Evaluation of etiology of lymphadenopathy in different age groups using Fine Needle Aspiration Cytology: A retrospective study

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Citation

Abstract
Background: Lymphadenopathy is a common presenting symptom in various diseases. Lymph nodes react to various stimuli and undergo changes leading to vast array of neoplastic or non-neoplastic proliferations. FNAC is a simple, quick and inexpensive method that is used to sample superficial masses and is now considered a valuable diagnostic aid.

Objective: The present study was undertaken to evaluate the usefulness of FNAC as a diagnostic tool in cases of lymphadenopathy, to find the frequency and cause of lymph node enlargement in patients of different age groups and analyze the different cytomorphological patterns associated with various lymphadenopathies.

Settings and design: Retrospective study conducted in the Department of Pathology, Subharti Medical College, Meerut from July 2006 to June 2009 (3 years).

Material and Methods: Total 1350 patients of lymphadenopathy who underwent FNAC were divided into 3 groups: Group I including pediatric patients (i.e. 0-15 years), Group II including adolescent and middle aged patients (i.e. 16-45 years) and Group III with elderly patients (i.e. >45 years).

Observation: Maximum number of patients with lymphadenopathy was in Group II with 640 patients (47.4%), followed by Group I: 498 patients (36.89%) and Group III: 212 patients (15.7%). Commonest causes of lymphadenopathy in different groups were found to be: In Group I- reactive hyperplasia 353(70.88%), Group II- Tubercular lymphadenitis 261(40.78%) and Group III- Metastatic carcinoma 115(54.25%).

Conclusion: It was concluded that different etiological factors play role in causation of lymphadenopathy in different age groups and that aspiration cytology provided a reliable, safe, rapid and economical method of screening these patients with accuracy.

INTRODUCTION
Aspiration of lymph nodes for diagnostic purpose was reported as early as 1904 by Grieg and Gray who used this procedure in the diagnosis of trypanosomiasis. In 1921, Guthrie attempted to correlate lymph node aspiration cytology with various disease processes. FNAC is particularly helpful in the work-up of cervical masses and nodules because biopsy of cervical adenopathy should be avoided unless all other diagnostic modalities have failed to establish a diagnosis.

FNAC is nowadays recognized as a rapid diagnostic technique because of its simplicity, early availability of results, minimal trauma and absence of complications.

The aim of this study was: 1) To evaluate the role of FNAC in patients presenting with lymph node enlargement 2) To find out the frequency of lymphadenopathy in different age groups 3) To find out the etiological factors causing lymphadenopathy in different age groups 4) To study the different cytomorphological patterns associated with various lymphadenopathies.

MATERIALS AND METHOD
The present study on 1350 patients of lymphadenopathy was conducted in the Department of Pathology, Subharti Medical College, Meerut over a period of 3 years from July 2006 to June 2009. FNAC of the enlarged lymph nodes was performed with informed consent of the patient. Detailed history was noted. Palpable nodes were aspirated in the
cytology department while guided FNAC (USG, CT) was performed in deep seated ones.

Procedure was done using a 23-25 G needle and 10ml syringe with the help of Franzen handle where required. Smears were stained with Geimsa, Hematoxylin and Eosin (H&E) and Pap stains depending upon the clinical presentation of the patient. In elderly patients more smears (atleast 50%) were fixed in alcohol and stained with Pap and H&E stains. In all cases where there was strong clinical or cytological suspicion of tuberculosis, Ziehl-Neelsen staining was performed to see the presence of acid fast bacilli. The smears prepared were studied to arrive at a probable diagnosis.

**OBSERVATIONS**

A total of 1350 FNAC from various groups of lymph nodes was performed during the course of 3 years (July 2006-June 2009). These cases were divided into three groups depending on their age: Group I including pediatric patients (i.e. 0-15 years), Group II including adolescent and middle aged patients (i.e. 16-45 years) and Group III with elderly patients (i.e. >45 years).

In Group I there were 498 patients with M:F ratio of 2.25:1; in Group II total 640 cases and M:F ratio was 0.7:1; in Group III there were 212 cases with M:F ratio of 3.4:1 (Table 1).

**Figure 1**

Table 1: Age and sex distribution of patients in different groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Age</th>
<th>No. of Patients</th>
<th>% of population</th>
<th>Male</th>
<th>Female</th>
<th>M:F Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0-15</td>
<td>498</td>
<td>36.89</td>
<td>235</td>
<td>263</td>
<td>2.25:1</td>
</tr>
<tr>
<td>II</td>
<td>16-45</td>
<td>640</td>
<td>47.41</td>
<td>263</td>
<td>377</td>
<td>0.7:1</td>
</tr>
<tr>
<td>III</td>
<td>&gt;45</td>
<td>212</td>
<td>15.7</td>
<td>164</td>
<td>48</td>
<td>3.4:1</td>
</tr>
</tbody>
</table>

The commonest chain of lymph nodes involved was cervical chain constituting of 1230 cases (91.1%) followed by axillary lymph nodes in 78 cases (5.78%) (Fig 1).

It was observed that in each of the three groups, the commonest cause of lymphadenopathy was different. In Group I, the most frequent cause of lymphadenopathy was found to be reactive lymphoid hyperplasia with 353 cases (70.88%) followed by tubercular lymphadenitis in 80 cases (16.06%). In Group II, the commonest etiology of lymphadenopathy was found to be tubercular with 261 cases (40.78%) followed by reactive lymphoid hyperplasia with 197 cases (30.77%). Metastasis was observed as the most frequent causative agent of lymphadenopathy with 115 cases (54.25%) in Group III, followed by tubercular lymphadenitis in 26 cases (12.26%) (Table 2).

**Figure 2**

Table 2: Result of FNAC showing frequency distribution of various pathological conditions in each group

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Cases</td>
<td>% of cases</td>
<td>No. of Cases</td>
<td>% of cases</td>
</tr>
<tr>
<td>Reactive Hyperplasia</td>
<td>353</td>
<td>70.88</td>
<td>197</td>
</tr>
<tr>
<td>Tubercular</td>
<td>80</td>
<td>16.06</td>
<td>261</td>
</tr>
<tr>
<td>Suppurative</td>
<td>19</td>
<td>3.81</td>
<td>45</td>
</tr>
<tr>
<td>Metastatic Carcinoma</td>
<td>0</td>
<td>0</td>
<td>45</td>
</tr>
<tr>
<td>NHL</td>
<td>5</td>
<td>1.00</td>
<td>6</td>
</tr>
<tr>
<td>HD</td>
<td>6</td>
<td>0.00</td>
<td>3</td>
</tr>
<tr>
<td>Histoplasmosis</td>
<td>2</td>
<td>0.40</td>
<td>8</td>
</tr>
<tr>
<td>Immuneoblastic lymphadenopathy</td>
<td>3</td>
<td>0.60</td>
<td>3</td>
</tr>
<tr>
<td>Castleman’s Disease</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Granulomatosis</td>
<td>17</td>
<td>3.41</td>
<td>39</td>
</tr>
<tr>
<td>Inadequate</td>
<td>19</td>
<td>3.81</td>
<td>39</td>
</tr>
</tbody>
</table>

Out of total 160 cases of metastatic carcinoma, squamous...
cell variety was predominant (53.12%) followed by adenocarcinoma (Table 3). All patients who had breast lump along with axillary lymphadenopathy were not included in the study.

**Figure 4**

Table 3: Cytomorphological pattern of metastatic carcinoma

<table>
<thead>
<tr>
<th>Type of Metastatic Carcinoma (Total cases)</th>
<th>Group I (No. of patients)</th>
<th>Group II (No. of patients)</th>
<th>Group III (No. of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous Cell Ca</td>
<td>85</td>
<td>21</td>
<td>64</td>
</tr>
<tr>
<td>Adeno Ca</td>
<td>34</td>
<td>11</td>
<td>23</td>
</tr>
<tr>
<td>Poorly Differentiated Ca</td>
<td>19</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Basocellular Ca</td>
<td>7</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Sealf Cell Ca</td>
<td>6</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Large cell Ca</td>
<td>6</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Thyroid Ca</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Adrenal Ca</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total no. of Patients</td>
<td>169</td>
<td>45</td>
<td>115</td>
</tr>
</tbody>
</table>

The cytological diagnosis of reactive hyperplasia was established by presence of high cell density, polymorphic cell population and considerable number of tingible body macrophages.

The diagnosis of tubercular lymphadenitis was made in presence of positive Ziehl-Neelsen stained smears and typical cytological features like epithelioid cell granuloma with or without caseous necrosis (Fig 2).

**Figure 5**

Fig. 2: H & E (x 40X) smear reveals epithelioid cells and multinucleate giant cell

Most of the aspirated cells were mature but a careful search for hyperchromatic irregular nuclei showed more malignant features which were important for confident diagnosis. This is because on rare occasions, the branchial or epidermal cyst aspirate with its content of mature squamous cells may closely mimic a differentiated metastatic carcinoma.\(^1\)

In metastatic adenocarcinomas, the individual cells were large cuboidal to columnar with abundant lacy cytoplasm, often with a pale blue extra cellular mucinous fluid background. Some cells even exhibited vacuoles with definite signet ring cell morphology. The nuclei were round to oval with irregularly thickened nuclear membranes and prominent nucleoli, sometimes making it difficult to rule out a poorly differentiated squamous carcinoma.\(^1\)

Non-Hodgkin’s lymphoma smears showed a monomorphic cell pattern, consisting of lymphoblasts or lymphocytes, the cells being singly scattered. Hodgkin’s lymphoma showed a mixed cell population with characteristic Reed-Sternberg cells.

Histopathological examination was advised in 40 cases comprising of lymphoma, histiocytosis and immunoblastic lymphadenopathy, of which correlation was possible in only 30 cases. In all cases of histiocytosis and Castleman disease
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(angiofollicular lymphoid hyperplasia), histological corroboration was seen where sensitivity and specificity was found to be 100% in our study.

Out of 28 lymphoma cases, cytohistological correlation was possible in only 18 cases. All these showed exact corroboration.

**DISCUSSION**

FNAC is a useful diagnostic adjunct to conventional method of diagnosis in cases of mass lesions. It is a simple, cost effective, safe and time saving procedure. Lymphadenopathy is one of the common clinical presentation of various ongoing disease process inside the body. This study was carried out to find out the relative frequencies of various pathologies presenting as lymph node enlargement in different age groups. The lesions arising in the lymph node can be found in patients ranging from early to advanced age. In our study the youngest patient was 3 months old and oldest was 85 years of age. These figures come in close comparison to other studies.

Fine needle aspiration cytology was performed in 1350 cases of lymphadenopathy, both superficial and deep. The male preponderance seen in our study correlates well with studies done by Ahmad, Hag and Izhar et al.

As observed by Tariq et al and Ruchi et al, in our study also the most common group of lymph nodes involved was cervical group (91.1%) followed by axillary group (5.78%) and inguinal lymph nodes (3.18%).

Various causes have been found to be responsible for lymphadenopathy and their frequency varies according to the age of the patient. It was observed that in pediatric age group the commonest cause of lymphadenopathy was reactive hyperplasia (70.88%) while tubercular lymphadenitis outnumbered other causes of lymph node enlargement in adolescents and middle aged patients (40.78%). This was noted in concordance with other studies done by Ruchi et al.

Metastatic carcinoma constituted as a major cause of lymphadenopathy in patients above 45 years of age (54.24%). The most common tumor metastatizing to the neck nodes was the squamous carcinoma (53.12% of all metastatic lymph nodes) arising commonly in the tongue, alveolus, buccal mucosa and palate followed by adenocarcinoma (21.25%). Metastatic adenocarcinomas commonly originate from either salivary glands, thyroid, breast, lung, kidney, prostate and gonads, etc. Aspirates with papillary branching, three-dimensional groups of cells may originate from thyroid, salivary glands, breast, lung and rarely even the ovary.

Out of total 1350 patients, the most common etiological factor in lymphadenopathy was Reactive with 412 (30.5%) cases followed by tubercular with 367 (27.1%) cases which is comparable with studies done by Ahmad et al and Hirachand et al. (Table 4)

**Figure 7**

Table 4: Comparison of different studies with present study

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Duration of study (years)</th>
<th>Reactivenspecific lymphadenitis (%)</th>
<th>TB lymphadenitis (%)</th>
<th>Metastatic (%)</th>
<th>Inconclusive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present Study</td>
<td>1350</td>
<td>3</td>
<td>53.6</td>
<td>38.2</td>
<td>11.3</td>
</tr>
<tr>
<td>Ahmad et al</td>
<td>1000</td>
<td>3</td>
<td>53.6</td>
<td>39.0</td>
<td>17.4</td>
</tr>
<tr>
<td>Kamal F et al</td>
<td>847</td>
<td>3</td>
<td>32.8</td>
<td>42.7</td>
<td>15.3</td>
</tr>
<tr>
<td>Rechi K et al</td>
<td>656</td>
<td>1</td>
<td>32.8</td>
<td>41.3</td>
<td>13.7</td>
</tr>
<tr>
<td>Hirachand et al</td>
<td>130</td>
<td>1</td>
<td>32.8</td>
<td>42.7</td>
<td>13.7</td>
</tr>
</tbody>
</table>

Hirachand et al and Hajdu et al also noted that the commonest type of metastatic carcinoma to lymph node was of squamous cell variety followed by adenocarcinoma. Lymphoma (both NHL and Hodgkin’s) was found in 2% cases which is lower than the result reported in other studies. Out of 40 cases of lymphoma, histiocytic and immunoblastic lymphadenopathy and Castleman disease 30 were confirmed histopathologically. Of the 28 lymphoma cases histological correlation was possible in 18 cases. Diagnostic accuracy was observed to be 100% in these cases. Ruchi et al, Gupta et al (1977) and Tripathi et al (1985) reported it as 84%, 82% and 80% respectively in their study of lymphoma cases.
CONCLUSION

We conclude that there were different etiological factors playing role in causation of lymphadenopathy in different age groups.

Commonest causes of lymphadenopathy in 0-15 years age group was reactive hyperplasia, in 16-45 years tubercular lymphadenitis and metastatic carcinoma in patients more than 45 years of age. Considering these statistical data it can be suggested that while doing lymph node FNAC in patients >45 years of age, a precaution should be taken to make wet fixed smears more and also should keep unstained smears for special histochemical stains e.g. for mucin etc. Though the diagnostic accuracy of FNAC is low as compared to histological examination, it is a valuable and reliable screening tool in outpatient clinics. Following the cytodiagnosis, decision regarding the requirement of histological examination can be made and patient managed with a curative or palliative approach.

References

2. Tariq Ahmad, Mohammad Naeem, Siddique Ahmad, Ambreen Samad. Fine Needle Aspiration Cytology (Fnac) And Neck Swellings In The Surgical Outpatient, J Ayub Med Coll Abbottabad 2008; 20(3): 30-32
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