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ORIGINAL RESEARCH

Small myxoid spindle cell tumors in adults – A diagnostic enigma

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ABSTRACT

Background: The term "spindle cell tumors" is commonly used by pathologists for neoplastic lesions when it is difficult to find the lineage of differentiation without ancillary studies like immunohistochemistry. The spindle cell tumors encompass a broad, heterogeneous group of diverse histogenesis and of different grades with a higher risk of malignancy when tumor size is more than 5 cm. Although the malignant soft tissue tumors account for approximately 1% of adult cancers, the malignancy rate among soft tissue lesions of less than 5 cm accounts for approximately 23% (Felix GG et al.). The T1 stage of malignant tumors is defined by the American Joint Committee on Cancer (AJCC) as a lesion with a diameter < 5 cm. As the smaller tumors are likely assumed to be benign clinically and excised without adequate resection margins, preoperative cytological assessment plays a pivotal role in the triage of patients and early clinical decision-making. A variety of spindle cell tumors are associated with myxoid matrix augmenting diagnostic perplexity (Akshay DB et al.).

Keywords: Spindle cell tumors, Soft tissue neoplasms, Preoperative cytological assessment, Small tumor malignancy risk

INTRODUCTION

FNAC is an established modality as an initial investigation for palpable masses, which is cost-effective, rapid, and provides valuable information about the nature of soft tissue lesions. We discuss here the challenges and the clues of cytological analysis in three cases of spindle cell tumors of less than 5 cm in size exhibiting myxoid background.

DESIGN

This retrospective study analyzes rare cases of spindle cell tumors encountered in the cytopathology unit at PES University of Medical Sciences Hospital in early 2024. Clinical details and imaging reports were reviewed, and written consent was obtained for FNAC. FNAC was performed under aseptic precautions using a 22G needle and 5ml syringe, without USG guidance, as the lesions were superficial. Smears were prepared from the myxoid material and stained with Leishman and PAP stains. Cytological diagnoses were made by correlating findings with clinical and imaging data.

The cytodiagnoses were compared to histopathological results from excised specimens, which were received in 10% buffered formalin. After orienting the specimen and marking the external surface, tumor size, margin status, and cut surface appearance were noted. Representative tissue samples were processed into paraffin-embedded blocks and stained with H&E. Immunohistochemistry was performed as needed. Tumors were graded using the FNCLCC system based on cellular differentiation, nuclear pleomorphism, mitosis, and necrosis. All cases were followed for over six months after surgical resections.

RESULTS

Case 1: A 46-year-old man presented with a painless swelling in the left posterior triangle of the neck, gradually increasing over 3 years. On examination, the swelling measured 3x3 cm, was mobile, non-tender, and the overlying skin appeared normal. Ultrasound suggested a peripheral nerve sheath tumor or epidermoid cyst. FNAC showed moderate to marked cellularity with plump fibroblast-like cells, regular oval nuclei, and dense myxoid stroma, along with clumps of adipose cells, endothelial cells, and ropy collagen fibers. A diagnosis of benign myxoid mesenchymal tumor, possibly spindle cell lipoma (WHO category 2), was made, with an excision biopsy recommended.

Intraoperatively, a capsulated swelling was found in the subcutaneous plane above the muscular fascia. Gross examination revealed a soft to firm 3 cm nodule

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with a delicate capsule, and the cut surface showed grayish-yellow, homogeneous areas with a gelatinous appearance. Microscopic examination demonstrated uniform spindly cells arranged in sheets and fascicles within a myxoid background, with scattered mature adipose cells. No necrosis or mitosis was observed. These findings were consistent with the diagnosis of spindle cell lipoma.

Case 2:A 72-year-old woman presented with a 6-month history of swelling in the right submandibular region, without associated dysphagia, fever, or pain. She had no weight loss or appetite changes and was a known hypertensive and diabetic patient. On examination, the swelling measured 3.5 x 2.5 cm, was firm, mobile, and skin-pinchable, with no palpable lymph nodes. Blood tests, including glucose, HBA1c, liver, renal function, and CBC, were normal. Flexible pharyngoscopy revealed a smooth swelling on the right side, possibly adenoid tissue. Dental examination showed chronic periodontitis. USG suggested a pleomorphic adenoma of the submandibular gland, and CECT Head and Neck indicated a well-demarcated mass, likely an enlarged lymph node. FNAC revealed moderately cellular smears with oval to spindly cells exhibiting mild anisonucleosis and nuclear atypia, along with myxoid tissue fragments. The features were suggestive of spindle cell myoepithelioma with focal atypia (WHO Category 3), and excision biopsy was recommended.
Intraoperative findings revealed the right submandibular swelling arising from the lateral pole of the right submandibular gland, adherent to the skin. The excision specimen consisted of normal salivary tissue attached to a partially circumscribed mass (3 x 2.5 cm), with a piece of skin (2 x 0.8 cm) and scant skeletal muscle. The cut surface showed a gray-white tumor with minimal gelatinous areas and irregular margins.
Microscopically, the tumor exhibited loose interlacing bundles of spindle cells in myxoid and collagenous areas, with mild to moderate pleomorphism, occasional mitosis (1/10 HPF), and no necrosis. The cells infiltrated skeletal muscle and dermis, separated from normal salivary tissue by a thick fibrous capsule. The diagnosis of low-grade spindle cell sarcoma, possibly fibromyxoid sarcoma, was made, and an IHC panel was recommended. Immunostains were positive for SMA and negative for MUC4, CD34, S100, EMA, p63, and Ki67, confirming low-grade myofibroblastic sarcoma. Surgical margins were clear.

Case 3: A 63-year-old man presented with a 4x3.5 cm painless lump on the lateral aspect of his left leg, present for 4 months, clinically suspected to be a soft tissue tumor. USG suggested a hypoechoic lesion indicative of a peripheral nerve sheath tumor.
FNAC showed moderately cellular smears with myxomatous tissue, pleomorphic polygonal and spindly cells, occasional giant tumor cells, and curvilinear blood vessels. The cytological features, along with clinical and imaging findings, led to a diagnosis of myxofibrosarcoma (WHO category 5), and excision biopsy was recommended. Gross examination revealed a gray-white tumor with myxoid and necrotic areas and focal irregular margins. Microscopically, fascicles of pleomorphic spindle cells with tumor giant cells, mitoses (8/10 HPF), blood vessels, and abundant myxoid stroma and necrosis were noted. The diagnosis was high-grade myxofibrosarcoma with free resection margins. IHC markers were negative for CD34, S100, MUC4, SMA, and EMA, and further tests were advised to exclude other myxoid sarcomas.

DISCUSSION

Spindle cell lesions encompass a range of neoplastic or reactive proliferations arising from fibroblasts, myofibroblasts, muscle, neural, epithelial, melanocytic, myoepithelial, endothelial, histiocytic, dendritic, adipose, or osseous origins (Hena Paul Singh et al.). Peripheral nerve sheath tumors are the most common benign spindle cell tumors, while undifferentiated pleomorphic sarcoma is a frequent malignant type. Common myxoid soft tissue tumors include pleomorphic liposarcoma, intramuscular myxoma, myxofibrosarcoma, and aggressive angiomyxoma (Akshay DB et al.). This report describes two rare myxoid tumors: benign spindle cell lipoma and low-grade myofibroblastic sarcoma. Cytological features of the latter were initially misinterpreted as myoepithelioma, based on USG findings suggesting a submandibular gland tumor.
Histopathological examination revealed an infiltrative soft tissue tumor, microscopically favoring fibromyxoid sarcoma. Immunostaining was non-reactive to MUC4 and reactive to SMA, indicating a diagnosis of myofibrosarcoma. Mentzen et al. reported 18 cases of myofibrosarcoma, with 12 arising from the oral cavity or extremities and a mean mitotic rate of 2/10 HPF. This tumor, particularly related to the salivary gland, is extremely rare, as noted in a case reported by Bisceglia et al..
Daniela et al. published 13 cases of low-grade myofibroblastic sarcoma, with 12 from the oral cavity and maxillofacial region. Guo Zhao Meng et al. described 20 cases of LGMS, with SMA positivity in 18 cases and 9 patients showing local recurrence during a 4-year follow-up.
A rare case of spindle cell tumor was correctly diagnosed through cytology, showing a mixture of adipose cells and predominantly spindly cells in a myxoid background, with occasional mast cells. Subash Yadav reported 6 cases of spindle cell lipoma (SCL), often found in the head and neck region, similar to our patient. Histologically, the tumor had sparse adipose tissue and prominent fibromyxoid areas. Immunostaining was not performed due to the tumor's encapsulation and free resection margins. SCL is typically positive for CD34 and Bcl-2, as

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reported by Yasmeen Khatib et al.

Myxofibrosarcoma (MFS), though uncommon, accounts for 13% of soft tissue tumors. Our patient presented with a superficial lump, and FNAC revealed myxoid tissue fragments, pleomorphic spindle cells, multinucleated giant cells, and atypical mitoses. The diagnosis of MFS was confirmed after resection. Paul EW et al. found arborizing blood vessels and a myxoid background with pleomorphic spindle cells were common in MFS diagnoses, with cytology showing 64% diagnostic accuracy. IHC was not particularly helpful in their study.

In this study, three patients with myxoid spindle cell tumors were evaluated cytologically. One case was diagnosed as benign, while the other two were categorized as intermediate and malignant. These cytological interpretations were consistent with the histopathologic findings. All three tumors were under 5 cm in size, which is notable given that most soft tissue sarcomas are typically larger at presentation. However, the malignancy rate in soft tissue masses smaller than 5 cm is reported to be 22.41% (Obaid et al.).

Cytological evaluation of soft tissue tumors can be challenging due to varying cellularity, different cell morphologies, and the presence of myxoid material. Accurate interpretation requires thorough examination of the stained smears. The sensitivity and specificity of cytology for assessing myxoid soft tissue tumors as benign or malignant are 98% and 100%, respectively (Carla Saoud et al.). The WHO reporting system has proven useful in categorizing myxoid lesions on FNA. Our experience suggests that FNAC, when combined with clinical details, is a reliable tool for early categorization of these tumors, even with limited imaging data.

No recurrence was observed in all three patients after 6 months of clinical follow-up.

CONCLUSION

An early diagnosis of small soft tissue tumors depending on the cytomorphology is of utmost significance in the clinical decision-making about the extent of surgery. FNAC is likely to be the initial mainstay investigation in the proper interpretation of myxoid spindle cell tumors as per the WHO system of reporting soft tissue tumors. We attempted to share our experience in dealing with the role of FNA in accurately diagnosing small and rare myxoid spindle cell tumors.

Figures

Fig.1(Case1)–

a. Grossspecimen-capsulatedgrayishyellowtumorrevealingglisteinggelatinouscutsurface.
b. Cytomorphology (Leishman stain x20) - revealing myxoid tissue fragments with spindle cells &adiposecells.
c. Histopathology(H&Estainx40)-revealinguniformspindlecellswithinterveningadiposecells.
d. Ultrasonogram-revealingwellcircumscribedtumor.

Fig.2 (Case 2) –

a. Gross specimen - cut section revealing circumscribed tumor attached to salivarygland.
b. Cytomorphology(Papstainx40) - revealingcellularclustersofspindlecellswithmildanisonucleosisina delicate myxoid background.
c. Histopathology(H&Estainx20)-revealingfasciclesofspindlecellsinwhorled patternandinterveningmyxoidmatrix.
d. Histopathology (H&Estainx20)-revealingspindlecellsinvadingadjacentskeletalmuscle.
e. Immunohistochemistry (Ki67x20)-revealingscatterednuclearpositivity.
f. IHC(SMA x40)-revealingstrongmembranouspositivityofspindlecellsintramtrackpattern.
g. IHC(MUC4x20)-revealingnon-immunoreactivespindlecells.

Fig.3 (Case 3) –

a. Gross specimen - cut section of irregular tumor revealing myxoid, necrotic &graywhiteareas.
b. Cytomorphology(Leishmanstainx40)-revealingabundantmyxoidpoolwithpleomorphicspindlecells&curvilinearbloodvessels
c. Histopathology(H&Estainx20)-revealinginterlacingfasciclesofmoderatelypleomorphicspindlecellswithprominentcurvedblood vessels.
d. Histopathology(H&E stain x20) - revealing abundant myxoid areas with spindly and stellatecells

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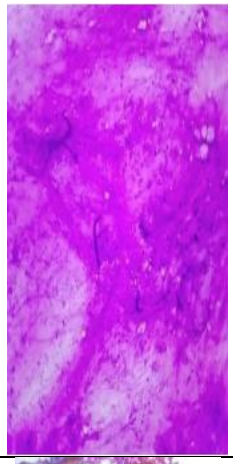
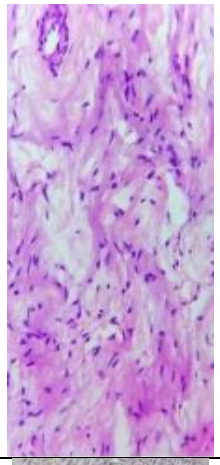
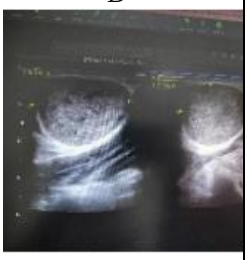
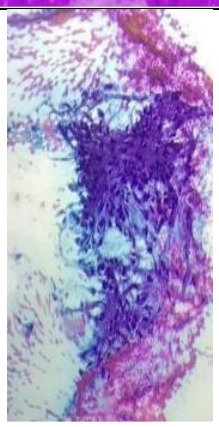
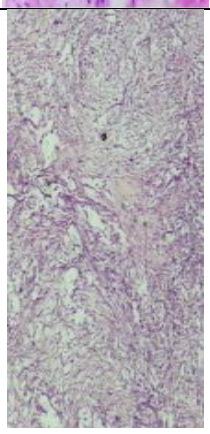
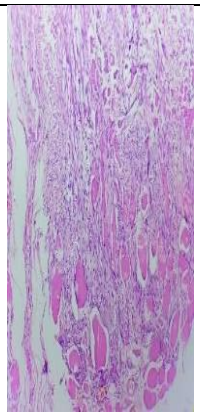
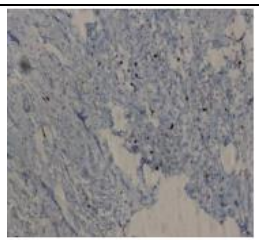
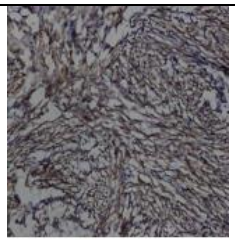
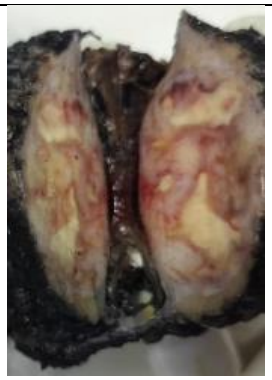
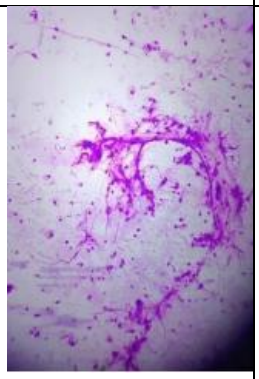
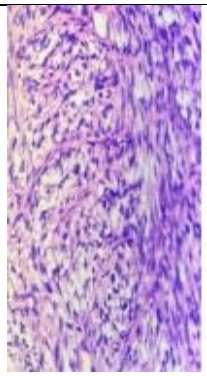
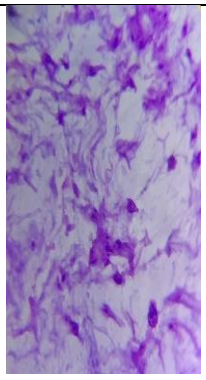
Case1 Spindle celllipoma	A 	B 	C 	D 
Case2 Myofibroblasticsarcoma				
2E,2F,2G				
Case3				

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