

Original Article

Fine Needle Aspiration Cytology of Lymph Nodes : A Mirror in The Diagnosis of Spectrum of Lymph Node Lesions

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Abstract

Background: Fine Needle Aspiration Cytology (FNAC) is a diagnostic technique useful in management of lymphadenopathies

Objective of study: The aim of this study was to study the cytological features of lymphadenopathies and categorize them and to determine the utility and predictive value of FNAC in diagnosing lymphomas and metastatic deposits.

Methods: Smears from 300 cases of lymphadenopathies were reviewed. The period of study was from May 2005 April 2007. Histopathology was done in 29 cases (21 cases of metastasis and 08 cases of lymphomas). SPSS package was used for descriptive analysis and calculation of p-value, p-value < 0.05 was considered significant.

Results: There was male preponderance of cases. Benign lymphadenopathies constituted 66 % of cases. Metastatic deposits constituted 26 % of cases, lymphomas constituted 6 % of cases. Aspirates were inadequate in 2 % of cases. The positive predictive value of diagnosing metastatic deposits and Non Hodgkins Lymphoma on Fine Needle Aspiration Cytology were 98 % and 90 % respectively. There were no false positive cases. The p - value in both metastatic deposit and NHL was > 0.05.

Conclusion: Fine needle aspiration is safe, rapid and minimally invasive procedure and can be used as an initial investigative tool in management of lymphadenopathies.

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Introduction

Lymph nodes are part of peripheral immune system located along the course of lymphatics. They act as a mirror of underlying disease process. Enlargement of lymph node - lymphadenopathy may be due to infections, autoimmune diseases, metabolic disorder, malignancies etc. Very often lymphadenopathy may be the only manifestation of underlying occult malignancy.^[1]

Lymphadenopathies are one of the most common clinical presentations attending both outpatient and inpatient departments in many hospitals. Before the advent of fine needle aspiration cytology definite diagnosis of lymphadenopathies were done after surgical excision followed by histopathological examination. With the introduction of fine needle aspiration cytology, all the peripheral nodes that can be easily needled and deep nodes needled through ultrasonography guidance can be assessed to arrive at a workable diagnosis.

Further, lot of data is available regarding the etiology of lymphadenopathies from urban population and little from rural population. This has compelled us to take up this study with an aim of

1. To study cytological features in various lymphadenopathies and categorize them
2. To study spectrum of lesions with respect to age
3. To study and record cytomorphological features of rare lesions,
4. To determine the utility and positive predictive value of FNAC in diagnosing metastatic deposit and NHL.

MATERIALS AND METHODS

Prospective study of 300 cases of lymphadenopathy presenting to department of Pathology, SDUMC for duration of 2 years was taken up for our study. All patients with enlarged superficial lymph nodes, patients with enlarged deep lymph nodes presenting to our department were included in our study. Very tiny nodes (less than 0.5 centimeters) were excluded from our study.

These patients were clinically evaluated and informed consent was obtained. The limitations and complications of *FNAC* were explained to the patient. After doing FNAC of both superficial and deep nodes (accessed through USG) four smears were made; two of them were fixed in a fixative containing ethyl alcohol, later to be stained with *PAP* and *H & E*. Two smears were air-dried followed by staining with *MGG*, *ZN* stain and *PAS*.

In cases where fluid was aspirated, fluid was centrifuged and smears were made from the sediment followed by above staining methods.

Lymph node biopsy was done in 29 cases (21 cases of metastasis and 08 cases of lymphomas) the number of cases available for histopathological analysis was less because reactive lymph nodes and tubercular lymph nodes were treated conservatively. Few patients with malignancies were lost for follow up. Lymph nodes were fixed in formalin; bits were given from entire node. Tissue was processed routinely. Clearing of the slides was done, which was followed by *H & E* staining. Special stains such as Reticulin and *PAS* were used whenever required.

For descriptive statistical analysis *SPSS* package was used.

RESULTS

Fine needle aspiration was done in 300 patients who had lymphadenopathies. Results are as follows:

The age of the patients varied from 2 months to 85 years. Male to female ratio was 5:4. The maximum numbers of cases were seen in the age group of 20 - 29 years and only 5 cases were

seen in age group of 80 - 89 years.

Out of 300 cases 198 cases were benign lymphadenopathies, 80 cases of metastasis, and 16 cases of lymphomas. In 6 cases the aspirate was inadequate and hence inconclusive.

The distribution of benign lymphadenopathies is represented in Table 1. In 69 cases ZN staining was done to demonstrate AFB. Thirty-seven cases (52%) were positive for AFB. Among 32/37 cases (86.5%) were of granulomatous lymphadenitis, (Fig 1 showing numerous epithelioid granulomas in a background of lymphocytes) 3/37 (8.5%) were from necrotic material, 1/37 case each from suppurative and calcified lymph node.

In our study a total number of seven cases were positive for HIV antibody test. Three had granulomatous lymph node, two had reactive nodes and two had non Hodgkin's lymphoma.

Cytological evidence of metastasis was present in 80 cases. Of this 48 cases were from squamous cell carcinoma, 15 cases were from adenocarcinoma, 6 were from poorly differentiated carcinoma and 4 were from papillary carcinoma of thyroid. There were 3 cases of metastasis of seminoma and 1 case each of metastasis from nasopharyngeal carcinoma, malignant melanoma, germ cell tumor and carcinoid.

Squamous cell carcinoma was the most frequently diagnosed (60 %) metastatic deposits in lymph nodes. The primary sites of origin were from malignancies of head and neck region, lung, cervix and anal canal. Cytohistopathological correlation was done in 7 cases and all cases correlated.

Diagnosis of adenocarcinoma was made

in 19 % of metastatic deposits. (Fig 2 showing tumor cells arranged in glandular pattern. Few cells showing prominent nucleoli). The primary sites of origin were from malignancies of breast, stomach, anal canal and lung. Histopathology was done in 2 cases. Both cases correlated.

We diagnosed 6 cases of poorly differentiated carcinoma. Histopathology was done in 4 cases. 3 cases on cytology correlated with histopathology while one case turned out to be adenocarcinoma on histopathology. Four cases of papillary carcinoma of thyroid deposit were diagnosed on cytology. Histopathology was done in all 4 cases and cytohistopathological correlation was positive in all 4 cases.

Metastatic seminoma was diagnosed in three men aged less than 40 years of age. Histopathological correlation was correct in 2 cases while one case turned out to be Immunoblastic lymphoma on histopathology.

One case each of metastasis from nasopharyngeal carcinoma, malignant melanoma, germ cell tumor and carcinoid were diagnosed. One case of carcinoid turned out to be non Hodgkin's lymphoma on histopathology.

Sixteen cases of lymphomas were diagnosed, 12 were categorized as NHL and 4 cases were of Hodgkin's lymphoma. Four cases of Hodgkin's lymphoma had characteristic bimodal age distribution was diagnosed, of them three cases were less than 20 years of age while one case was in a 80 year old person.

Subtyping was done in four cases of Hodgkins lymphoma. Two cases were subtyped as mixed cellularity, one case as nodular sclerosis variant and one case as lymphocyte predominance. Histopathological examination

was done in three cases of Hodgkin's lymphoma. All three cases correlated with cytological diagnosis. Subtyping of NHL was done on FNAC in all 12 cases.(Fig 3 showing small lymphocytic lymphoma with mature small lymphocytes). Histopathological examination was done in five cases of non Hodgkin's lymphoma. All five cases correlated with cytological diagnosis.

Statistical analysis was done using chi-square test. Positive predictive value in diagnosing metastatic deposit on FNAC is 98%. Positive predictive value in diagnosing NHL on FNAC is 90%. P value in both was >0.05. p value of > 0.05 was considered as not significant.

DISCUSSION

FNAC of lymph nodes is one of the routinely used diagnostic procedures in patients presenting with lymphadenopathy. Male preponderance of cases correlated with study by *Gupta et al.*^[2]

Adequate material was obtained in 98% of the cases. No untoward complications occurred in any of the cases during guided aspiration. Our study correlated with study by *Gupta et al.*^[2] Where adequate material was obtained in 85.2 % of cases.

Aspirates were benign in 66 % of cases; metastatic deposits were found in 26 % of cases and lymphomas in 6 % of cases. Same findings has been reported by other authors.^[3,4,5]

We diagnosed 87 cases of reactive lymphadenopathy (44 %) two cases were of infectious mononucleosis etiology in the age group of 0-9 years. The etiology in both cases was confirmed by Paul Bunnell test. A case of

reactive node was also reported in a patient with rheumatoid arthritis with raised rheumatoid factor. Our study correlated with studies by *Patra et al* where 39 % of aspirated nodes were reactive.^[4] Suppurative lymphadenitis was diagnosed in 9.5 % of cases. The distribution of cases correlated with other cases.^[6]

Granulomatous lymphadenitis was diagnosed in 78 (39 %) of cases. This finding correlated with studies by *Gupta et al.*^[3] (34 %), *Malakar et al.*^[7] (39 %). Maximum numbers of lesions were diagnosed in patients aged less than 40yrs. Similar age distribution was also found by *Ng et al.*^[8]

Ziehl Neelson staining for AFB was positive in 52% of our cases. *Ng et al* was reported positivity in 41.6 % cases while *Ahmed et al* have reported positivity in 46 % of cases.^[8,9] Out of 9 cases of necrotic aspirates ZN stain was done in 4 cases. AFB was positive in 3 cases. Similar findings were found in study by *Malakar et al.*^[7]

From a total of 300 patients seven were positive for HIV antibody test. There were two cases of reactive lymphadenitis and NHL. Three cases were granulomatous lymphadenitis with AFB positivity. Our findings correlated with other studies.^[10,11] Cases of metastatic deposits, fungal infections were not seen in our HIV antibody positive patients are due to less number of HIV cases in present study.

The diagnosis of sinus histiocytosis was made in 3 cases, who were more than 20 years of age with nodes measuring more than 3x2 centimeters. Our findings correlated with studies by *Stastny.*^[12] One case of dermatopathic lymphadenitis was diagnosed in a patient with a

Table 1- Distribution of Cases in Benign Lesions

Table 2: Distribution of metastatic deposits in various studies

Fig 1: Granulomatous Lymphadenitis showing epithelioid cell collections, giant cell in a background of lymphocytes. MGG x 400. Inset shows ZN stain positive for acid fast bacilli. (ZN x 1000)

Fig 2: Adenocarcinoma deposit showing cells in glandular arrangement. MGG x 1000
Inset shows individual cells with prominent nucleoli. (PAP x 400)

Fig 3: Non Hodgkins lymphoma. Small lymphocytic lymphoma showing monotonous Population of small lymphocytes. (MGG x 400)

scalp lesion. Cytological features were similar to cases described by *Sudilovsky et al.*^[13]

Lymph node aspirates in 80 cases showed metastatic deposits. The finding of metastatic deposit correlate well with other studies mentioned in Table 2.^[14,15] Compared to studies by *Lui et al.*^[16] and *Raghuveer et al.*^[5] in our study 60% of deposits were from Squamous cell carcinoma deposits 19% were from adenocarcinoma. This high incidence of squamous cell carcinoma in our study can be attributed to increased incidence of head and neck cancers in our region due to tobacco chewing.

One out of three cases of seminoma, showed immunoblastic lymphoma on histopathology.. The erroneous diagnosis was because of the similarity between seminoma cells and immunoblast. Similar findings were described by *Shek et al.*^[17]

There was one case of metastasis of carcinoid tumor in mediastinal lymph node, which turned out to be NHL on histopathology. Presence of neuroendocrine round to oval nuclei, stippled nuclear chromatin and inconspicuous nucleoli and plexiform background of small blood vessels helps to make a definitive diagnosis of carcinoid tumor.^[18]

Black colored fluid akin to melanin pigment was aspirated in a patient with history of amputation of great toe from inguinal node. A cytological diagnosis of malignant melanoma deposit was made. Similar findings were found by *Lori et al.*^[19] .

Lymphomas constituted 6% of our study. This was in accordance with other studies.^[20] In

one case of lymphocyte predominance numerous atypical cells and few RS cells were present. Inadequate sample, fibrosed nodes in advanced disease may be the cause of lack of RS cells. *Chhieng et al* also reported presence of such atypical cells on cytology.^[20]

However age of the patient, polymorphous population of cells and atypical cells should raise a suspicion of Hodgkin's lymphoma in presence of numerous atypical cells that the diagnosis can be confirmed by immunocytochemistry.

Fine needle aspiration of lymph nodes revealed 12 cases of Non - Hodgkin's lymphoma. An attempt to sub classify all 12 cases was made as suggested by *Katz et al.*^[21] Entities that can be diagnosed definitively on FNAC include high-grade lymphoma like small non-cleaved lymphoma, lymphoblastic lymphoma, Immunoblastic lymphomas, myeloblastic, lymphoblastic leukemia/lymphoma, Hodgkin's disease and Diffuse large cell lymphoma.^[22]

p-value in diagnosing both metastasis deposit and lymphoma on FNAC was >0.05 suggesting that there was no statistically significant difference between two procedures namely FNAC and histopathology in arriving at the diagnosis emphasizing that FNAC is as good as histopathological examination in diagnosing lymphomas and metastatic deposits

CONCLUSION

FNAC diagnosis will help the clinician to confirm or exclude the clinical differential diagnosis made at first visit of the patient on OPD basis and helps the clinician in early treatment without extensive surgical

interference. Hence biopsy was not indicated in benign lesions as they were treated conservatively. Because of this reason less number of cases were available for histopathological correlation.

Though the numbers of cases with histopathology correlation were less, the role of FNAC as an initial investigative procedure is undisputed. To define the role of FNAC in managing lymphomas a multiparametric approach has to be done involving larger population.

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