Diagnostic utility of fine needle aspiration cytology versus conventional histopathological study and immunohistochemistry of benign tumors and tumor like growths of the synovium

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ABSTRACT Aims: The aim of this retrospective study is to study the fine needle aspiration cytology of various clinically suspected benign tumors & tumor like growths of the synovium , its diagnostic utility & further confirmation of the lesions with biopsy study & immunohistochemical study

Methods: This study comprises analysis of 25 cases of clinically suspected benign tumors & tumor like growths of the synovium conducted at Department of Pathology, J.J.M Medical College, Davangere during period of 2 years from April 2002 to March 2004 contributing 23.8% of 105 total Fnacs & biopsies done for synovial lesions during the period respectively. Fine needle aspiration cytology (FNAC) was done for the clinically suspected cases and the smears were stained with haematoxylin and eosin, papinocolaus stain, geimsa & other romanowsky stains. The FNAC findings were further correlated with Histopathological study of Synovial biopsy Specimens which were processed routinely and stained with haematoxylin and eosin. Prussian blue stain for haemosiderrin were carried out in suspected cases of pigmented villonodular synovitis for the demonstration of haemosiderrin pigment. Wherever necessary the available clinical, radiological findings, immunohistochemical marker study were taken in to consideration to categorize the lesions.

Results: In our study, the common age groups affected were between 30-50yrs. Females were commonly affected with M: F 1:1.8 Most common symptoms seen were pain, swelling, restricted movements. The commonest joints involved were knee, wrist, interphalangeal joints of hand. Most common FNAC diagnosis made among the clinically benign tumors & tumor like growths of the synovium were pigmented localized nodular tenosynovitis followed by diffuse tenosynovial giant cell tumor, ganglion cyst and synovial chondromatosis. Later these lesions were further correlated with histopathological study of synovial biopsies & wherever necessary some of these lesions were further confirmed by immunohistochemical study . Conclusion: Definitive diagnosis & prognosis of the benign tumors & tumor like growths of the synovium can be accessed only by combination of FNAC findings, histopathological examination & immunohistochemical study in correlation with the clinical & radiological findings.
MATERIALS AND METHODS

This study comprises analysis of 25 cases of clinically suspected benign tumour like growths & true neoplasms of the synovium conducted at Department of Pathology, J.J.M Medical College, Davangere during period of 2 years from April 2002 to March 2004 contributing 23.8% of 105 total FNac’s & biopsies done for synovial lesions during the period respectively.

Materials for study were obtained from Bapuji Hospital, Chigateri District Hospital, Woman and Children Hospital and from other well equipped private and Government Hospitals in and around Davangere.

Clinical information required for the study were obtained from the respective medical faculty and were recorded chronologically in the proforma and later categorized accordingly, which included complete clinical details, necessary investigations and procedures adapted to obtain them material.

Fine needle aspiration cytology (FNAC) was done for the clinically suspected cases and the smears were fixed in 10% methanol, processed & stained routinely with haematoxylin and eosin, papinocolau’s stain, geimsa & other romanowsky stains including the special stains like Prussian blue stain to demonstrate haemosiderin pigment in case of pigmented villonodular synovitis. Detailed morphological study of the clinically suspected cases of benign tumors & tumor like lesions of the synovium was done.

The FNAC findings were further correlated with Histopathological study of Synovial biopsy Specimens, most of which were obtained by whole tissue excision. After obtaining the specimens detailed gross examination was done and salient morphological features were recorded and the whole biopsy material was fixed in 10% formalin for 24-12 hours. Finally representative bits were given. Tissues were processed routinely and paraffin blocks were prepared and stained with haematoxylin and eosin. Prussian blue stain for haemosiderin were carried out in suspected cases of pigmented villonodular synovitis for the demonstration of haemosiderin pigment. Wherever necessary the available clinical, radiological findings, immunohistochemical marker study was done using microwave tissue processing.

OBSERVATIONS AND RESULTS

A total of 25 clinically suspected cases of benign tumour like growths & true neoplasms of the synovium were choosen out of total 105 synovial lesions which came to Pathology, J.J.M. Medical College, Davangere for FNAC & histopathological study during the period of 2 years (April 2002 to March 2004) contributing 23.8% of 105 total FNac’s & biopsies done for synovial lesions during the period respectively.

The common benign tumors & tumor like growth encountered are shown in (table -1)

The mean age group affected by these lesions were in the age group of 20-50yrs (table-2)

Amongst the 25 cases highest incidence of 20 patients (57.14%) was noted in female patients compared to males of 15 patients (42.9%) with male to female ratio of 1:1.8. (table-3)

Pain & swelling were the predominant clinical features encountered in most of these patients with only few patients showing difficulty in movements in patients with diffuse/local giant cell tumor of tendon sheath.

Knee was the common site involved in this study and interphalangeal joints were commonly involved in diffuse/localized tenosynovial giant cell tumor (table-4)

Ganglion cyst:

FNac findings:

The aspirated material from 7 cases were thick, colourless & jelly like.

Smears from the aspirated material showed a small number of single cells with abundant cytoplasm and small oval nuclei over a background of abundant myxoid material which showed a drying artifact. (fig-1)

Histopathology:

Macroscopically they appeared as pearly white to grey white masses measuring from 0.5cm – 4cm and the cut section showed cystic change in 2 patients and it was grey white in remaining 5 patients.

Microscopically the presence of Cyst wall was the most persistent feature in all the 7 patients of ganglion, chronic inflammatory infiltrates were seen in 4 patients (57.14 %), fibroconnective tissue in the cyst wall and the less common features like myxoid change was seen in 2 patients (28.6%), fibrofatty vascular connective tissue and flattened epithelial lining of cyst wall was seen in 1 patient (14.3%). (fig-2)

Baker’s cyst:

FNac findings:

The 6 clinically suspected cases showed very scanty aspirate comprising of few scattered fibroblasts, occasional synovial cells & few scattered chronic inflammatory cells.

Histopathology:

Macroscopically Specimens were grey white to grey yellow. They were irregular in shape.

The predominant microscopic findings were fibrocollagenous wall lined by low cuboidal to flattened epithelium and chronic inflammatory cell infiltrates in stroma.

Synovial chondromatosis: Radiologically loose bodies in joint space were seen in all the 3 patients. All the routine laboratory investigations were within normal limits in these 3 patients.

FNac findings:

Did not yield any material.

Histopathology:

Macroscopy: Bony bits were received along with grey white soft tissue in all 3 patients, measuring 4 - 6 cm in diameter and were pearly white to grey white in colour, globular masses with irregular surface. Cut section was grey white. (Fig-3)

Microscopically Section studied from the synovial tissue showed mild villous hypertrophy, focal infiltration of macrophages and lymphocytes, blood vessel proliferation in one patient. Section studied from all the loose bodies showed a circumscribed nodule lined by synovium and foci of hyaline cartilage and ossification were seen.

2 cases of histopathologically diagnosed localized TGCT were subjected to immunohistochemical study, the mononuclear cells & the giant cells showed positivity for CD68 indicating their synovialcell origin.
Diffuse/Localized Tenosynovial giant cell tumour (TGCT):

A total of 9 (25.7%) patients of tenosynovial giant cell tumours were encountered. Amongst them 7 patients (77.8%) had localized tenosynovial giant cell tumours and 2 (22.2%) patient had diffuse tenosynovial giant cell tumour. All were between 21-50 years and females were commonly affected (66.7%). ESR was 36-40mm/hr in 2 patients, 27 and 28mm/hr in 4 patients respectively and in the other patient the ESR was within the normal limits.

FNAC findings:
In 2 clinically suspected cases of diffuse/pigmented villonodular synovitis FNAC yielded pale yellow to pale brown coloured fluid aspirate, smears from the centrifuged sediment from fluid showed sheets of synovial cells with occasional papillary clusters and macrophages containing brown cytoplasmic granules of hemosiderin, occasional tuton type of multinucleated giant cells were seen. (fig-4)

Histopathology:
Macroscopically specimens of TGCT were grey white to grey yellow, pale brown in colour and were globular masses, irregular membranous soft tissue with tiny nodules on its surface with shaggy villous structures was seen in 1 patient which measured from 2-4cm in diameter.

Microscopically the most common findings seen in all the 9 patients were multinucleated giant cells admixed with round to polygonal cells and fibrocollagenous stroma. Cleft like spaces were seen in 2 nodular and diffuse TGCT. Features like cells arranged in clusters, groups and strands were seen in all patients. Haemorrhage with hemosiderin deposits and inflammatory infiltrates were seen in 3 patients, foamy cells were seen in 2 patients. Malignant features were not seen in any of the sections. (fig 5,6)

Prussian blue staining for hemosiderin pigment was done in 4 patients and was positive in 3 patients. (Fig.7).

In 2 cases we demonstrated immunohistochemical positivity for CD68 similar to the localized TGCT.

Table 1. Incidence of benign tumour like growths & true neoplasms of the synovium

<table>
<thead>
<tr>
<th>Benign tumour like growths and true neoplasms of synovium</th>
<th>No. of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Ganglion cyst</td>
<td>7</td>
<td>28</td>
</tr>
<tr>
<td>b. Baker’s cyst</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>c. Synovial chondromatosis</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>d. Diffuse TGCT /localized TGCT (nodular synovitis)</td>
<td>9</td>
<td>36</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>25</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

Table-2 Age distribution

<table>
<thead>
<tr>
<th>Tumors &amp; tumor like lesions of the synovium</th>
<th>11-20</th>
<th>21-30</th>
<th>31-40</th>
<th>41-50</th>
<th>51-60</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ganglion cyst</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>7</td>
</tr>
<tr>
<td>Baker’s cyst</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Synovial chondromatosis</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Diffuse/Localized tenosynovial giant cell</td>
<td>-</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>-</td>
<td>9</td>
</tr>
<tr>
<td>tumour</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2</strong></td>
<td><strong>4</strong></td>
<td><strong>8</strong></td>
<td><strong>6</strong></td>
<td><strong>5</strong></td>
<td><strong>25</strong></td>
</tr>
</tbody>
</table>

Table-3. Sex Distribution of benign tumour like growths & true neoplasms of the synovium

<table>
<thead>
<tr>
<th>Pathological lesion</th>
<th>Sex</th>
<th>M:F Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Ganglion cyst</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Baker’s cyst</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Synovial chondromatosis</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Diffuse/Localized TGCT</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>9</td>
<td>16</td>
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Table-4 Joints involved

<table>
<thead>
<tr>
<th>Pathological lesions</th>
<th>Knee</th>
<th>Elbow/Forearm</th>
<th>Wrist</th>
<th>Hand (L.P.)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ganglion cyst</td>
<td>-</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Baker’s cyst</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Synovial chondromatosis</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>Diffuse/Localized tenosynovial giant cell tumour</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>11</td>
<td>1</td>
<td>5</td>
<td>8</td>
<td>25</td>
</tr>
<tr>
<td><strong>Percentage</strong></td>
<td>44</td>
<td>4</td>
<td>20</td>
<td>32</td>
<td>100</td>
</tr>
</tbody>
</table>
DISCUSSION

Exploratory arthrotomy and synovial biopsy are recognized procedures for early diagnosis of joint diseases particularly when clinical and radiological findings are inconclusive. In our study of 7 cases, smears from the aspirated material showed a small number of single cells with abundant cytoplasm and small oval nuclei over a background of abundant myxoid material which showed a drying artifact. Similar observations were made by Dodd & Layfield (1996). Punia RS, Gupta S, Handa u, etal.

In the present study a total of 7 patients (28%) of ganglion were diagnosed histopathologically. Females dominated males in sex incidence with a M:F ratio of 1:2.5 and wrist was the commonest joint involved. Similar observations were made by many authors that, ganglion develops most frequently on the dorsal aspect of wrist proximal to the thumb. Over usage of wrist and fingers is the cause for this frequent location. Sometimes a history of injury preceding ganglion formation may exist. It forms as a result of synovial or bursal tissue, which becomes pinched off or trapped under a ligament or tendon.
The lining of the cysts varies from a continuous layer of cells resembling synovium to a partial lining or no lining at all. Some ganglia are not completely cystic being composed partially of tissue resembling synovium. The lesion may be multilocular and enlarges through coalescence of adjacent areas of myxoid change but however, there is no communication with joint space.¹

**Baker's cyst:**

Herniation of synovium through a joint capsule or massive enlargement of bursa may produce a synovial cyst. A well recognized example is the synovial cyst that forms in the popliteal space in the setting of rheumatoid arthritis (Baker cyst). The synovial lining may be hyperplastic and contain inflammatory cells and fibrin.²

There were 6 patients of Baker's cyst which were diagnosed histopathologically with maximum incidence in the age group of 51-60 years. Females were commonly affected. All these lesions had a cyst wall consisting of dense connective tissue lined by low cuboidal to flattened epithelium with mononuclear cell infiltration. David G. Palmer (1969) reported such cystic swellings seen frequently in rheumatoid disease and are obviously related to bursae, tendon sheaths and joints. These cysts develop as fluid exudation in to spaces lined by synovium.

**Synovial Chondromatosis:**

Synovial chondromatosis may be seen in a wide variety of disturbances of synovial membrane of joints and bursae like infection, trauma and metaplastic transformation of synovial tissues.³

Robineau in 1919 counted up to 1200 loose bodies in one joint. The loose bodies have a clear center and a shell of calcification and may appear in typical attached grape like formation. Secondary osteoarthritis and severe synovitis may result from the presence of loose bodies.⁴ similarly all the 3 cases in our study showed loose bodies.

Baun Gaard Philip and Bernt B. Nielsen observed histologic variants in 8 cases of primary synovial chondrometaplasia which consisted of cystic degeneration, variation of chondroid cells and their nuclei, tumor like accumulation of metaplastic nodules apart from connective tissue invasion, calcification and ossification which were most frequent.¹⁵ In our study 2 out of 3 cases showed similar histological features.

Knee, elbow and hip of middle aged and young adults are the most commonly involved sites. It has a male predominance and pain is the most common symptom.⁶

Only 3 patients (12%) of synovial chondromatosis were diagnosed histopathologically during 2 years. Knee was the only joint involved in both patients. loose bodies were seen in all 3 patients similar observations were noted in the study of Rainav and S.B. Kohli with only 3 patients in a period of 5 years, in 1977. Sviland L and AJ. Marcolon in 1995 also observed the similar histopathological findings like lobulated masses of hyaline cartilage and few foci of ossification.¹⁵

**Localized Tenosynovial Giant Cell Tumour:**

The localized form of giant cell tumour is characterized by a discrete proliferation of rounded synovial-like cells accompanied by a variable number of multinucleated giant cells, inflammatory cells, siderophages, and xanthoma cells.⁷ This tumour was first described by chassaignac.⁸

The appearance of the giant cell tumor varies depending on the proportion of mononuclear cells, giant cells, xanthoma cells, and the degree of collagenization. Most tumors are moderately cellular and are composed of sheets of round or polygonal cells that blend with hypocellular collagenized zones in which the cells appear slightly spindled. Clef like spaces are occasionally present, particularly in lesions arising near large joints. Some probably represent synovium lined spaces, whereas others are artificial spaces caused by shrinkage and loss of cellular cohesion. Multinucleated giant cells are scattered throughout the lesions. In the typical case they are relatively numerous but become sparse in highly cellular lesions, particularly recurrent ones. Xanthoma cells are also frequent, tend to be located geographically in these tumors, and often contain fine hemosiderin granules. Cartilaginous and osseous metaplasia is a rare focal finding in these tumors. Similar variations were noted in our 9 cases of tenosynovial giant cell tumors.

The diagnosis of giant cell tumor is rarely difficult, but the evaluation of certain atypical features can be problematic. For instance, the presence of mitotic figures occasionally leads to a mistaken diagnosis of a malignant neoplasm.⁹

Rao and vigorita documented 3 or more mitotic figures per 10hpf in more than 10% of their cases.ⁱ⁰ Although it may indicate an actively growing lesion that is likely to recur, there is no evidence to suggest such lesions are at increased risk to metastasize. Similar observations were made in our 1 case out of 7 localized TGCT.

Occasionally, benign lesions located in the vicinity of the tendon sheath are confused with giant cell tumours, including foreign body granulomas, necrobiosis granulomas, tendinous xanthomas, and fibromas of the tendon sheath.¹ⁱ

O’Connell IX, cavaliere, malu demonstrated immunohistochemical markers like CD68, HAM56, MAC387 & PG-M1 in their study.¹⁰¹⁹²¹ Similarly in our study we demonstrated CD68 in 2 cases.

**TENSOYNOVIAL GIANT CELL TUMOR, DIFFUSE TYPE**

(Proliferative synovitis, florid synovitis, extraarticular pigmented villonodular synovitis, pigmented villonodular bursitis).

Diffuse tenosynovial giant cell tumor can be regarded as the soft tissue counterpart of pigmented villonodular synovitis of the joint space. In most instances the lesion probably represents extraarticular extension of a primary intraarticular process, a contention supported by the similarity in age, location, clinical presentation, and symptoms of the two processes. In rare instances this disease resides completely outside a joint, in which case its origin must be ascribed to the synovium of the bursa or tendon sheath.²²²³²⁵

In 2 clinically suspected cases of diffuse /pigmented villonodular synovitis FNAC yielded pale yellow to pale brown coloured fluid aspirate, smears from the centrifuged sediment from fluid showed sheets of synovial cells with occasional papillary clusters and macrophages containing brown cytoplasmic granules of hemosiderin, occasional tunet cell type of multinucleated giant cells were seen. Similar observations were reported by chieng et al (1997).²⁶

Ray A. Ronne, et al reported Trisomy 7 in 24 of 75 (35%) metaphases obtained from short term culture of cells from pigmented villonodular synovitis and concluded that some cases of pigmented villonodular synovitis represent clonal neoplastic proliferations.²⁷
O’Connell John et al., did immuno histochemical study of 35 specimens of GCTS, 12 specimens of PVNS and 3 cases of reactive synovitis and concluded that GCTS/PVNS are tumors of synovial cell origin and do not support an association between GCTS and fibroma of tendon sheath.11

TGCT was diagnosed histopathologically in 9 patients in our study constituting 36% of benign tumour like growths & true neoplasms of the synovium and showed a female preponderance, commonest age group affected was 31-50 years. Interphalangeal joints of hand & knee were the common joint involved, similarly in Srinivas Rao and Vincent J, Vigorita study in 1984, 81 pigmented villonodular synovitis patients were encountered and found that the average age of involvement was around 41.5 years with a female predominance. Knee and fingers were the most commonly involved location in their study.

The histopathological features observed in 81 patients of nodular synovitis by Srinivas Rao and Vincent J, Vigorita showed an incidence of giant cells in 96%, fibrosis in 89%, haemosiderin in 85%, foam cells in 60% and inflammation in 25% of biopsies. In our study giant cells were seen in all the 9 patients, fibrosis in all cases but haemosiderin and inflammation were seen in 3 patients and foam cells in 2 patients only.

CONCLUSION

- Definitive diagnosis of the benign tumor like growths & true neoplasms can be made by combination of fnac, histopathological findings & necessary special stains & immunohistochemistry in certain tumors along with clinical & radiological findings.
- Benign tenosynovial giant cell tumors needs to be distinguished from malignant pigmented villonodular synovitis by looking for the absence of thypical histopathological features.
- Majority of these lesions could be classified into various subgroups by histopathological study.

BIBLIOGRAPHY