not specific, TLE1 in context with other markers like bcl2, vimentin, cytokeratins and epithelial membrane antigen can lead to the diagnosis of a synovial sarcoma.[ ]

The biological behavior of SS is variable and independent of histological subtype.[ ] Factors negatively changing the prognosis are poorly differentiated histological subtype, tumoral dimension > 5 cm, lymph nodal involvement and presence of metastases (mainly pulmonary). Since the tumor is chemo-sensitive, the treatment includes neoadjuvant therapy with wide local excision.

Conclusion

The diagnosis of SS on FNAC smears is often overlooked because of considerable cytological overlap. With increasing experience in cytomorphology, the characteristic and well established cytomorphologic features of SS are recognized. A high index of suspicion, especially for material drawn from rare sites, helps in considering it as an initial differential. FNAC is a minimally invasive technique for embarking on a cytologic diagnosis of SS and obviates the need for a biopsy, provided a dedicated pass for cell block is considered to lock the diagnosis.

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