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SPECTRUM OF LYMPHNODE LESIONS ON CYTOLOGY :A RETROSPECTIVE STUDY.

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ABSTRACT:

Objective

Fine Needle Aspiration Cytology (FNAC) is first line of investigation in diagnosing a variety of superficial and deep lesions. It is a easy, quick, cost effective,well tolerated and reliable technique done as a outpatient department procedure. Lymphadenopathy is clinically important in a myriad of conditions ranging from simple reactive lymphadenitis to neoplastic etiology. In this study, we explain the utility of FNAC in lymph node lesions ranging from infectious etiology to malignant lesions and we highlight Tuberculous Lymphadenitis.

Methods: This was a retrospective study and includes a total of 256patients of all age groups and both sexes presenting with palpable lymphnodes at FNAC clinic of our institute over a period of 3 years .FNAC was conducted with 22-24 Gauge disposable needles attached to 5/10c.c syringes. Smears were fixed in 95% ethyl alcohol and stained with Hematoxylin and Eosin stain. Leishman stain was done on air dried smears. Ziehl- Neelsen (ZN) staining was done wherever required.

Results: Out of a total of 256 patients with lymphadenopathy subjected to FNAC the commonest site was cervical lymphnodes(57.03%) .Females(54.68%) outnumbered males(45.31%) in our study .The commonest lesion was found to be Granulomatous lymphadenitis(51.95%,followed by reactive lymphadenitis(23.82%),non suppurative lymphadenitis(10.1%),acute suppurative lymphadenitis(6.25%),Metastatic deposit(5.07%),chronic suppurative lymphadenitis(1.95%) and HodgkinsLympoma(0.78%).

Conclusion: FNAC is a easy to perform,reliable in expensive method in diagnosing lymphadenopathy.In our study the predominant cause of lymphadenopathy was Tuberculous lymphadenitis,followed by reactive lymphadenitis.

Keywords: FNAC, Lymphadenopathy, Tuberculous lymphadenitis, Metastatic lymphadenitis

INTRODUCTION:

The reticuloendothelial system comprises of lymphnodes,lymphatics,Monocytes,Macrophages,Thymus,Spleen,Bone marrow and the Mucosa associated Lymphoid tissue of the Viscera.(1). The reticuloendothelial system, a major component of immune system (RES) plays a vital role in the clearance of particles and soluble substances in the circulation and tissue.Reticuloendothelial system is also called as Mononuclear Phagocytic System(MPS) as phagocytosis is its major role. Lymph nodes are kidney shaped glands penetrated by afferent and efferent lymphatic vessels.

The Lymphnodes are located along the course of lymphatic vessels and are commonly located in cervical,axillary,retroperitoneal,mediastinal and inguinal regions.The main function of lymphnodes is to clear the antigens from extra cellular fluid.Lymphnodes are divided into cortex and Medulla. Cortex comprises of subcapsularsinus,cortical sinus and lymphoid nodules. Medulla comprises of medullary cords and sinuses.Lymphadenopathy refers to the nodes which are abnormal in size, consistency and number and constitutes one of the frequent clinical presentations of patients visiting the Out Patient Department(2). The Spectrum of the underlying cause of lymphadenopathy can be secondary to bacterial, viral, or fungal infections, autoimmune disease, and malignancy(3). The treatment of these lesions varies considerably and hence FNAC plays a critical role in the initial diagnosis. Lymphadenopathy can be localized or generalised.

About 75% of most lymphadenopathies are localized, and about 50% of those occur in the head and neck regions. Generalized lymphadenopathy, which involves two or more non-contiguous regions, is reported to occur in 25% of lymphadenopathies(4).Ultrasound examination gives preliminary data regarding whether a Lymphnode is benign or malignant(5).However the gold standard for diagnosis of lymphadenopathy is histopathological examination(6).Fine needle aspiration Cytology (FNAC) is the study of cells aspirated from lesions or masses in various body sites by using a needle attached to syringe.FNAC is a important diagnostic test in the evaluation of clinically palpable lesions like lymphnodes,Breast swellings and Thyroid swellings.

FNAC has evolved as a important diagnostic tool over the years with support from radiological techniques ,immune histochemistry,Immunophenotyping and Cytogenetics.Guided FNAC can be done in evaluation of deep seated visceral lesions(7).Fine needle aspiration cytology is considered as the first line diagnostic investigation inlymphadenopathy and is an useful alternative to excision biopsy(8).Excision biopsy can lead to sequale like scar formation and bleeding(9).FNAC is a simple,rapid,inexpensive,minimallyinvasive,welltolerated,out patient department procedure in assessment of superficial palpable masses(10,11,12,13).Usually the diagnostic material obtained by FNAC is considered of inferior quality when compared to histopathological sections. However, there are many advantages of FNAC over trucut biopsy. First, it's an office procedure without the need for any specific prior hematological workup. Second, the adequacy of material obtained on FNAC can be checked onsite and repeat FNAC can be done immediately. Another advantage of FNAC is an extremely low complication rate.FNAC gives a accurate diagnosis in reactive lymphadenitis,granulomatous lymphadenitis and in metastatic malignancy.Metastatic malignancy diagnosed on FNAC often propels to look for Occult Carcinoma(14).FNAC also plays a important part in staging of primary Lymphoid malignancies and recognizing residual disease(15).Surgicaly inaccessible lymphnodes can be assessed by FNAC.FNAC when supported by immunophenotyping and genotyping helps in accurate diagnosis of Malignant Lymphoma.Tuberculosis is a common disease of developing countries manifesting as Pulmonary and extra Pulmonary Tuberculosis.Extra Pulmonary Tuberculosis presents a miliary Tuberculosis, meningeal Tuberculosis,TuberculousLymphadenopathy.InExtra Pulmonary

Tubercuosis,Tuberculous lymphadenopathy is the most common presentation seen in about 40% of cases and these constitute 15–20% of all cases of tuberculosis in India(16,17,18,19).HIV infection is common in extra Pulmonary Tuberculosis.Cervical Tuberculous Lymphadenopathy is most common presentation in of Tuberculous Lymphadenopathy(20).In a developing country like India, tuberculous lymphadenitis is one of the most common presentations at OPDs where a definitive diagnosis is needed before the initiation of anti-tubercularthерapy.The most reliable criteria for diagnosing tubercular lymphadenitis is demonstration of acid fast bacilli (AFB) by ZiehlNeelson (ZN) stain, auramine rhodamine stain,histopathological examination of excised tissue and polymerase chain reaction or culture of bacilli from aspirates. Cytology with acid fast staining or culture is an invaluble aid in the diagnosis of Tuberculosis.FNAC is economical and rapid when compared to culture studies which are time consuming and need expertise,while Polymerase chain reaction is expensive and needs training.FNAC has sensitivity and specificity of 88-96% in diagnosing Tuberculous Lymphadenitis. The present study highlights the role of FNAC in diagnosis of Lymphadenopathy with emphasis on Tuberculous Lymphadenopathy.The objective of the study is to study the Spectrum of lymphnode lesions diagnosed on fine needle aspiration Cytology with emphasis on Tuberculous Lymphadenopathy.

MATERIAL AND METHODS:

This is a retrospective descriptive study on Lymphadenopathy cases at the Government General Hospital Mahabubnagar,TelanganaState,India. All Cytological reports of Fine needle aspiration Cytology of Lymphadenopathy cases issued from August 2018 to July 2021 were reviewed.A brief clinical history followed by physical examination was carried out in all the cases presenting with lymphadenopathy.FNAC of the lymphnode was performed under strict aseptic conditions with through cleaning of the site with spirit swab.The palpable swelling was fixed with one hand andFnac was performed using 22 Guage needle attached to 5cc or 10 cc syringe.After insering the needle into the swelling negative suction was applied and the needle was moved to and fro and sideways gently till some material was visualized in the needle hub. The needle was withdrawn after the release of negative pressure.The aspirated material was blown on a clean glass slides and with the help of spreader slide Smears were prepared. The smears were fixed in 95% ethanol and stained with Hematoxylin

and Eosin.Slides were through examined for celluarity,background,nuclear and cytoplasmic features.ZiehlNeelsen staining was employed in suspicious cases for Tuberculosis like necrotic aspirate, patients presenting with symptoms of weight loss,evening rise of temperature and family history of Tuberculosis or with a past history of Tuberculosis. In cases where fluid was aspirated on FNAC, the fluid was centrifuged and smears were made from the sediment followed by the above staining methods. The diagnoses were categorized broadly as Tuberculous lymphadenitis, Reactive lymphadenitis, acute suppurativelymphadenitis , metastatic lymphadenopathy and lymphomas.

Statistical analysis was done by Chi square test or Fishers exact test basing on sample size to test for variation in proportions with the help of open source epidemiologic statistics for Public Health(21). A "P value" less than 0.05 was considered to be statistically significant.

INCLUSION CRITERIA:

1.All cytology cases of Lymphadenopathy in the time period between 2018 August to 2021 July with adequate cellular adequacy.

EXCLUSION CRITERIA:

2. All cytology slides time period between 2018 August to 2021 july without cellular adequacy and slides where aspirated material showed blood and blood cellular elements.

RESULTS:

A total of 256 cases were studied during the defined time period with the patient age ranging between with a male to female ratio of 0.82:1.The cytological diagnosis varied from 9 years in youngest patient to 80 years in most oldest patient.TubercuousLymphnodes were firm,multiple and matted,reactive lymphadenopathy were discrete,while the metastatic lymphnodes showed a hard and fixed consistency.The most common site of lymphadenopathy was Cervical Lymphadenopathy followed by Axillary Lymphadenopathy.In the cytological diagnostic perspective out of the total 256 cases of Lymphadenopathy , Tuberculous Lymphadenitis dominated the the picture as being the most common diagnosis with 133 cases(51.95%) followed by reactive lymphadenitis which accounted for 61(23.8%) cases. The cases of Tuberculous lymphadenitis cases on

the basis of Cytology were further divided into three groups; group1: Granulomas without necrosis - 43/133(32.33%), group 2: Caseating epithelioid granuloma - 83/128(62.40%) and group 3: Necrotizing lymphadenitis - 8/133(6.01%).Acid fast bacilli stain was positive in 29 cases(37.12%).A total of 15 cases(5.8%) of Malignancy were encountered of which Hodgkins Lymphoma were 2(13.33%) and secondary deposits were 13 (86.66%).Acute suppurative Lymphadenitis cases were 16((6.25%) and chronic Suppurative Lymphadenitis were 5((1.95%).

TABLE 1:TOTAL NUMBER OF CASES

TOTAL NUMBER OF CASES(n=256)	
YEAR	CASES
2018-2019	124(48.43%)
2019-2020	64(25%)
2020-2021	68(26.56%)

TABLE 2:SITE OF LYMPHNODE INVOLVEMENT

SITE OF LYMPHNODE INVOLVEMENT(n=256)	
Cervical	146(57.03%)
Axillary	83(32.42%)
Inguinal	20(7.81)
Multiple	5(1.95%)
Extremities	2(0.78%)

:SEX DISTRIBUTION OF LYMPHADENOPATHY

SEX DISTRIBUTION OF LYMPHADENOPATHY		
YEAR	MALES	FEMALES
2018-2019	56	70
2019-2020	31	31
2020-2021	29	39
TOTAL	116(45.31)	140(54.68%)

TABLE4: CYTOLOGICAL DIAGNOSIS

CYTOLOGICAL DIAGNOSIS	**2019**	**2020**	**2021**	**TOTAL**
TUBERCULUS LYMPHADENITIS	64	30	39	133(51.95%)
REACTIVE LYMPHADENITIS	25	18	18	61(23.82%)
CHRONIC SUPPURATIVE LYMPHADENITIS	4	0	1	5(1.95%)
NON SUPPURATIVE LYMPHADENITIS	11	8	7	26(10.1%)
ACUTE SUPPURATIVE LYMPHADENITIS	16	0	0	16(6.25%)
HODGKINS LYMPHOMA	0	2	0	2(0.78%)
METASTATIC DEPOSIT	6	4	3	13(5.07%)

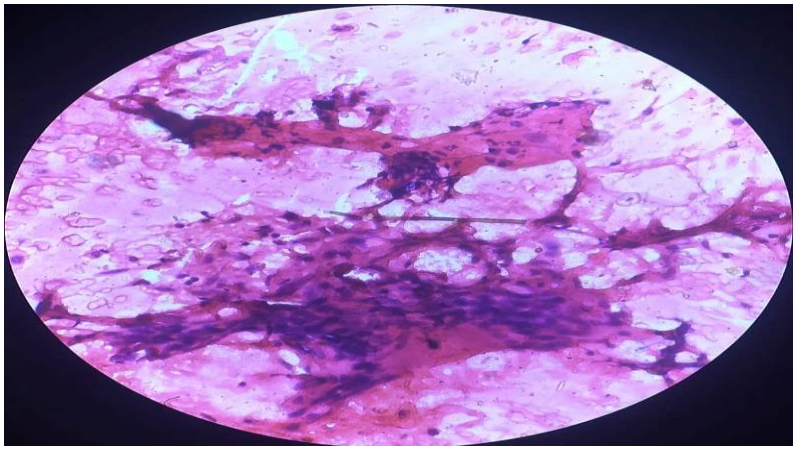

Fig1:Tuberculous Lymphadenitis with Cluster of epitheloid cells.

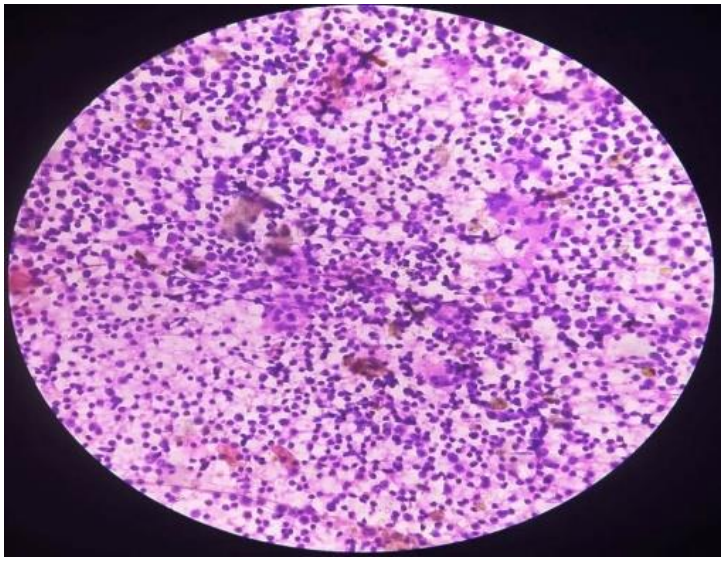

Fig 2.Reactive Lymphadenitis

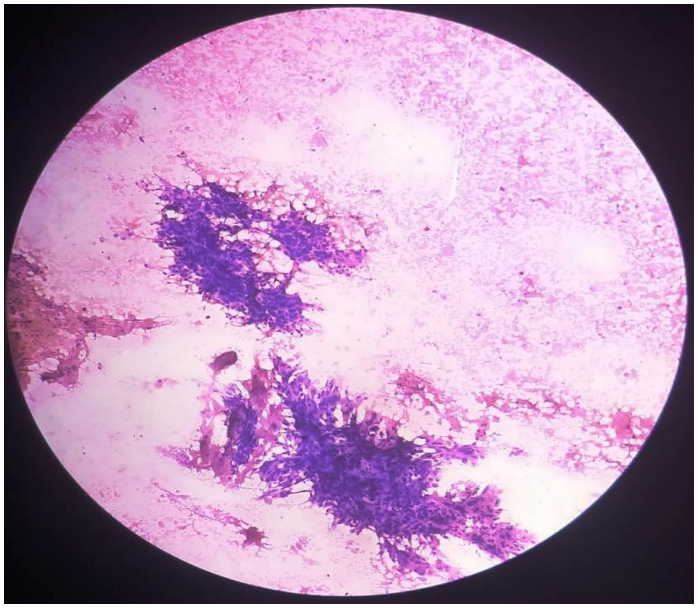

Fig3.Secondary deposit inLymphnode

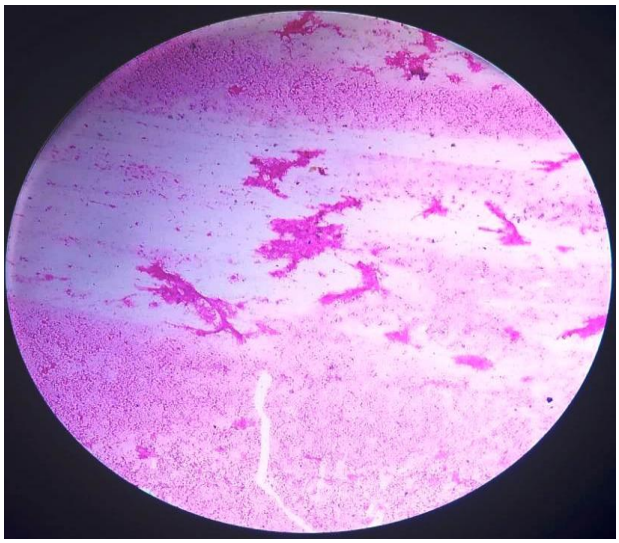

Fig4.Caseous Necrosis

TABLE 5:Age Distribution of Cytological Diagnosis of lymphadenopathy

AGE	TB		REACTIVE		CHRONIC		NON SUPPURATIVE		ACUTE SUPPURATIVE		HODGKINS		METASTASIS		Total
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	
0-9	7	4	8	4	1	1	1	6	2	2	0	0	0	0	36
10-19	13	17	7	6	0	1	1	5	2	0	1	0	0	0	53
20-29	8	23	2	11	0	0	2	4	3	1	0	0	0	0	54
30-39	15	15	5	7	0	1	0	3	0	1	0	0	0	0	47
40-49	10	9	1	1	0	0	1	2	0	0	0	0	1	0	25
50-59	5	4	3	3	1	0	0	0	1	2	0	1	1	2	23
60-69	2	0	0	1	0	0	1	0	0	0	0	0	4	0	8
70-79	0	0	2	0	0	0	0	0	1	1	0	0	5	0	9
80-89	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
TOTAL	61	72	28	33	2	3	6	20	9	7	1	1	11	2	256

TABLE 6

AGE	TB	REACTIVE	CHRONIC	NON SUPPURATIVE	ACUTE SUPPURATIVE	HODGKINS	METASTASIS
	“P”Value	“P”Value	“P”Value	“P”Value	“P”Value	“P”Value	“P”Value

0-9	0.418	0.266	0.954	0.032	0.914	0.0000001	0.0000001
10-19	0.753	0.496	0.547	0.165	0.200	0.452	0.0000001
20-29	0.716	0.279	0.0000001	0.744	0.067	0.0000001	0.0000001
30-39	0.188	0.951	0.574	0.180	0.574	0.0000001	0.0000001
40-49	0.658	0.960	0.0000001	0.564	0.0000001	0.0000001	0.520
50-59	0.586	0.910	0.478	0.0000001	0.526	0.521	0.607
60-69	0.107	0.125	0.0000001	0.875	0.0000001	0.0000001	0.500
70-79	0.0000001	0.777	0.0000001	0.0000001	0.222	0.0000001	0.444
80-89	0.0000001	0.0000001	0.0000001	0.0000001	0.0000001	0.0000001	0.0000001

DISCUSSION:

Fine needle aspiration Cytology plays a pivotal role in diagnosis of lymphadenopathy. FNAC is inexpensive, safe and rapid technique performed as an out patient procedure with minimal riskto the patient.The first aspiration of lymphadenopathy was done in a patient suffering from sleeping sickness by Griey and Gray in 1904(22).Reactive lymphadenitis,Suppurative Lymphadenitis diagnosed on cytology subside after a course of antibiotics.FNAC as a tool in the diagnosis of Tuberculous lymphadenopathy was first employed by Dudgeon and Patrick(23).Tuberculosis is more common in people with low socio economic status,Diabetics and in HIV infected individuals. The present study, focuses on the cytomorphological spectrum and epidemiological pattern of lymph node lesions. The commonest age group in which lymphadenopathy was recorded in our study was 10-19 years while in other studies it was 21-30 years.(24,25,26,27,28). Cervical lymph nodes were the most common group of lymph nodes involved, which is similar to that observed by Pavithra et al(24)Chandanwale et al(28), Kochhar et al(29) and Mohanty et al(30). Tuberculous lymphadenitis was the most common lesion and was reported in 51.95% cases and maximum number of these cases were in the age group 10-19

years with a female preponderance (M:F = 0.76:1) followed by 20-29 years and 30-39 years.ReactiveLymphadentis were the next commonest lesion observed after Tuberculosis accounting for 23.82%. The female preponderance of TB Lymphadenitis was similar to the study of Sharma P et al(31) Pavithra et al(24) Fatima et al(32) and Chand et al(33).The predominance of TB in females can be attributed to malnutrition and Poverty. Cervical lymph nodes (57.03%) were more commonly involved by Tuberculosis, followed by axillary group (32.42%) in our study . Similar observations were made by Pavithraet al.,(24),Sharma et al (31) Chand et al.(33)and Khajuria et al(34) and Das et al(35). ZN staining for acid fast bacilli was seen in 26.67% cases in our study, while Chand et al.(33)reported 44.54% cases, Bezabih et al.(36)The areas of necrosis are associated with abundance of proliferation of tubercle bacilli which yield more AFB while lymphocytes,epithelioid cells and multinucleated giant cells wall off the Tuberculous Bacilli(35,37,38)**.** In our study those cases where on cytology the yield showed epithelioid cells ,lymphocytes,Langhan giant cells a diagnosis of Granulomatous Lymphadenitis was favored,in those cases where caseating necrosis with epitheloidcells,Langhan giant cells were seen a diagnosis of Caseating Lymphadenitis was given,while large areas of confluent necrosis with nuclear debris a diagnosis of necrotic Lymphadenitis was suggested.Apart from Tuberculosis Granulomas can be seen in a myriad of conditions like sarcoidosis, Crohns disease, Histoplasmosis,cat scratch disease.(39)However the cytological diagnosis of granulomatous Lymphadenitis in an area where Tubercuosisis is common usually favors a diagnosis of Tuberculosis.(38).In our study only necrosis was seen in 8 cases which were AFB positive similar to the study by Sharma P et al(31),our study was a 3 year study while the study of Sharma et al(31) was a two year study.A P value of 0.032 was observed in 0-9 years in non suppurative lymphadenitis which was significant.In the age group 0-9 years the commonest diagnosis was reactive lymphadenitis followed by Tuberculosis.In the age group 10-19 years Tuberculosis was the major disease diagnosed on Cytology followed by reactive lymphadenitis.In the age group 20-29 years Tuberculosis cases exceed the other cases with Reactive lymphadenitis coming next.A similar trend of Tuberculosis cases on diagnosed on Cytology followed by reactive lympadenitis were seen in the age group of of 30-39 years,40-49 years,50-59 years.We observed only on one case in the extreme age group of 80-89 years which was diagnosed as Tuberculosis.Two cases of Hodgkins Lymphoma were encountered one in 10-19 years and the other in 70-79 years reflecting the

bimodal age distribution(40).In the metastatic deposits 9 cases out of 13 were found above the age of 60 years indicating the propensity of metastatic tumors to arise in the elderly. Males outnumbered female in the total number of metastatic deposits.A P value of 0.000001 was observed in many age groups and in both the sexes and this can be attributed to the inadequate number of cases in that age groups.All the primary malignancies in our study were of Hodgkins Lymphoma and secondary deposits accounting for a total of 15 cases (5.8%).Of the malignanciesHodgkins Lymphomas accounted for only 2 cases((0.78% of the total cases) while Metastasis(5.07%) accounted for majority of the Malignancies. The studies by Sharma et al,Bhaskaran et al reported 0.41 and 0.74% of Hodkins

Lymphomas respectively.Those cases with only hemorrhagic aspirates were observed or inadequate cellularity was observed were omitted from the study.

CONCLUSION:

Lymphadenopathy is a commonly encountered clinical presentation in the out patient department where FNAC is the first line of investigation .FNAC is rapid, safe,reliable technique which is well tolerated by the patient and can be performed in extremes of age as it is a simple, procedure. FNAC is pivotal in diagnosing Tuberculous Lymphadenitis asthese cases are spared from excision as a course of anti Tubercular therapyinduces regression of lesions.FNAC plays an important role in diagnosis of Lymphnode malignanciesand can be the only tool providing a clue to occult carcinoma when metastasis is diagnosed in Lymphnode.Even in cases of known primary FNAC is invaluable in the follow up of these cases.For the diagnosis of lymphoma it gives basic diagnosic information which can be further confirmed by histopathology and then by Immunohistochemistry.In the present study the various cytomorphological patterns of lymphadenopathy are highlighted with a emphasis on Tuberculous lymphadenitis.

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