



Reaffirming the Diagnostic Role of Fine Needle Aspiration Cytology in an Analytical Study of Clinico-pathological Profile of Peripheral Lymphadenopathy

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Authors' contributions

This work was carried out in collaboration between all authors. Authors KB, DD and PR designed the study, performed the statistical analysis, wrote the protocol and the first draft of the manuscript and literature searches which was guided by author GK and was reviewed by author PB. All authors read and approved the final manuscript.

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ABSTRACT

Background: Lymphadenopathy is one of the commonest manifestations of a variety of diseases of diverse etiology. Tuberculosis, metastasis, acute suppurations and lymphomas are some of the entities. Fine needle aspiration cytology is a precise diagnostic technique for evaluation of different causations of lymphadenopathy and is comparable to the gold standard test excision biopsy and histopathological examination.

Aims and Objectives: The study was designed to evaluate the clinicopathological profile of patients presenting with peripheral lymphadenopathy, establishing the role of fine needle aspiration cytology in the etiological diagnosis and to assess its sensitivity and specificity to correlate the findings with histopathological examination.

Materials and Methods: One year single centered hospital based prospective analytical study

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was conducted in a tertiary care teaching hospital in north eastern India among 100 adult patients aged above 15 years presenting with accessible peripheral lymphadenopathy.

Results and Observation: A male preponderance with maximum occurrence in the age group 15-40 years with features of neck swelling, fever, night sweats, unilateral cervical lymphnode involvement, anemia and raised ESR were common. Fine needle aspiration cytology was successfully done in 98% cases whereas excision biopsy in 90% cases. Diagnosis arrived on the basis of aspiration cytology and histopathology were tubercular in 52.04% vs 52.22%, metastasis in 25.51% vs 28.88%, nonspecific reactive lymphadenitis in 17.34% vs 13.33%. Hodgkin's and Non-Hodgkin's lymphoma in 2.04% vs 2.22% and 3.06% vs 3.33% cases respectively. The respective sensitivity and specificity of aspiration cytology vis-a-vis histopathology obtained in various groups are statistically significant ($p < 0.0001$) in each of tuberculosis 95.65% vs 100%, metastasis 96% vs 100%, nonspecific reactive lymphadenitis 100% vs 96%, Hodgkin's lymphoma and Non-Hodgkin's lymphoma 100% vs 100%.

Conclusion: Peripheral lymphadenopathy is a manifestation of a variety of diseases and fine needle aspiration cytology is a convenient and accurate diagnostic tool in evaluation of lymphadenopathies.

Keywords: Anemia; biopsy; fine needle aspiration cytology; lymphadenitis; Hodgkin's lymphoma and Non-Hodgkin's lymphoma.

1. INTRODUCTION

Lymphadenopathy is classically described as a lymph node larger than 1 cm although this varies in different lymphatic region. Palpable supraclavicular, iliac or popliteal node of any size, epitrochlear nodes larger than 5 mm or inguinal nodes >1.5 cm are said to be clinically significant [1,2,3]. Lymphadenopathy is classified as "Generalised" if lymph nodes are enlarged in two or more non-contiguous areas and "Localised" if only one area is involved [4]. It can be either acute or chronic. In acute condition, the nodes are enlarged and tender along with various constitutional symptoms like fever, malaise, local pain and tenderness etc. whereas in chronic variety the nodes are painless and non-tender with delayed development of constitutional symptoms [5].

In developing countries like India, acute respiratory infections, suppurative skin lesions and tuberculosis are the major causes of regional lymphadenopathy. TB has been a major cause of suffering and death in the world wide with a major adverse impact on the developing nations. Tubercular lymphadenitis is the commonest form of extra pulmonary tuberculosis (EPT) and is seen in 35% of EPT and constitutes 15-20% of all TB cases. Metastatic involvement of lymph nodes forms the next common group [6,7,8].

Fine needle aspiration cytology (FNAC) is a simple, convenient and precise diagnostic procedure used not only to differentiate between benign and malignant nodes but also is quite

helpful in pinpointing the actual diagnosis [9,10]. Diagnosis of lymphadenopathy depends mainly on excision of the gland and subsequent histopathological examination (HPE) [11]. FNAC on the other hand is a rapid, simple, cost effective and safe alternative investigative technique and is helpful in diagnosing conditions like reactive hyperplasia, infections, granulomatous lymphadenitis and metastatic diseases [8].

1.1 Aims and Objectives

1. To study the clinico-pathological profile in adult patients presenting with peripheral lymphadenopathy.
2. To evaluate the role of FNAC in establishing the etiology of peripheral lymphadenopathy.
3. To assess the sensitivity and specificity of FNAC in the etiological diagnosis of peripheral lymphadenopathy and to correlate the findings of FNAC with HPE.

2. MATERIALS AND METHODS

A one year single centered hospital based prospective analytical study was conducted at the Department of Medicine, Silchar Medical College and Hospital, Silchar, Assam which is a tertiary care teaching hospital in north eastern India catering the needs of patients from four southern districts of Assam viz Cachar, Karimganj, Hailakandi and Dima Hasao and the neighboring states of Tripura, Manipur and Mizoram.

100 cases of peripheral lymphadenopathy meeting the selection criteria attending the above hospital were selected for study.

2.1 Inclusion Criteria

Patients aged above 15 years presenting with peripheral lymphadenopathy like cervical, iliac, epitrochlear, axillary, popliteal, inguinal and other accessible lymph node.

2.2 Exclusion Criteria

Patients aged less than 15 years or those with central and clinically inaccessible nodes or epitrochlear nodes <5 mm or inguinal nodes <1.5 cm or cases already diagnosed with or without specific therapy.

3. RESULTS AND OBSERVATIONS

In the present study, the age of patients varied from 15 to 76 years, the commonest being in the age group 21-30 years (24%) followed by the age group 15-20 and 31-40 years respectively with an incidence of 18% in each. The number of males were 59 (59%) and the remaining 41(41%) cases were females, the male female ratio being 1.43: 1. The mean age was 37.98±17.19 years for males and 37.97±16.92 years for females respectively.

Clinical features included neck swelling in 73 (73%), fever in 28 (28%), night sweats in 19 (19%), weight loss in 16 (16%), dysphagia and cough in 11(11%) each, hemoptysis in 6 (6%) and hoarseness of voice in 5 (5%) of cases respectively. Duration of symptoms were <30 days in 54 (54%), 31-60 days in 20 (20%) and >61 days in 26 (26%) cases respectively. Distribution of lymph nodes were unilateral in 90 (90%) of cases right sided being commoner than the left sided ones, bilateral in 4 (4%) and generalized in 6 (6%) cases respectively. Cervical nodes accounted for 79 (79%) of cases followed by axillary in 9 (9%), inguinal and generalized nodes in 6 (6%) cases each respectively. Discrete nodes were seen in 60 (60%) cases while the remaining 40 (40%) had matted nodes. Single node were seen in 9 (9%) cases whereas 54 (54%), 35 (35%) and 2 (2%) presented with two, three and four nodes respectively.

Blood parameters showed Hb>11.0 gm/dl in 32 (32%) cases, 8-10.9 gm/dl in 56 (56%) and <7.9

gm/dl in 12 (12%) while ESR (at the end of first hour) <20 mm in 32 (32%) and >20 in 68 (68%) of cases.

FNAC was done successfully in 98 (98%) cases whereas in 2 (2%) cases aspirated material was inadequate despite repeated attempts. The diagnosis arrived on the basis of FNAC were tubercular (TB) in 51 (52.04%), metastasis (MET) in 25 (25.51%), non-specific reactive lymphadenitis (NSRL) in 17 (17.34%), Hodgkin's lymphoma (HL) in 2 (2.04%) and Non-Hodgkin's lymphoma (NHL) in 3(3.06%) cases respectively.

HPE was done in 90 (90%) of cases including the two cases where FNAC was unsuccessful. However, 10 (10%) cases opted out due to various reasons. The diagnosis based on HPE which is considered as gold standard were TB in 47 (52.22%), metastasis in 26 (28.88%), NSRL in 12 (13.33%), HL in 2 (2.22%) and NHL in 3 (3.33%) cases respectively.

In the present study, the results of HPE were considered as the final diagnosis in those 90 cases where HPE was done. FNAC results were considered as final in only those 10 cases where HPE was not done.

Both FNAC and HPE was done successfully in 88 cases and the results are compared in the Table 2.

Among 15 cases of NSRL diagnosed on the basis of FNAC, 2 were later diagnosed as TB and 1 as metastasis on the basis of HPE (Table 2).

The Sensitivity and specificity of FNAC considering HPE as the gold standard is depicted in Table 3.

Table 1. Showing the etiological diagnosis based on HPE and FNAC and FNAC only

Final diagnosis	Both FNAC and HPE results	FNAC result only	Total (pc)
TB	47	7	54(54%)
Metastasis	26	1	27(27%)
NSRL	12	2	14(14%)
HL	2	0	2(2%)
NHL	3	0	3(3%)

(TB- tuberculosis, NSRL- nonspecific reactive lymphadenopathy, HL- Hodgkin's, NHL- Non Hodgkin's lymphoma, FNAC- Fine needle aspiration cytology, HPE- Histopathological examination)

Table 2. Comparison of findings in FNAC and HPE

Diagnostic test	TB	Metastasis	NSRL	HL	NHL	Total
FNAC	44	24	15	2	3	88
HPE	46	25	12	2	3	88

Table 3. Sensitivity and specificity of FNAC

Diseases	FNAC results	Final diagnosis (HPE results)	Sensitivity	Specificity	P value
TB	44	46	95.65%	100%	<0.0001
Metastasis	24	25	96%	100%	<0.0001
NSRL	15	12	100%	96%	<0.0001
HL	2	2	100%	100%	<0.0001
NHL	3	3	100%	100%	<0.0001

In the present series, age varied from 15-76 years. The commonest age group involved were in TB lymphadenitis 21-30 years (37.03%, p<0.05), metastatic lymphadenitis in 61-70 years (33.33%, p<0.0001) and NSRL in 15-20 years (50%, p<0.05) respectively. In the age group 51-60 years 1 case each of HL and NHL and in the age group 61-70 years 1 case of HL and 2 cases of NHL in the age group 71-80 years were observed (Fig. 1). The mean age for TB, metastasis, NSRL, HL and NHL were (30.98±12.44), (52.33±11.36), (26.92±12.27), (61.5±10.6) and (69.33±9.86) years respectively. The male female ratio in different etiologies are 1.16:1 in TB, 1.7:1 in metastatic, 1.33:1 in NSRL while all the cases of HL and NHL were males. The overall male female ratio in all cases of lymphadenopathy in the present series was 1.43:1.

The clinical features of different etiologies of peripheral lymphadenopathy are shown in the Table 4.

4. DISCUSSION

In the present study the age of the patients varied from 15-76 years with a maximum (24%) in the age group 21-30 years, which is in agreement with Chawla, Nitin et al. [12] who reported maximum incidence of 27% cases in the same age group.

In the present series 59% of cases were male and 41% female with a male to female ratio of 1.43:1 observed is in agreement with a larger series by Quadri, Sumyra Khurshid et al. [13] where the reported ratio was 1.5:1.

The clinical features in the present series included neck swelling (73%), fever (28%), night

sweats (19%), weight loss (16%), cough and dysphagia in 11% each, hemoptysis (6%) and hoarseness of voice (5%), with 54% of total cases reporting with symptoms of < 30 days duration whereas local swelling in 75.6% and fever in 32.9% with other symptoms like night sweats, weight loss etc. were reported by Abdulla, A. Abba et al. [13].

In the present series, cervical, axillary, inguinal and generalised lymphadenopathy were observed in 79%, 9%, 6%, and 6% of cases respectively which is in agreement with Singh, Arjun et al. [14] who observed involvement in 81.12%, 8.98%, 3.1% and 6.7% in cervical, axillary, inguinal and generalised lymphadenopathy respectively.

In the present series, 90% of the cases had unilateral involvement and 4% and 6% had bilateral and generalised involvement respectively. Right sided involvement were seen in 54% of the cases and single nodal involvement in 9% cases whereas two, three and four nodal involvement were seen 54%, 35% and 2% cases respectively. Right sided involvement of 46.84% and 47% were observed by Shrivastava, Jyoti Priyadarshini et al. [15] and Abhishek Maheshwari et al. [16] respectively which is in agreement with the present series though a higher bilateral involvement (20%) were observed by the later. Distribution of the lymph nodes observed in present series could not be compared with other studies due to paucity of adequate literature in this field.

In the present series, all the patients had varying degrees of anemia. Mild, moderate and severe anemia was noted in 32%, 56% and 12% of cases respectively. Due to inadequacy of literature in this field comparative studies with other workers were not possible.

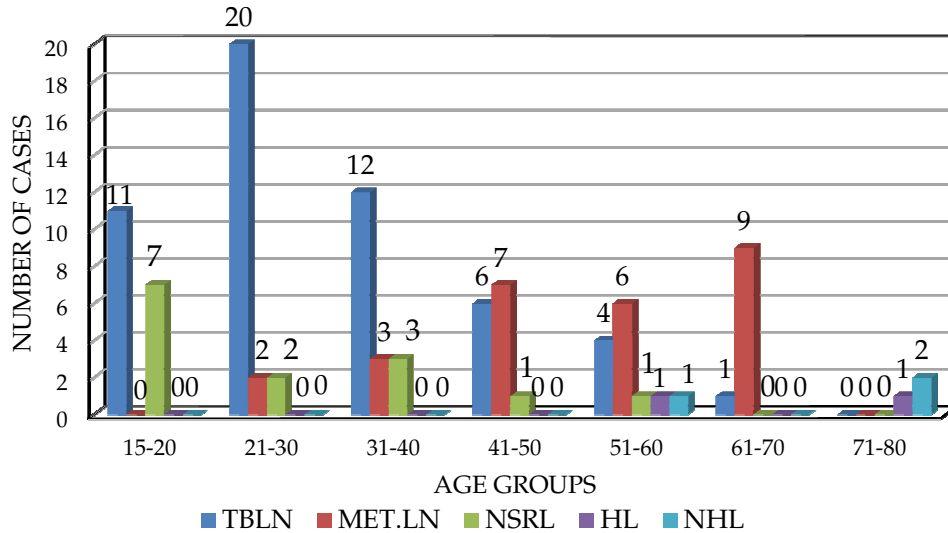


Fig. 1. Age distribution in different causes of peripheral lymphadenopathy

Table 4. Clinical spectrum of diseases of peripheral lymphadenopathy

Clinical features	TBLN (54 cases)	MET.LN (27 cases)	NSRL (14 cases)	HL (2 cases)	NHL (3 cases)
Neck swelling	43 (79.62%)	16 (59.25%)	10 (71.42%)	2 (100%)	2 (66%)
Fever	18 (33.33%)	3 (11.8%)	4 (28.57%)	1 (50%)	2 (66%)
Cough	6 (11.11%)	4 (14.81%)	1 (7.14%)	0 (0%)	0 (0%)
Weight loss	8 (14.81%)	5 (18.51%)	0 (0%)	1 (50%)	2 (66%)
Dysphagia	1 (1.85%)	10 (37.03%)	0 (0%)	0 (0%)	0 (0%)
Night sweats	8 (14.81%)	8 (29.62%)	2 (14.28%)	1 (50%)	0 (0%)
Hemoptysis	1 (1.85%)	5 (18.51%)	0 (0%)	0 (0%)	0 (0%)
Hoarseness of voice	1 (1.85%)	4 (14.81%)	0 (0%)	0 (0%)	0 (0%)
No symptoms	4 (7.40%)	1 (3.70%)	2 (14.28%)	0 (0%)	1 (33%)

In the present series, diagnosis of lymphadenopathy on the basis of FNAC were tubercular, metastatic, NSRL, HL and NHL in 52.04%, 25.51%, 17.34%, 2.04% and 3.06% of cases respectively which is almost similar with the findings of Patel, Mandakini et al. [17] series who observed tubercular, metastatic, reactive lymphadenitis and lymphoma in 50.52%, 27.06%, 14.66% and 2.76 % cases of lymphadenopathy respectively.

In the present series, among 100 cases, biopsy and histopathological examination were done in 90 cases and remaining 10 dropped out due to various reasons.

Diagnosis of lymphadenopathy on the basis of HPE were tubercular (52.22%), metastatic (31.11%), NSRL (13.33%) , HL (2.22%) and NHL (3.33%) of cases respectively whereas Kamat, Girish C [18] in a relatively larger series of 244 cases reported similar findings in TBLN

(58.19%), HL (3.27%) and NHL (0.4%) and dissimilar findings in metastatic (7.37%) and NSRL (30.73%) of cases respectively.

In the present study, the sensitivity and specificity of FNAC in diagnosing tubercular lymphadenitis are 95.65% and 100% respectively whereas observations by Shilpa G et al. [19] and Ahmad, S. Shamshad et al. [20] were 97.2% vs 100% and 97% vs 97.5% respectively.

In the present series, the sensitivity and specificity of FNAC in diagnosing metastasis was 96% and 100% similar to the findings of Singh, Arjun et al. [14] (97.5% and 100%) and Qadri, Sumyra Khurshid, et al. [21] (97.9% and 99.1%) respectively.

The sensitivity and specificity of FNAC in NSRL in the present series was 100% and 96% respectively which is in agreement with Singh, Arjun et al. [14] (100% and 97.3%) and Ahmad, S. Shamshad, et al. [20] (91.6% and 99%) respectively.

The sensitivity and specificity of FNAC was 100% each in the present series as well as that of D. Malakar et al. [22] in the diagnosis of lymphoma.

In the present study, final diagnosis was made on the basis of FNAC and histopathological studies. FNAC was conducted in all 100 cases, however inadequate specimen were obtained in 2 cases where a definitive diagnosis was not possible. Histopathological examination was done in 90 cases including those 2 cases of inadequate specimen. FNAC was considered as final diagnostic tool in those 10 cases where HPE was not possible due to different reasons.

In present series, out of 100 cases of peripheral lymphadenopathy the etiological diagnosis arrived on the basis of HPE and FNAC and FNAC alone were TBLN in 54% cases, followed by metastatic in 27%, NSRL in 14%, HL in 2% and NHL in 3% respectively. Patel, Mandakini et al. [17] and Pavithra P, Geetha JP [23] in their respective series revealed TBLN (50.52% and 42.31%), metastatic (27.06% and 20.06%), NSRL (14.66% and 17.55%) and lymphoma (2.76% and 1.56%) which is comparable to the present study.

Peak incidence of TBLN was found in 21-30 year age group (37.03%, $p= 0.0285$) similar to the findings (32.3%) of Nidhi, Paliwal, et al. 2011 [24]. The metastatic disease of lymph node were more commonly seen in 61-70 year age group

(33.33%, $p< 0.0001$), whereas 81.47% of the total number of cases of metastasis were above 40 years of age and on the other hand the respective figures were 88% and 84.9% in the series by Khajuria, Ruchi et al. [25] and Shilpa, G et al. [19]. In the present series, 50% of NSRL were in the age group 15-20 years ($p=0.0031$) whereas Abba, Abdullah A et al. [13] reported 44% of NSRL below 20 years of age. Hodgkin's lymphoma was observed in only 2 cases (2%), both of which were above 50 years of age. Siddiqui, Neelam et al. [26] found similar results with majority of the cases above 50 years. Incidence of NHL was only 3 (3%), one of whom was in 51-60 year age group and remaining two in 71-80 year age group respectively whereas Khajuria, Ruchi et al. [25] observed 5 out of 8 cases above 50 years of age.

In the present series male preponderance were observed in all groups with respective male and female ratio in TBLN, metastatic lymphadenopathy, NSRL of 1.16:1, 1.7:1, 1.33:1 whereas all HL and NHL were males. The sex ratio observed by Qadri, Sumyra Khurshid, et al. [21] were 1.23:1, 1.37:1, 1.35:1, 3:1 and 2.81:1 for TBLN, metastasis, NSRL, HL and NHL respectively which is comparable to the present series.

Common symptomatology in TBLN in the present series included neck swelling, fever and weight loss in 79.62%, 33.33%, and 14.81% respectively similar to the findings (79.3%, 34.1% and 13.5%) by Abdullah, A. Abba et al. [13] in TBLN. Clinical spectrum of metastatic lymphadenopathy in the present series and the series by Abdullah, A. Abba et al. [13] were 59.25% vs 58.8%, 29.62% vs 29.4%, 18.51% vs 11.8% and 37.03% vs 0% for neck swelling, night sweats, and weight loss and dysphagia respectively. In NSRL important features of neck swelling, fever, night sweats and cough observed in the present series and that by Abdullah, A. Abba et al. [13] were 71.42% vs 69.4%, 28.57% vs 27.8%, 14.28% vs 13.9% and 7.4% vs 5.6% respectively. Matted and discrete lymph nodes were noted in 61.11% and 38.88% of cases in TBLN as compared to 73% and 27% cases respectively in the series by Sharma, Puja, et al. [27] whereas 60% of matted lymph node was reported in the series by Ahmad, S. S. et al. [28].

5. CONCLUSION

The present observational study revealed tuberculosis as the commonest cause followed by metastatic lymphadenopathy, NSRL, HL and

NHL in decreasing order of frequency. Tuberculosis was common in young adults and malignancy in elderly. Male predominance was noted in all categories of patients.

Neck swelling especially the unilateral cervical involvement was the commonest presentation followed by fever, night sweats, weight loss, anemia and raised sedimentation rate and other constitutional features in all cases. Peripheral lymphadenopathy is a morbid presentation of a variety of diseases of diverse etiology presenting with similar clinical and hematological features, the diagnosis of which can be clinched cytologically or histopathologically.

FNAC is a very convenient diagnostic tool for evaluation of peripheral lymphadenopathies and correlates well in terms of sensitivity and specificity with histopathological examination which is the gold standard. However, in cases of inadequate aspiration or obscure diagnosis HPE is the ultimate tool.

The results and observations obtained in the study are in agreement with the previous studies reviewed.

6. LIMITATIONS OF THE STUDY

As this study comprises of limited numbers of patients for a limited duration in a single center, a larger multi-centric study for longer duration is required for detailed assessment and definite conclusion.

CONSENT

Necessary informed consent was taken from each patient during enrolment in the study.

ETHICAL APPROVAL

Permission from the Institutional Ethical Committee was taken before undertaking the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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