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Cytomorphological profile of lymph nodes at a tertiary care centre in Uttar Pradesh: A retrospective study

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Abstract
Fine Needle Aspiration Cytology (FNAC) is a quick, reliable, minimally invasive and cost effective diagnostic modality for evaluation of superficial lymph nodes and has been accepted as a first line investigation in most centres. The aim of the study was to identify the patterns of pathologies in aspiration cytology of lymph nodes in a tertiary care hospital located in Uttar Pradesh, India. The study was undertaken as a retrospective study using data in the Department of Pathology, G.S Medical College and Hospital, Uttar Pradesh, India. 235 lymph node FNACs that were performed during the two year span of 2018-19 were analysed. Females comprised 59.6% of the total patients who underwent lymph node FNAC procedure, 95 (40.4%) were males. The youngest patient was a 3 month old and the oldest happened to be 78 years. Lymph node enlargement was traced to malignant processes exclusively above 40 years of age. Uptill that age, tuberculosis seems to be the major cause underlying lymphadenopathy, mostly presenting as granulomatous lymphadenitis. Out of all cases which showed granulomatous or necrotic features, 27% showed the presence of AFB, hence confirming tuberculosis. A vast majority of the FNACs were performed for cervical lymphadenopathy (92.8%). 42.1% of the FNACs revealed reactive morphology. This diagnosis was closely followed by granulomatous lymphadenitis in 29.4% patients. Together with a definite diagnosis of tuberculous lymphadenitis, patients with granulomatous lymphadenitis comprised 42.6% of all diagnoses. 12 patients received a diagnosis of suppurative lymphadenitis, 9 received necrotizing lymphadenitis. 12 patients were diagnosed as metastatic carcinoma and 1 was suggestive of lymphoma. Most of the lymph nodes whose sizes were under 1 cm were reactive on cytology. Lymphadenopathy due to malignant etiology presented with lymph nodes measuring at least 2 cm. Granulomatous/tuberculous lymphadenitis presented in lymph nodes of varying sizes, from as small as 0.5 cm to larger ones.

Keywords: cytomorphological, lymph nodes, tertiary care centre

Introduction
Lymphadenopathy is one of the commonest clinical presentations in out-patient departments. Fine Needle Aspiration Cytology (FNAC) is a quick, reliable, minimally invasive and cost effective diagnostic modality for evaluation of superficial lymph nodes and has been accepted as a first line investigation in most centres [1].
While histopathological evaluation of surgically excised lymph nodes is a more specific and accurate diagnostic modality, it is relatively more costly, time consuming and invasive. Additionally, it may not be warranted in every patient [2].
The aim of the study was to identify the patterns of pathologies in aspiration cytology of lymph nodes in a tertiary care hospital located in Uttar Pradesh, India.

Materials and Methods
The study was undertaken as a retrospective study using data in the Department of Pathology, G.S Medical College and Hospital, Uttar Pradesh, India. FNACs performed during the two year span of 2018-19 were analysed. All swellings referred for FNAC as "neck swelling" were retrieved; however swellings other than lymph nodes were excluded from the study. Lymph node FNACs which yielded inadequate material were excluded from the study. Adequacy was defined by the presence of tingible-body macrophages in the smears.

Epidemiological features such as age and gender were studied. Cytological diagnosis was recorded. The usual approach included studying the clinical details and investigations of each patient. The patients underwent FNAC evaluation of the lymph node(s), using a 22 or 23 gauge needle attached to a 10 cc disposable syringe. Consent of the patients was obtained in each case. Smears were prepared on clean glass slides as per standard techniques, and the smears wet fixed by immersing the slides in 95% methanol and air dried. Where aspirate was scanty, all slides were air – dried only. Wet fixed smears were stained by Papanicolaou's (Pap) stain. Air dried smears were stained by May Grunwald Giemsa stain. Ziehl–Neelsen stain (ZN) stain for Acid□Fast Bacilli (AFB) was done whenever required. Standard guidelines for cytological diagnosis were followed.

Reactive lymph node hyperplasia was diagnosed by the presence of a polymorphous population of lymphoid cells and tingible body macrophages. Granulomatous lymphadenitis was diagnosed by the presence of epithelioid cell granulomas, with or without caseating necrosis. Necrotizing lymphadenitis was diagnosed by the presence of predominantly necrotic material with insufficient viable cellular content or epithelioid granulomas. All cases which showed the presence of epithelioid granulomas and/or necrosis were subjected to AFB stain. A diagnosis of tuberculous lymphadenitis was rendered on the presence of AFB; in other cases, granulomatous or necrotizing etiology was ascribed as applicable. Suppurative lymphadenitis was diagnosed by the presence of a predominantly acute inflammatory infiltrate. Correlation with histopathological diagnoses was not undertaken during this study, as only a few lymph nodes of these were excised and received for histopathological evaluation.

Results

Table 1: Age and gender profile of patients in our study

Age in years	Male	Female	Total
0-10	41	29	70
11-20	19	48	67
21-30	10	41	51
31-40	10	13	23
41-50	5	7	12
51-60	4	0	4
>60	6	2	8

Table 2: Categorization of diagnoses received by our patients

Age/Diagnosis	Reactive lymphadenitis	Granulomatous Lymphadenitis	Tuberculous Lymphadenitis	Necrotizing Lymphadenitis	Suppurative Lymphadenitis	Metastatic	Lymphoma
0-10	51	12	4	1	2	0	0
11-20	20	24	11	6	6	0	0
21-30	14	24	9	2	2	0	0
31-40	11	5	5	1	1	0	0
41-50	1	3	2	1	1	4	0
51-60	2	0	0	0	0	2	0
>60	0	1	0	0	0	6	1
Total	99	69	31	11	12	12	1

Table 3: Comparison of size of lymph node with cytological diagnoses

Lymph node size/ Diagnosis	Reactive Lymphadenitis	Granulomatous Lymphadenitis	Tuberculous Lymphadenitis	Necrotizing Lymphadenitis	Suppurative Lymphadenitis	Metastatic	Lymphoma	Total
Upto 0.5 cm	21	3	0	1	0	0	0	25
Upto 1 cm	20	4	4	3	0	0	0	31
Upto 2 cm	8	15	2	3	5	1	0	34
Upto 3cm	0	5	1	2	4	2	0	14
Upto 4 cm	0	1	1	1	0	2	1	6
More than 4 cm	0	0	3	1	0	1	0	5
Total	49	28	11	11	9	6	1	115

A total of 235 patients reported for the FNAC evaluation of superficial lymph nodes in the two year span of 2018-2019.

Age and gender

140 patients were females which comprised 59.6% of the total patients who underwent lymph node FNAC procedure, 95 (40.4%) were males (Table-1).

The youngest patient was a 3 month old and the oldest happened to be 78 years. Lymph node enlargement was traced to malignant processes exclusively above 40 years of age, the youngest patient was 41 years old. Uptill that age, tuberculosis seems to be the major cause underlying lymphadenopathy, mostly presenting as granulomatous lymphadenitis. The youngest patient who received a diagnosis of granulomatous lymphadenitis was a 3 month old baby (Table-2).

Site

A vast majority of the FNACs were performed for cervical lymphadenopathy (92.8%). The other lymph node groups examined in our study were axillary, inguinal, supraclavicular and post-auricular.

Diagnosis

Many of the FNAC slides revealed reactive morphology (42.1%). This diagnosis was closely followed by granulomatous lymphadenitis in 29.4% patients. Together with a definite diagnosis of tuberculous lymphadenitis, patients with granulomatous lymphadenitis comprised 42.6% of all diagnoses. Out of all cases which showed granulomatous or necrotic features, 27% showed the presence of AFB, hence confirming tuberculosis. 12 patients received a diagnosis of suppurative lymphadenitis, 9 received necrotizing lymphadenitis. 12 patients were diagnosed as metastatic carcinoma and 1 was suggestive of lymphoma (Table-2).

Size

An analysis of size of lymph nodes (Table-3) revealed that most of the lymph nodes whose sizes were under 1 cm were reactive on cytology. In our study, suppurative lymphadenitis presented among lymph nodes measuring 2-3 cm. Lymphadenopathy due to malignant etiology presented with lymph nodes measuring at least 2 cm. Granulomatous/tuberculous lymphadenitis presented in lymph nodes of varying sizes, from as small as 0.5 cm to larger ones with accumulation of necrotic material.

Discussion

FNAC is a valuable diagnostic tool for establishing a diagnosis in cases of superficial lymphadenopathy [3]. The use of this technique has limited the need for excision of enlarged lymph nodes, especially in cases of reactive and tubercular lymphadenitis [4]. It is a simple, cost effective procedure that is minimally invasive with almost no complications. Results obtained by FNA are quick as compared to histopathology. FNAC of superficial lesions needs no anesthesia, eliminating the risk of complications associated with anesthesia. No scar is formed at the site of FNA; other diagnostic modalities like incision biopsy or excision biopsy leave a scar [5].

The lesions arising in lymph nodes can be found in patients ranging from an early to advanced age [6]. In the present study also, the age of patients requiring FNAC of lymph node lesions ranged from 3 months to 78 years. Other studies have also confirmed the presentation of lymphadenopathy through all age groups [1, 7, 8].

More number of the patients who presented with lymphadenopathy to our FNAC clinic were females (60%). Kamaal M *et al.* also found female patients in the range of 57% [1]. In the study by Fatima S *et al.*, 60.7% patients were females [5]. Other studies also found female patients in the range of 40-60% [4, 5, 8]. No specific reason could be ascribed for this trend. In our study, metastatic lymphadenopathy was diagnosed in 5.1% of the total cases. One patient was diagnosed as lymphoma. In the study by Arul P, benign lesions consisted of 81.7% and malignant lesions including suspicion of malignancy category consisted of 18.3% [7]. The cytological features were observed to be benign in 86.32% and malignant in 13.68% in the study by Malhotra AS *et al.* [8]. Metastatic deposits in the enlarged lymph nodes were diagnosed in 4.34% cases by Duraiswami R *et al.* [4]. 15.4% of the lymph node FNAC's yielded malignant diagnoses in the study by Wilkinson AR [9]. In the developing world, lymphadenopathy due to infectious causes dominates the picture of cytological diagnoses on FNACs, and diagnosis of metastatic lymphadenopathy ranges from 4-15% in various studies. The cervical group is the most common group of lymph nodes to be involved and the primary is most often from the oral cavity [9]. Findings in our study concurred with these findings. Malignancies in lymph nodes in our country are predominantly metastatic in nature with an incidence varying from 65.7% to 80.4% and lymphomas range from 2% to 15.3% among lymph nodes aspirated from all sites. Additionally, most of the metastatic malignancies arise from squamous cell carcinomas [9]. In our study too, most of the metastatic lesions comprised of squamous cell carcinomas. The sensitivity of FNAC for metastatic lesions to lymph nodes has varied from 97.9% to 100%, whereas the specificity has been found to be 100%. For the lymphomas the sensitivity has been found to be 80% and specificity 100% [10]. We found that a total of 42.6% patients were diagnosed with either granulomatous or tuberculous lymphadenitis. Considering that in our region, granulomatous lymphadenitis is mostly caused by tuberculosis, tuberculosis appeared to be the most common cause of lymphadenopathy in our study. The study by Malhotra AS also found tuberculous lymphadenitis to be the most common finding [8]. These findings reflect the burden of tuberculosis in our region of northern India. Studies from other parts of the country reflect similar trends. In the study by Arul P, tuberculous lymphadenitis was seen in 44.1% of patients with lymphadenopathy [7]. Several series from Pakistan have found tuberculosis as the most common diagnosis among enlarged lymph nodes [11, 12]. Though earlier studies from the western world did not report a high incidence of tuberculosis in their studies, in the recent times it is being reported as a significant cause of cervical lymphadenopathy in the western world. This trend is probably a result of an increase in the immunocompromised population due to various diseases like HIV and organ transplantation [5]. A study by Koo *et al.* from Ireland reported the following etiologies for 18 cases of FNAC diagnosed granulomatous lymphadenitis: four Hodgkin's lymphoma, two non-Hodgkin's lymphoma, five tuberculosis, two toxoplasmosis, one sarcoidosis and four benign reactive changes [13]. Out of all cases which showed granulomatous or necrotic features, 27% showed the presence of AFB, hence confirming tuberculosis. The various causes of granulomatous lymphadenitis are tuberculosis, Hodgkin and non- Hodgkin Lymphoma, metastasis, carcinoma drainage associated granulomas. Less common causes include sarcoidosis, toxoplasmosis and atypical mycobacteria [13]. In the study by Kamaal M, the AFB positivity rate was high, being 66.7% [1]. Vimal *et al.* reported AFB positivity of 40.74% [14]. The frequency of AFB positivity ranges from 10-70 % in various studies [15].

AFB was most commonly observed in slides which consisted predominantly of necrotic material. This finding is reiterated by findings in the study by Vimal *et al.* who found AFB positivity rate as high as 87.5 % in cases with necrosis without granulomas [14]. Bhattacharya S pointed that necrotic features whether acellular or accompanied by neutrophilic infiltrate were often misdiagnosed as suppurative abscesses. Such smears however showed high AFB positivity [16].

41.6% of the patients received a diagnosis of reactive lymphoid hyperplasia. In the study by Duraiswamy *et al.*, reactive lymphadenitis was the most frequent diagnosis in patients with enlarged lymph nodes [4]. (40%). As per the findings in our study, most of the children received a diagnosis of reactive lymphadenitis. This can be explained by the many upper respiratory tract infections that abound in this age group. A significant number of children also had granulomatous/ tuberculous cause. This finding reflects the burden of tuberculosis in our country. Most of the cases with tuberculous/granulomatous lymphadenitis were concentrated between 11-30 years. Lymph node enlargement was traced to malignant processes exclusively above 40 years of age, the youngest patient was 41 years old.

We received a 60 year old female patient with multiple enlarged cervical lymph nodes on one side of the neck with sizes ranging from 1 cm to 4 cm. The lymph nodes were firm and fleshy. A previous FNAC done outside had been reported as tuberculous lymphadenitis, but the patient had not been responding to anti-tuberculous treatment. Aspiration was done from the largest lymph node which revealed a rather monotonous population of medium sized

lymphoid cells, in a background of other polymorphous lymphoid cells. There were occasional ill-defined epithelioid granulomas and an inflammatory infiltrate comprising of few eosinophils and neutrophils. Based on these findings, lymphoma was suspected; excision and histopathological examination was advised. The biopsy revealed effaced architecture of the lymph node with extracapsular extension. Typical Reed-Sternberg cells were, however, not evident. A diagnosis of lymphoma was made and the patient was referred to a higher centre for immunophenotyping. The presence of granulomata in an aspirate may thus indicate the presence of a neoplastic process. The background cell population needs to be observed in such a case. Granulomata may be encountered in both Hodgkin's disease and non-Hodgkin's lymphoma, particularly T-cell lymphoma. Hodgkin's lymphoma is characterised by the classic Reed-Sternberg cells in a background of sarcoid-like granulomata, reactive lymphoid cells and occasional eosinophils [13, 17]. FNAC plays a greater role in the management of Hodgkin's disease as it helps in the primary diagnosis, staging of the patient and monitoring the recurrence of the disease [14]. The present case illustrates how grey areas still exist in the establishment of an exact diagnosis especially in the case of primary lymphoproliferative disorders, where distinguishing them from a reactive hyperplasia may pose a diagnostic conundrum even in experienced hands [4].

We observed that size of the lymph node also provides information regarding the etiology underlying its enlargement. An analysis of size of lymph nodes (Table-3) revealed that most of the lymph nodes whose sizes were under 1 cm were reactive on cytology. Lymph nodes under 1 cm do not usually require to be sampled, and are subjected to FNAC when the clinician is trying to investigate the etiology of certain symptom like for instance Pyrexia of Unknown Origin. We found a significant number of lymph nodes between 0.5-1 cm harbouring epithelioid granulomas with or without evidence of AFB positivity. Granulomatous/tuberculous lymphadenitis presented in lymph nodes of varying sizes, from as small as 0.5 cm to larger ones with accumulation of necrotic material. Maximum number of nodes with granulomatous/ tuberculous etiology ranged in size from 1-3 cm. In our study, suppurative lymphadenitis presented among lymph nodes measuring 2-3 cm. Lymphadenopathy due to malignant etiology presented with lymph nodes measuring at least 2 cm. Reddy *et al.* concluded that in cervical and axillary region lymph node size of 1 cms, more than 1.5 cms in the inguinal region and more than 0.5 cm at any other site are to be considered significant [18].

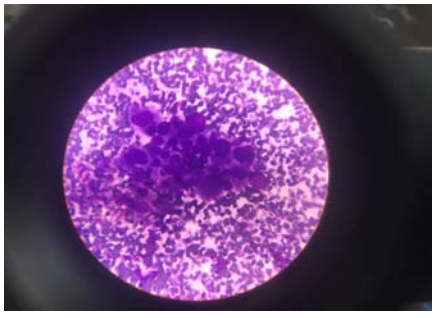

Fig 1: Photomicrograph of FNAC lymph node slide showing dysplastic cells of metastatic squamous cell carcinoma carcinoma. (MGG, 400X)

Fig 2: Photomicrograph of FNAC lymph node slide showing reactive population along with tangible body macropage. (MGG, 400 X)

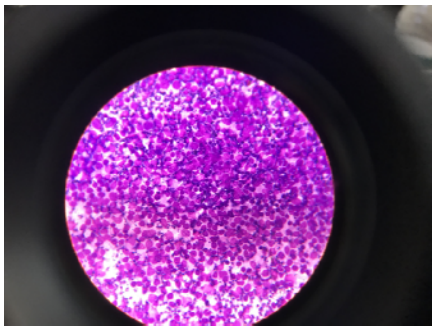

Fig 3: Photomicrograph of FNAC lymph node slide showing abnormal lymphoid cell population, subsequently diagnosed as lymphoma on biopsy. (MGG, 400X)

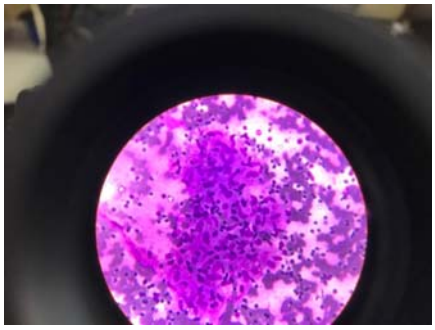

Fig 4: Photomicrograph of FNAC lymph node showing epithelioid cell granuloma (MGG, 400X)

Conclusion

FNAC is a convenient, relatively painless and rapid method of diagnosing the underlying pathology in cases of superficial enlarged lymph nodes. Most of the FNACs revealed reactive lymphoid hyperplasia, granulomatous and tuberculous lymphadenitis. 5% patients were diagnosed as metastatic carcinoma. Age of the patient and size of lymph node are important clues regarding the underlying etiology.

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