



Cytopathology of Lymphadenopathy in Patients of Chenab Valley

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Abstract

Background: Fine-needle aspiration (FNA) cytology is a simple, economical, highly accurate tool in the diagnosis of tuberculous and non-tuberculous lesions of Lymph nodes. It is also used for sample collection for ancillary studies such as Zeihl-Nelsen (Z-N) stain for acid fast bacilli (AFB) and CBNAAT (Cartridge based nucleic acid amplification testing) for confirmation of Mycobacterium tuberculosis and rifampicin resistance as well as culture and molecular biologic studies.

Enlarged Lymph nodes are a prime target for Fine Needle aspiration (FNA). In an adult, lymphadenopathy is an immediate source of concern and unless the cause is evident, the enlarged node is usually aspirated. In children lymphadenopathy is common and usually the result of reactive hyperplasia ;for this reason it is often watched and not aspirated .Nevertheless, FNA is easily applicable to children also if lymphadenopathy persists.

In studies involving multiple sites, AFB positivity by Z-N ranges from 23% to 45%. The positive rate of mycobacterium culture from FNA material ranges from 20.8% to 83%. A few limitations include sampling and interpretation error and differential diagnostic problems.

Material and Methods: This prospective observational study was conducted in the department of pathology GMC Doda over a period of 8 months from May2019- December 2019 .The study population included 47 cases.

FNAC of enlarged lymphnodes was done with 21-22 gauge needle and 20ml dispovan syringe using Frenzens Handle by the pathologists of GMC doda using all the aseptic precautions.

Results: 22 cases were diagnosed as Non-specific reactive lymphadenitis,18 as Chronic granulomatous lymphadenitis,2 as Acute Suppurative lymphadenitis,1 as Non –Hodgkins Lymphoma , 1 case as Metastatic deposits of P.D SCC,1 case as metastatic deposits of Malignant Melanoma, 1 case as metastatic deposits of Duct cell carcinoma breast and 1 case as small lymphocytic lymphoma /Chronic lymphocytic leukemia.

Conclusion: To conclude, FNA is non-invasive procedure and helps in making accurate diagnosis of various lesions in both superficial and deep nodes in the body without causing any complications to the patients and is done as an OPD procedure without any hospital stay and is a cost effective and relatively painless procedure. But whenever there is doubt in diagnosis, repeat sample can be taken without any delay for cytopathology as well as for Ancillary studies.

Keywords: Cytopathology, Tuberculosis, casseous necrosis, Lymphnode, Langhan giant cells.

Introduction

FNA is a non –invasive procedure for evaluating lymphadenopathy. It preserves lymph node architecture for evaluation of node whenever excision becomes necessary. It has advantages over surgical excision. FNAC is particularly helpful in patients with deep seated lymph nodes (e.g; mediastinal, retroperitoneal, abdominal) for which surgical intervention carries the risk of significant morbidity. Even with superficial e.g (Cervical, inguinal) lymphadenopathy FNAC is preferred over excision to prevent morbidity associated with excision like accessory spinal nerve injury¹

The Final diagnosis made by the cytopathologist is based up on the intergration of Clinical details, light microscopic analysis, and ancillary studies.²

The cytopathologist performing the FNAC has a responsibility to involve clinical history and physical findings into the final diagnosis.³

On FNAC (Fine Needle Aspiration Cytology) of lymphnodes, diagnosis of:

1. Tuberculous lesions depends upon demonstration of epithelioid granuloma with or without caseous necrosis in the smear
2. Non –specific reactive hyperplasia of lymphnode is based upon detection of polymorphic population of lymphoid cells in the form of predominantly small lymphocytes, centrocytes, centroblasts, immunoblasts and tangible body macrophages
3. Lymphoma depends upon the demonstration of monomorphic population of atypical lymphoid cells
4. Acute suppurative lymphadenitis depends on polymorphic population of lymphoid cells and abundance of acute inflammation.

Mycobacterial Lymphadenitis

Mycobacterial infections occur in individuals who are immunocompetent and immunosuppressed. FNA is particularly efficacious in endemic regions and its accuracy is lower in the US because of low

prevalence of disease and atypical clinical presentations.⁴

SMEARS may show granulomas with necrosis, granulomas without necrosis and sometimes necrosis only.⁵

In immunocompromised patients only histiocytic collections are seen .The “negative image” phenomenon ⁶due to lipid coating of bacillus resisting staining with Romanowsky stains is seen as clear rods or striations surrounded by stained proteinaceous or necrotic material either within the macrophages where they look like linear striations resembling “crinkled tissue paper” appearance of storage cells of Gauchers disease or extracellular.

Aims and Objectives

1. To study the role of Cytopathology in evaluating patients presenting with lymphadenopathy
2. TO know the role of Ancillary studies in confirmation of final diagnosis whenever there is doubt in diagnosis with cytopathology.

Materials and Methods

Inclusion Criteria

All patients irrespective of age and sex presenting to pathology department with Lymphadenopathy were included in the study.

Exclusion Criteria

1. Patients with known history of coagulation disorder were excluded from the study.
2. Patients with previously diagnosed tuberculosis and those on antitubercular treatment.

Study Period: This Prospective observational study was done over period of 8 months from May 2019-December 2019.

Study Population: This study included total of 47cases.

FNAC was done by pathologist. Pathologist also performed Rapid on-site evaluation (ROSE) for assessment of adequacy of material and repeated

procedure until adequate material was obtained. The on-site assessment was also used for the triage of material. If on ROSE pathologist found an evidence of infection (neutrophils, granulomas, necrosis, visible organisms) then a part of material was sent for CBNAAT examination Where-ever it was required.

Local Anaesthesia was not used for FNA. The area was cleaned by sterile alcohol/spirit swabs .In routine three separate passes were given (needle puncture with aspiration) was made with a 22-23 or 25 –gauge sterile needle .The procedure was performed either with needle only (This technique was used for (<1cm) nodes, freely mobile nodes that could not be immobilized) or needle attached to the syringe so that vacuum was applied. More material was obtained with the later procedure. Smears were prepared by spreading the material over the slide with the help of spreader by applying gentle pressure as lymphocytes are fragile and easily crush if too much of pressure is applied during the preparation of smear.

Most of the slides were airdried, fixed with Acetone free methyl alcohol and stained with MGG Stain a Romanowsky group of stains because it highlights the cytoplasmic details of lymphoid cells and lymphoglandular bodies. Samples in the form of needle rinses were also sent to DOTS center for CBNAAT when ever required for confirmation of diagnosis.

Results

Out of total 47 cases maximum number of cases were found in the age group of 0-10 years 13 cases followed by 11-20 years, I;e9 cases, followed by 21-30 years I;e8cases. (TABLE:1). Males were 21 in number and females were 26 in number with male to female ratio of 0.81:1.(TABLE:2). 27 Cases were showing cervical nodes ,6 cases as submandibular nodes,,4 as supraclavicular nodes, 4 as axillary nodes ,2 as inguinal nodes,2 involving multiple body site nodes, 1 preauricular node and 1 arm node . (Table 3).

Cytopathological diagnosis on FNA

22 cases were diagnosed as Non-specific reactive lymphadenitis (Fig -1),18 as Chronic granulomatous lymphadenitis (Fig- 2),2 as Acute Suppurative lymphadenitis (Fig -3),1 as Non – Hodgkin Lymphoma(Fig- 4), 1 case as Metastatic deposits of P.D SCC (Fig -5),1 case as metastatic deposits of Malignant melanoma(Fig- 6) , 1cases as metastatic deposits of Duct cell carcinoma breast (Fig -7) and 1 cases as Small lymphocytic lymphoma/Chronic lymphocytic leukemia (SLL/CLL) [Table -4]

Out of 18 cases diagnosed as Chronic granulomatous lymphadenitis,4 cases were found to have extensive casseous necrotic material and few vague epithelioid cell collections , 9 cases were found to have well defined epithelioid cell granulomas and langhan type of giant cells and five cases were showing reactive background with few epithelioid cell collections only .These patients were aspirated again and sample rinses were sent for CBNAAT for confirmation of diagnosis .These all 5 cases were finally diagnosed as tuberculosis cases on CBNAAT. (Table 5)

Table 1: Age wise distribution of patients

Age Group	Number of cases	Percentage
0-10	13	27.65%
11-20	9	19.14%
21-30	8	38.29%
31-40	5	10.63%
41-50	5	10.63%
51-60	7	14.89%
TOTAL	47	100%

Table 2: Sex wise distribution of cases

MALES	%age	FEMALES	%age	TOTAL	%age
21	44.68%	26	55.31%	47	100%

Table 3: Site wise distribution of lymphadenopathy

SITE	NUMBER OF CASES	PERCENTAGE
CERVICAL	27	57.44%
SUBMANDIBULAR	6	12.76%
SUPRACLAVICULAR	4	8.51%
AXILLARY	4	8.51%
INGUINAL	2	4.25%
MULTIPLE BODY SITES	2	4.25%
PREAURICULAR SWELLING	1	2.127%
ARM	1	2.127%
TOTAL	47	100%

Table 4: Cytopathologic Diagnosis on FNA

DIAGNOSIS	NUMBER OF CASES	PERCENTAGE
NON-SPECIFIC REACTIVE LYMPHADENITIS	22	46.80%
CHRONIC GRANULOMATOUS LYMPHADENITIS	18	38.29%
ACUTE SUPPURATIVE LYMPHADENITIS	2	4.25%
LYMPHOMAS(NHL)	1	2.127%
METASTATIC DEPOSITS OF P.D SCC	1	2.127%
METASTATIC DEPOSITS OF MALIGNANT MELANOMA	1	2.127%
METASTATIC DEPOSITS OF DUCTAL CELL CARCINOMA	1	2.127%
SMALL LYMPHOCYTIC LYMPHOMA(SLL)/CHRONIC LYMPHOCYTIC LEUKEMIA(CLL)	1	2.127%
TOTAL	47	100%

Table 5: Diagnosis on CBNAAT Where ever required

SAMPLES SENT FOR CBNAAT	TUBERCUOSIS PRESENT	TUBERCULOSIS ABSENT
5	5	-

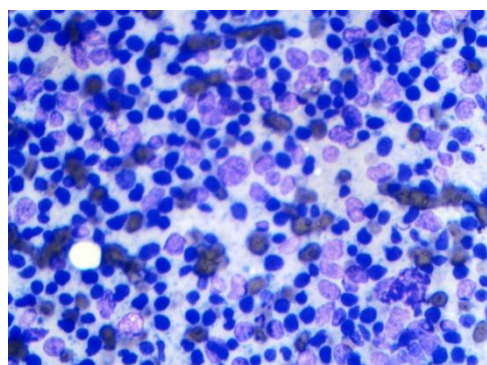


Fig 1: Photomicrograph showing polymorphic population of small lymphocytes, centrocytes, centroblasts and tinged body macrophages. (Non-Specific lymphadenitis)

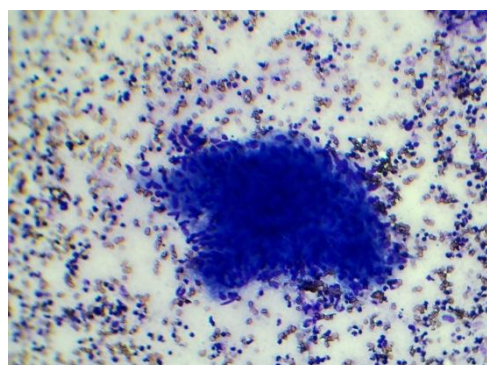


Fig 2: Photomicrograph showing epithelioid cell granulomas (Tuberculosis)

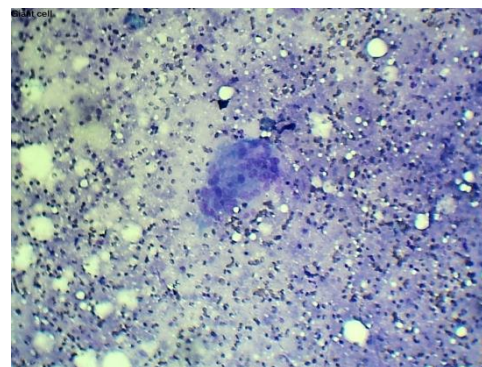


Fig 3: Photomicrograph showing Langerhans giant cell against a background of caseous necrosis (Tuberculosis)

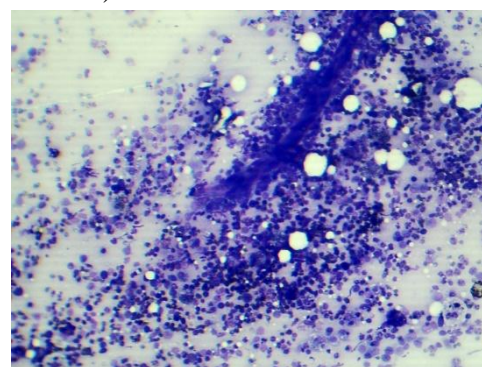


Fig 4: Photomicrograph showing predominantly neutrophilic infiltrates against an active node (Acute suppurative lymphadenitis)

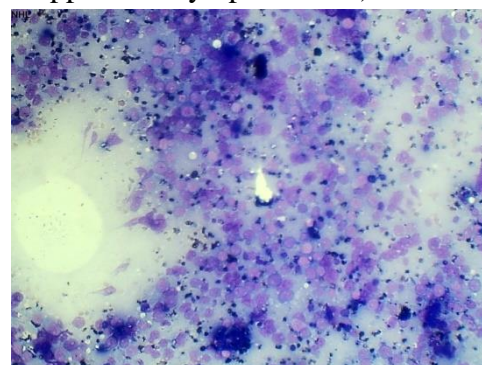


FIG 5: Photomicrograph showing monomorphic population of lymphoid cells (NHL)

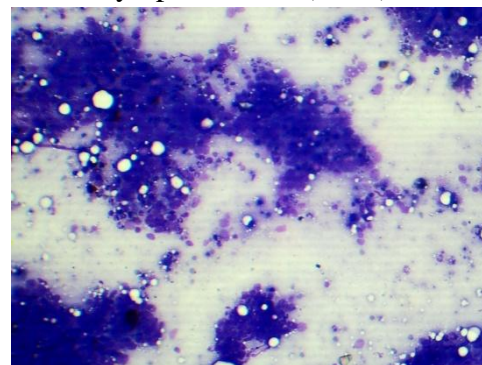


Fig 6: Photomicrograph showing sheets and clusters of tumour cells with a high N/C ratio. (PD SCC)

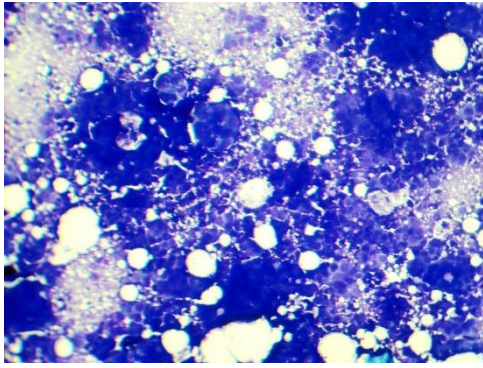


Fig 7: Photomicrograph show clusters of pleomorphic tumour cells against lymphoid background (Mets Ductal cell carcinoma breast)

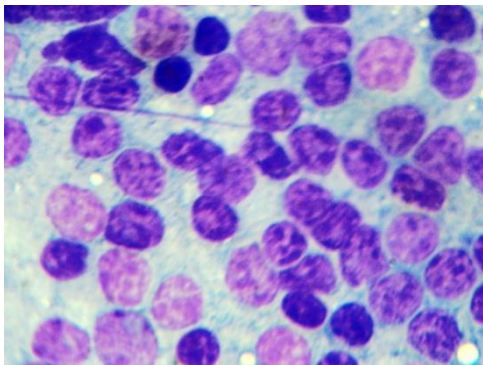


Fig 8: Photomicrograph showing Monomorphic population of lymphoid cells with socketball chromatin (Small lymphocytic lymphoma/Chronic lymphocytic leukemia/ CLL)

Discussion

Accurate and timely diagnosis along with effective anti TB drugs is the mainstay of TB care and control. A confirmed diagnosis of TB can only be given on isolating the *M. tuberculosis* on culture or finding specific DNA sequence of the bacteria in aspirates by either doing CBNAAT or PCR. In the developing countries, however, these tests are not within the reach of every individual. In these countries, cost-effective techniques for example FNAC. In cases of extrapulmonary tuberculosis, fine needle aspiration cytology (FNAC) is a very useful and reliable test. For Pulmonary TB, morphological features and sputum smear microscopy are the cornerstone of TB diagnosis. In areas where tuberculosis is prevalent, diagnosis of TB can be made by seeing the morphological features. Granulomatous inflammation is the common cytological

presentation of tuberculosis. However, there are many other infectious and noninfectious causes which can lead to granulomatous inflammation. Second important infectious cause of granulomatous inflammation is fungus.

In the present study FNAC of enlarged lymph nodes was done to diagnose various lesions.

Out of total 47 cases maximum number of cases were found in the age group of 0-10 years 13 cases followed by 11-20 years, i.e. 9 cases followed by 21-30 years i.e. 8 cases. This finding was in accordance with Bezabih et al. in which 69% were below 30.¹¹ Based on the facts, it can be inferred that lymphadenopathy was more commonly seen in young population and hence Tuberculosis.⁷ Males were 21 in number and females were 26 in number with male to female ratio of 0.81:1. Female gender was a slightly more affected (55.31%) in current study and was in concordance with other studies.⁸ However, there was slight male predominance in a study of Bezabih et al.⁷ 27 Cases were showing cervical lymphadenopathy, 6 cases as submandibular lymphadenopathy, 4 as supraclavicular lymphadenopathy, 4 as axillary lymphadenopathy, 2 as inguinal lymphadenopathy, 2 as multiple body site nodes, 1 preauricular enlarged node and 1 arm node. This shows that cervical node involvement occur in maximum number of cases.

Cytopathological diagnosis on FNA

22 cases were diagnosed as Non-specific reactive lymphadenitis (Fig 1), 18 as Chronic granulomatous lymphadenitis (Fig 2), 2 as Acute Suppurative lymphadenitis (Fig 3), 1 as Non – Hodgkin Lymphoma (Fig 4), 1 case as Metastatic deposits of P.D SCC (Fig 5), 1 case as metastatic deposits of Malignant melanoma (Fig 6), 1 case as metastatic deposits of Duct cell carcinoma breast (Fig 7) and 1 case as Small lymphocytic lymphoma/Chronic lymphocytic leukemia (SLL/CLL) (Fig:8). [TABLE -4]

Out of 18 cases diagnosed as Chronic granulomatous lymphadenitis, 4 cases were found to have extensive caseous necrotic material and few vague epithelioid cell collections, 9 cases

were found to have well defined epithelioid cell granulomas and langhan type of giant cells and five cases were showing reactive background with few epithelioid cell collections only .These patients were aspirated again and sample rinses were sent for CBNAAT for confirmation of diagnosis. These all 5 cases were finally diagnosed as tuberculosis cases on CBNAAT. (Table 4 & 5). The various morphological presentations of TB have been published locally .⁹ International data also supports this variation and studies tried to correlate morphological findings with the AFB staining and CBNAAT.¹⁰

In regions where TB is very common, the morphological findings of granulomatous inflammation is consistent with tuberculosis .¹¹ India is one among these along with Ethiopia and other African countries. Since epithelioid granulomas, caseation necrosis, giant cells, and AFB positivity are specific for TB, so in these countries excision biopsy can be avoided and antituberculous treatment can be given straightaway.⁸ Excision isnot free of complication and is expensive and time consuming, thus it can delay the treatment. Above findings conclude that FNAC with ancillary studies can solely help the physician to start the treatment in patients diagnosed of particular disease.

Recommendations

When physicians are confronted with enlarged lymph nodes, the node may be punctured with a sterile disposable needle, and if cheesy material is aspirated then the physician can strongly consider tuberculous lymph adenitisadenitisin are as where tuberculosis and immunodeficiency states are rampant and pathology services are lacking.

Limitation of Study

This study does not include comparison with histopathology because of unavailability of Later in the department.

Conclusion

To conclude Cytopathology (FNA) is non-invasive procedure and helps in making accurate diagnosis of various lesions in both superficial and deep nodes in the body without causing any complications to the patients and is done as an OPD procedure without any hospital stay and is a cost effective and relatively painless procedure. But whenever there is doubt in diagnosis, repeat sample can be taken without any delay for cytopathology as well as for Ancillary studies. Fine needle aspiration cytology (FNAC) is also very important investigation in the diagnosis of granulomatous inflammation. If it is supplemented with ancillary studies like, special stains as ZN, GMS, and PAS, and CBNAAT /PCR it may help to differentiate between many infectious causes of granulomatous inflammation.

In this region this procedure helped to diagnose Extra pulmonary Tuberculosis cases which were missed otherwise.

Conflict of interest: None

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