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GIANT CELL TUMOR OF TENDON SHEATH- CYTOMORPHOLOGIC SPECTRUM

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ABSTRACT

Aim of study was to know the role of cytomorphological findings in the diagnosis of giant cell tumor of tendon sheath (GCTTS) in twenty-four histologically proved cases. Archival records pertaining of 24 patients as Giant cell tumor of tendon sheath (GCTTS) diagnosed on fine needle aspiration cytology (FNAC) were studied. The detailed cytological findings were analyzed on smears stained with Papanicolaou and May-Grunwald-Giemsa. Patients ranged from 10 to 60 years, with slight female predominance. Small joint involvement was seen in most of the cases with equally involved upper and lower limb. Hemorrhagic material was aspirated in all the cases. The key cytological features were cellular smears with varying proportions of the stromal cell, osteoclastic type of giant cells and hemosiderin laden macrophages. Stromal cells showed a dispersed arrangement and composed of varying proportions of polygonal to spindle shaped cells. Nuclear grooves were found in almost all cases. Other features seen were cytoplasmic granules and vacuoles, focal mild pleomorphism and foam cells. Mitosis and necrosis were absent. Cytologic features were classified as constant when present in all cases and variable when present occasionally. The diagnosis of GCTTS is suggested strongly using fine needle aspiration cytology, since unique cytological features are sufficiently diagnostic, when evaluated in conjunction with clinico-radiological features.

INTRODUCTION

Giant cell tumor of tendon sheath (GCTTS) better known as localized nodular tenosynovitis[1] is a benign slow growing lesion most commonly presenting as soft tissue nodule with a peak incidence in the third to fourth decade of life. It arises from the synovium of tendon sheath, frequently affecting hands and feet. Pigmented villonodular synovitis term was previously used and it can be localized or diffuse. GCTTS is thought to arise from synovial lining cells, while the giant cells in GCTTS are structurally and functionally osteoclasts[2].

Although, the histopathological appearances are well established, but only few reports or series describe the cytomorphology of this lesion.[1-4]The present study describes cytomorphological features in 24 cases of GCTTS. We aimed to evaluate the diagnostic accuracy of FNA features of GCTTS.

MATERIAL AND METHODS

The series includes 24 histologically confirmed cases of GCTTS during the period July 1999 to July 2006, referred for pre-operative FNA. Archival records pertaining to clinical features, FNA smears, histology slides and their reports were analyzed. The aspirations were performed by a cytopathologist with 23-gauge needle attached to a plastic disposable syringe as an outpatient procedure. Alcohol-fixed smears were stained with Papanicolaou (PAP) and air-dried one with May-Grunwald-Giemsa (MGG).

The following parameters were looked for: cellularity of smears, presence of stromal cells as spindle cells and polygonal cells, hemosiderin-laden macrophages and foamy histiocytes. Other features looked were also studied, such as nuclear grooves, cytoplasmic vacuoles, prominent nucleoli and nuclear pleomorphism.

The nodules were subsequently excised and submitted for histopathological examination.

RESULTS

Clinical details of the patients are presented in Table I.

Table I: Clinical data on 24 cases of GCTTS

Clinical Features	No. Cases (n=24)	%
Age (Year)		
1-10	1	4.17
11-20	4	16.66
21-30	7	29.16

31-40	8	33.34
41-50	3	12.5
51-60	1	4.17
Sex		
Men	11	45.83
Women	13	54.17
Site		
Upper Limb		
Hand (fingers & thumb)	10	41.66
Wrist	2	8.33
Lower Limb		
Toes	8	33.33
Middle Malleolus	1	4.17
Shin of Tibia	1	4.17
Knee	2	8.33
Lytic lesion (on X-ray)	3	12.5

The age of the patients ranged from 10-60 years with a slight female predominance. All patients presented with a soft tissue swelling. Out of twenty four cases, twelve cases presented as swelling in the upper extremity, over the fingers, palm and wrist, twelve cases presented as swelling in lower extremity over the knee, ankle and toes. The duration of the lesion varied from 2 months to 18 years and size varied from 0.5 to 5.0 cm in greatest dimension. Radiological study revealed bone involvement in three cases. There was no history of antecedent trauma in any case.

The smears prepared from aspirated material were mild to highly cellular and revealed biphasic pattern of cells consisting of loose aggregates of round to ovoid cells with moderate to abundant cytoplasm along with small tissue fragments forming papillae at places. All cases showed an admixture of stromal and giant cells.

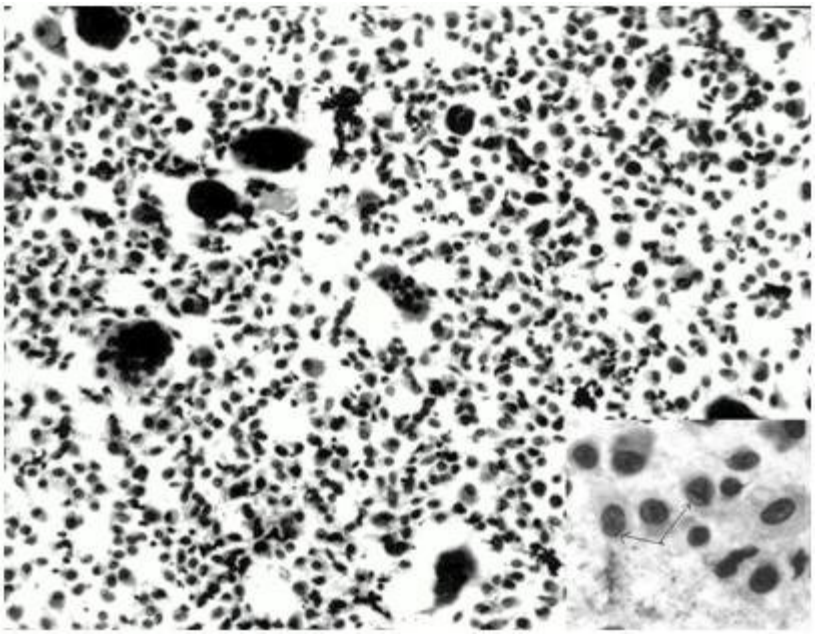

Figure:1- Smear showing admixture of stromal and giant cells. Inset show nuclear grooving in stromal cell (Arrow).

The stromal cells were either polygonal-shaped cells with abundant cytoplasm or spindle-shaped cells with scant cytoplasm. Polygonal cells were seen in larger numbers with varied shape and nuclear grooves were identified in most of the cases, although in variable frequency. Some polygonal stromal cells had rounded nuclei with prominent nucleoli and fine cytoplasmic vacuolation. The number and size of the giant cells varied from case to case. Most of the giant cells had large number of nuclei (10-15 nuclei), with 95% of cases showing at least one giant cells with more than 20 nuclei. Morphologically giant cells were similar to those seen in giant cell tumour of bone. Fair number of multinucleated giant cells, hemosiderin-laden macrophages and foamy histiocytes were also seen.Nuclear pleomorphism, mitosis and necrosis were absent.

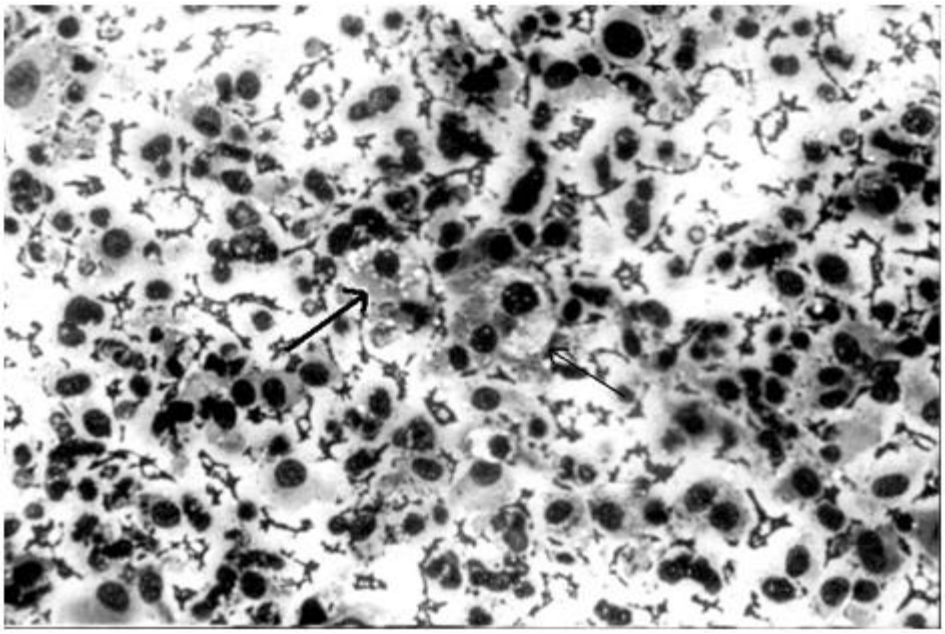

Figure 2: Smear showing presence of hemosiderin laden macrophages (Thin arrow) and foamy histiocytes (Thick arrow).

Details of cytological findings are given in Table II.

TABLE II: Cytological findings in 24 cases of GCTTS with histopathologically proved cases

	No. of Cases	%
Constant features		
Cellularity	24	100
Stromal cells	24	100
Polygonal	24	100
Spindle	15	62.5
Giant cells	24	100
HLM	24	100
Variable features		
Xanthoma cells	22	91.66
Nuclear grooves	22	91.66
Nuclear inclusions	2	8.33
Cytoplasmic granularity	2	8.33
Cytoplasmic vacuoles	12	50
Nuclear pleomorphism	4	16.66
Nucleoli	12	50

DISCUSSION

GCTTS was first described by Chassaignac[5], and subsequently Jaffe et.al[6] contributed most to the understanding of these tumours. In 1941, Jaffe et al characterised a variety of fibrohistiocytic tumour, which occurred within the large joints and termed them pigmented villonodular synovitis (PVNST). Localized tenosynovial GCT, diffuse tenosynovial GCT, PVNST and other related lesion represent a common family of lesion arising from the synovium of tendon sheath, bursa, and joints and having more or less similar cytological features.[7] These lesion have been considered reactive by some and neoplastic by others. GCTTS also known as localized nodular tenosynovitis usually present as a soft tissue nodule in relation to the tendon sheaths of the hand and feet [1] and can occur at any age but is most often seen in the third to fifth decade of life with slight female predominance.[1-2] In the present series most of the patients were in the second to fourth decade of life but with equal male: female ratio. GCTTS is a slow growing, asymptomatic, soft tissue mass and radiologically, a circumscribed, soft tissue mass without bony involvement in 50% of patients.[6] Common sites of involvement are interphalyngeal joints in the hand but can also present in the feet, ankle, knee, shoulder and elbow.[7,8]

Although, GCTTS is capable of local recurrence and considerable destruction of the joint and surrounding soft tissue, it does not appear to be capable of distant metastasis.[8] When destruction of bone is radiologically evident, chances of clinical misdiagnosis is high. In this series, out of 18 cases, 3 cases showed osteolytic lesion of bone. Two cases were misdiagnosed as osteogenic tumour and giant cell tumour of bone respectively. One case was diagnosed as GCTTS even with the presence of bony lesion, may be due to characteristic site of lesion i.e. middle phalynx of right hand.

The pathogenesis of this tumour still remains obscure. Antecedent trauma and hemorrhage in some cases favor reactive theory, while autonomous growth, capacity of local recurrence if inadequately excised, rare metastasis and recurrent chromosomal breakpoints[9] favor a neoplastic theory. Cytogenetic analysis reported by Ferrer J et al[10], the presence of a clonal population with 47 chromosomes and two different translocations, t(2;3) and der(8) t(8;12) further support neoplastic nature of this tumoral entity.[10] In this series history of trauma was not present in any of the cases. Chances of recurrence in GCTTS are 10-20%, with a remote

potential for distant metastasis.[8] Recurrence develops more frequently in lesions that are cellular and have increased mitosis. In patient undergoing simple enucleation, microscopic residue may be left behind leading to recurrence.[7]

Description of cytological features of GCTTS is still in its infancy, only few studies in the form of series and case reports are available.[1-4] Cytomorphological features observed by most of the authors are highly cellular lesion consisting of predominantly polygonal cells and numerous multinuclear giant cells without nuclear atypia. In our case series aspirates were mild to highly cellular, with presence of polygonal and spindle cells. Giant cells and hemosiderin laden macrophages (HSLM) with histiocytes-like cells were also present in all cases in good number. Iyer et al[2] and Batra et al noticed frequent presentation of nuclear groove, which were also noticed in our case series. Convolutions of the nuclear outline and occasional intranuclear inclusions in stromal cells but less frequently, the presence of HSLM in their series while HSLM were consistently present in our series. They suggested, the presence of osteoclastic like giant cell with the combination of typical stromal and hemosiderin-laden macrophages in aspirates of soft tissue tumor is virtually diagnostic of GCTTS, which are parallels with our findings. The similarity of nuclei between the giant cells and some stromal cells suggested the current understanding of the formation of osteoclasts in giant cell tumour of bone, as well as the molecular mechanisms underlying the formation of osteoclasts. Cytokines released from progenitor osteoblasts or other progenitor stromal cells cause recruitment of mononuclear cells of the marrow and their in situ fusion to form osteoclasts[2]. Recent studies suggest that Microphthalmia transcription factor (MITF) and tartrate-resistant acid phosphatase (TRAP) are expressed during osteoclast differentiation. A similar mechanism may underlie the presence of osteoclasts in GCTTS.[11]

The differential diagnoses considered are synovial sarcoma, benign fibrous histiocytoma, clear cell sarcoma of the soft part, giant cell tumor of bone,[5] solid aneurysmal bone cyst before giving a cytological diagnosis of GCTTS, when combination of stromal cells and giant cells are present. In case of synovial sarcoma and benign fibrous histiocytoma osteoclastic type giant cells are not present, whereas in clear cell sarcoma it is sometimes present in addition to monomorphic polygonal cells. Giant cell lesion of bone with soft tissue components may mimic GCTTS, including the presence of osteoclastic giant cell, however the peripheral

adherence of giant cells to the spindle cell is the feature of diagnostic significance in GCT of bone,[12] while closely associated mononuclear cells with dense, homogeneous, extracellular, matrix material is common in solid aneurysmal bone cyst.[13] Hence cytology should be interpreted in conjunction with radiological findings.

While, in our study cytologically all cases were diagnosed as GCTTS whereas clinically only three cases were suspected as GCTTS. However, two cases were misdiagnosed as malignant lesion clinically as synovial sarcoma with differential diagnosis of fibroma and osteogenic sarcoma respectively.

In conclusion, the diagnosis of GCTTS can be made or at least strongly suggested in light of clinico-radiological correlation and unique cytological findings such as presence of stromal cell, giant cell and hemosiderin-laden macrophages.

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