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Case Report

Synovial sarcoma- A potential diagnostic pitfall on FNAC

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ABSTRACT

Synovial sarcoma is a malignant mesenchymal tumour with an uncertain origin. It is most commonly seen in the extremities, particularly lower extremities. The diagnosis of synovial sarcoma can be challenging due to its morphological diversity. Histologically, it can be of three subtypes: Monophasic, Biphasic and Poorly differentiated. The transcriptional corepressor, Transducin-Like Enhancer 1(TLE1) is a sensitive and specific marker for synovial sarcoma which helps in distinguishing it from histologic mimics. This case report presents a 48 year old female with swelling over right forearm since 1 year which was misdiagnosed on FNAC as Benign spindle cell lesion, probably Schwannoma. Surgery was done and on histopathological examination, it was diagnosed as Biphasic synovial sarcoma. It was confirmed by TLE1 immunohistochemistry which showed diffuse strong nuclear positivity. FNAC can sometimes fails to sample the epithelial component in biphasic synovial sarcoma, which complicates accurate diagnosis. The exact subtyping of spindle cell tumours is difficult on cytology owing to their complex heterogeneity. Though, Synovial sarcoma is an aggressive tumour, it responds well to treatment including surgery and chemotherapy. Therefore, correct and early diagnosis of synovial sarcoma is vital.

1. Introduction

Synovial sarcoma is an uncommon soft tissue malignancy of uncertain differentiation.[1] It predominantly affects adolescents and young adults, typically between 15–35 years and show a slight male predominance.[2] Although it can arise in any anatomic site, it most frequently presents in the extremities, particularly the lower extremities. The trunk is the second most common site, followed by head and neck regions.[3,4]

Historically, synovial sarcoma was identified as a biphasic tumor featuring both epithelial and uniform spindle cell components.[3] This neoplasm exhibits significant morphological and immunohistochemical heterogeneities. Despite its morphological diversity, synovial sarcoma is molecularly characterised by a specific genetic alteration: the (X;18)(p11.2;q11.2) translocation, which involves the SS18 gene on chromosome 18 and one of several synovial sarcoma X (SSX) genes on chromosome X.[3]

Diagnosis of synovial sarcoma relies on a combination of its distinct morphological features, immunohistochemical markers, and the identification of the characteristic driver translocation.

Gene expression profiling has identified TLE1 (Transducin-Like Enhancer of Split-1) as a valuable diagnostic tool for synovial sarcoma. TLE1, a member of the Groucho/TLE gene family, acts as a transcriptional corepressor involved in epithelial and neuronal differentiation.[5] It is considered a highly sensitive and specific marker for synovial sarcoma, particularly when moderate to strong staining is observed, aiding in distinguishing it from other histologic mimics.[6]

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While molecular testing remains the diagnostic gold standard for diagnosing synovial sarcoma, TLE1 can serve as an effective immunohistochemical marker, especially in small biopsies or in conjunction with classical histopathological features, providing dual confirmation alongside molecular analysis when needed.[5]

2. Case Report

2.1. Clinical history

A 48year old female presented with complaints of swelling over ventral aspect of right forearm for 1 year, not associated with pain. On examination, a solitary swelling was noted over the distal part of right forearm measuring around 5x4cm, firm in consistency, non-tender, mobile on muscle contraction.

2.2. Radiology

Ultrasonography of the swelling showed a well-defined, solid, heterogeneously iso – hyper echoic lesion below the muscular plane in the flexor aspect of forearm- likely neoplastic etiology (?Peripheral nerve sheath tumour)

Figure 1: Clinical presentation

2.3. Cytological examination

Fine needle aspiration of the swelling was done which yielded hemorrhagic smears showing thick tissue fragments and dispersed spindle cells. The nuclei of these cells are wavy, giving fish hook appearance with tapered ends and abundant filamentous cytoplasm. The features suggestive of Benign spindle cell neoplasm – Probably Schwannoma.

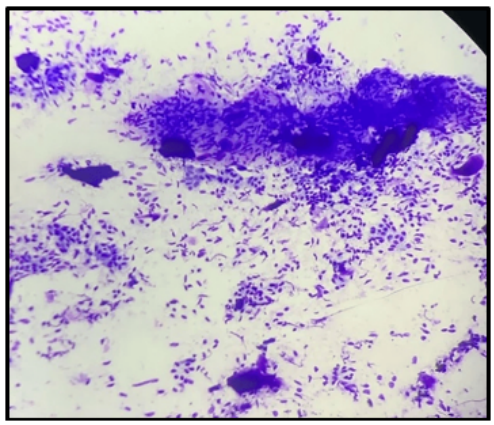

Figure 2: FNAC showing features suggestive of Benign spindle cell neoplasm(Giemsa, 10X)

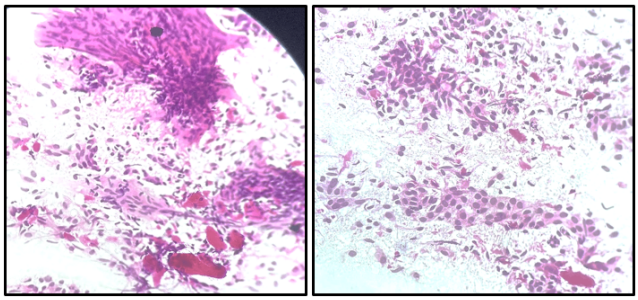

Figure 3: FNAC showing features suggestive of Benign spindle cell neoplasm (H&E, 20X)

Figure 4: Soft tissue mass with homogenous grey white areas

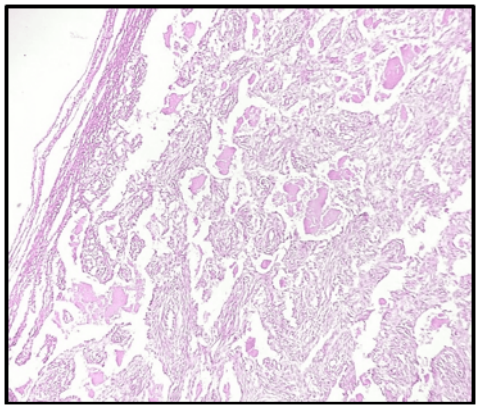

Figure 5: Well circumscribed neoplasm (H&E,10X)

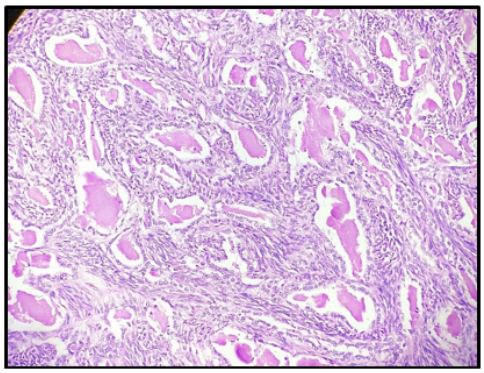

Figure 6: Biphasic neoplasm arranged in glands and long fasicicles (H&E,20X)

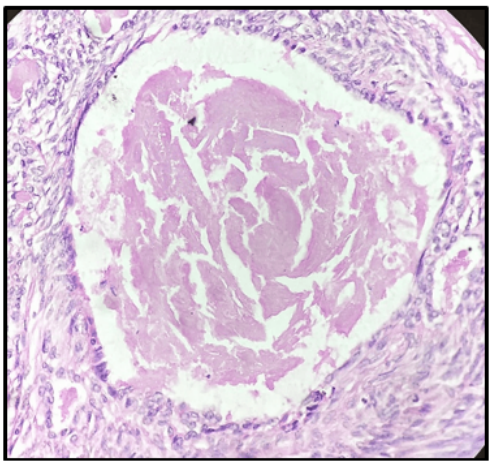

Figure 7: Glands surrounded by tumour cells with lumen showing eosinophilic material (H & amp; E,20X)

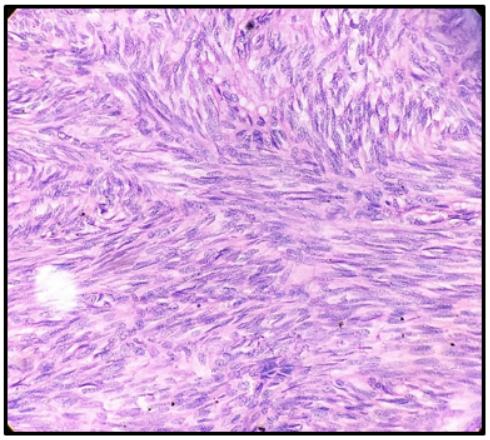

Figure 8: Tumour cells arranged in long fascicles (H & amp; E,20X)

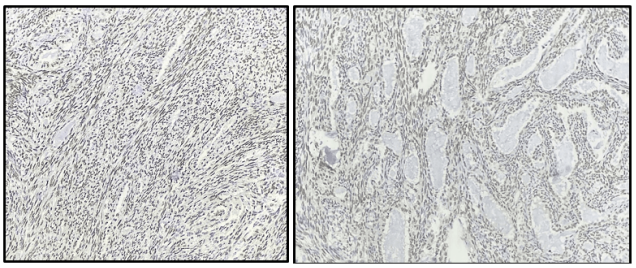

Figure 9: TLE 1 Nuclear positivity (20X)

2.4. Gross examination

Received a globular soft tissue mass measuring approximately 5x5x3cm, External surface is lobular, and capsule is present. Cut surface shows homogenous grey white to grey brown areas.

2.5. Microscopic examination

Multiple sections studied from the tissue bits shows a well circumscribed biphasic tumour with cells arranged in glands and long fascicles. The glands are lined by epithelial cells which are ovoid with dispersed chromatin and moderate amount of cytoplasm. The lumina of the glands show eosinophilic material.

The tumour cells are also arranged in long fascicles in between these glands and show ovoid to spindle nucleus with dispersed chromatin, inconspicuous nucleoli and scant cytoplasm. Mitotic figures: <2/10hpf noted.

Features suggestive of **Bi**phasic synovial sarcoma.

2.6. Immunohistochemistry

Immunohistochemical study of this tumour showed diffuse nuclear positivity for TLE1.

3. Discussion

Synovial sarcoma is a type of malignant mesenchymal tumor with an uncertain origin, most frequently occurring in the lower extremities. Synovial sarcoma shows a diverse clinicopathological spectrum. A palpable mass associated with or without pain is the most common presenting finding.[7]

Radiologically, these tumors often appear as ill-defined, lobulated, or rounded soft-tissue masses near a joint, sometimes associated with peripheral calcification.[7]

Despite its aggressive nature, synovial sarcoma can respond well to treatment options, including chemotherapy, highlighting the importance of accurate diagnosis.[5] Diagnosis of synovial sarcoma relies on a combination of its distinct morphological features, immunohistochemical markers, and the identification of the characteristic driver translocation.

On cytology, Synovial sarcoma yields cellular smears showing uniform cells in clusters and singles with these cells showing bland, oval nuclei and scant, delicate tapering cytoplasm. Occasional fragments of myxoid extracellular matrix and thin branching capillaries may be seen.[8] However according to a study done by Kanika Rastogi et al., sensitivity and specificity of FNAC in diagnosis of spindle cell lesions were 83.3% and 92.3% respectively.[9]

The complex heterogeneous nature of soft tissue tumors is a limiting factor in their exact categorization. Particularly in biphasic synovial sarcoma, cytological diagnosis can be challenging as it may miss the epithelial component, complicating accurate diagnosis. Therefore, appropriate subtyping of these tumors is not always possible on cytology alone. Clinical and radiological correlation, alongside histopathological examination, is crucial for precise subtyping.[10]

Histologically Synovial sarcoma can be classified into three different subtypes: (1) monophasic (2) biphasic and (3) poorly differentiated. The monophasic variant is characterized by spindle-shaped cells arranged in interlacing fascicles with the cells showing pale, scanty cytoplasm and tapering nuclei. The biphasic subtype features variable proportions of spindle cells and epithelial cells, which may form glands, nests or cords. The poorly differentiated variant resembles the small round blue cells seen in Ewing's or primitive neuroectodermal tumors.[7]

Immunohistochemistry plays a significant role in diagnosing synovial sarcoma. Common markers like cytokeratins, bcl-2 and epithelial membrane antigen lack sensitivity and specificity for this tumor type.[6] However, gene expression studies have identified TLE1 (Transducin-Like Enhancer of Split-1) as a reliable marker, being frequently overexpressed in synovial sarcoma. The transcriptional corepressor, TLE1, a member of the Groucho/TLE gene family, is involved in various developmental processes like embryogenesis, neurogenesis and hematopoiesis. TLE proteins are part of the Wnt/β-catenin signaling pathway, which is linked to synovial sarcoma. The intensity of nuclear staining for TLE1 is assessed as weak, moderate, or strong.[6]

A study done by Foo et al.[6] on 73 cases of synovial sarcoma showed 60 cases(82%) positive for TLE1, out of which 22 cases were monophasic, 18 cases were biphasic and 20 cases were poorly differentiated. TLE1 expression demonstrated an overall sensitivity of 82% and specificity of 92% for diagnosing synovial sarcoma.[6]

Cytogenetically, synovial sarcoma is marked by the chromosomal reciprocal translocation t(X;18) (p11.2;q11.2), which fuses the SYT gene on chromosome 18 with either the SSX1, SSX2, or SSX4 gene on the X chromosome (Xp11). This translocation is present in up to 90% of synovial sarcoma cases. While molecular analysis remains the definitive diagnostic 'gold standard', practical constraints may limit its availability in resource-limited settings[11–14]

The initial FNAC diagnosis of the current case was a benign spindle cell lesion, likely Schwannoma, owing to complex heterogeneity of the lesion and the tendency of cytology to miss the epithelial component in biphasic tumors, which complicates accurate diagnosis. However, the histological examination confirmed the diagnosis as biphasic synovial sarcoma, which is considered the gold standard. Further validation was achieved through immunohistochemistry using TLE1, a marker known for its high sensitivity and specificity for synovial sarcoma, showing strong 4+ nuclear positivity. Following the immunohistochemical confirmation, a re-evaluation of the cytological smears revealed good cellularity, a few mitotic figures, and scattered single cells within a background of occasional fragments of homogeneous eosinophilic matrix.

4. Conclusion

In summary, synovial sarcoma is an uncommon soft tissue neoplasm of mesenchymal origin, typically found in the lower extremities of young individuals. Accurate diagnosis of synovial sarcoma relies on a combination of histological examination, immunohistochemical profiling, and detection of the characteristic genetic translocation.

5. Source of Funding

None.

6. Conflict of interest

None.

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