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EVALUATION OF GRANULOMATOUS LYMPHADENITIS ON FINE NEEDLE ASPIRATION CYTOLOGY – DIAGNOSTIC DILEMMA

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ABSTRACT

Aims: *Granulomatous lymphadenitis is one of the most common cause of lymphadenopathy. Fine needle aspiration cytology (FNAC) is the most economical, safe and easy way of its diagnosis. In developing countries like India, the most common cause is Tuberculosis. Definitive and correct diagnosis is essential for early treatment. Aim of this study is to review cytomorpholgy of granulomatous lymphadenitis on FNAC in respect to their aetiology.* ***Methods****: Cytomorphological features of 217 cases showing epithelioid cells on FNAC lymph nodes were reviewed in respect to their aetiology.* ***Results:*** *Definitive diagnosis of tuberculosis was achieved in 69.58 %(n=151) cases on FNAC based on epithelioid cells and caseation necrosis and or Acid Fast Bacilli (AFB)/AFB culture positivity. Two cases were diagnosed as lymphoma. In remaining 64 cases based on clinical signs and symptoms, therapeutic trial of standard antitubercular treatment (ATT) was advised.* ***Conclusion****: Definitive diagnosis of lymph node tuberculosis on FNAC requires epithelioid cells and caseation necrosis and/or AFB/culture positivity for AFB. Culture positivity is gold standard for diagnosis of tuberculosis. Cases in which definitive diagnosis is not achieved, therapeutic trial of ATT should be given based on clinical signs and symptoms.*

KEYWORDS

Fine needle aspiration, Fine needle aspiration cytology, Acid fast bacilli, Granulomatous, lymphadenitis.

INTRODUCTION

Granulomatous lymphadenitis is a manifestation of several disorder and is mainly caused by infections, sarcoidosis , foreign body reactions , lymphomas and lymph nodes draining carcinomas. Infectious causes include tuberculosis, atypical mycobacteriosis, brucellosis, fungi and pneumocystis carinii. Most notable are tuberculosis with a reported frequency of 59.4% and fungal causes with a reported frequency of 20.4%. [1-3] Tuberculosis has been declared as a global emergency. More than two billion people equal to one third of the world's population is infected with Mycobacterium Tubercle bacilli. One third of all new cases are in India and China. Lymph node tuberculosis constitutes 20 to 40% of extra pulmonary tuberculosis[4.5] Cervical lymph nodes are most commonly affected followed by mediastinal , mesenteric , axiallary , and inguinal group. Pertaining to broad differential diagnosis, tuberculous lymphadenitis remains a diagnostic challenge. Early diagnosis is a cornerstone of tuberculosis control strategies.[6] Aim of this study is to study cytomorphological features of granulomatous lymphadenitis on FNAC in respect to their aetiology.

MATERIAL AND METHODS

The study included 217 cases. Inclusion criteria for study was cases irrespective of age and sex, fine needle aspirates (FNA) of lymph nodes showing epithelioid granuloma/epitheloid cells. Exclusion criteria for the study was known cases of tuberculosis and or any patient receiving antitubercular treatment (ATT). Over the period of 5 years from June 2006 to July 2011, 217 cases were included in the study. Eight cases were HIV seropositive. With prior consent of the patients, FNA were performed using 10 ml of disposable plastic syringe and 22 gauge needle. Aspirates were smeared on glass slides and

smears were prepared and air dried. 2 smear were stained with Leishman's stain and 1 smear was stained with Ziehl Neelsen (Z.N.) stain for AFB. Additional smears if any were stained with Grocott Gomori methanamine sliver stain for fungi in 22 cases. Culture examination For AFB was done in 46 AFB negative cases. Biopsy of the lymph node was done in 12 cases. Tissue was fixed in 10% formalin and Paraffin processed 3 to 5 micron thick section were cut and stained with hematoxylin and eosin (H& E) stain.

RESULTS

Clinical details of 217 cases of lymph nodes aspirates in which epithelioid cell were seen were retrieved from the medical records. **Table 1** show detailed age and sex distribution of cases. Ages of the patients ranged from 3 to 69 years with 68.20% (n=148) in the age group of 21 to 40 years followed by (n=39) in the age group of 21 to 40 years. 51.62 %(n=112) were females while males were 43.8 %(n=105). In our study 96.72% (n=204) had cervical lymphadenopathy followed by axillary lymphadenopathy in 10.85 %(n=5) and inguinal and generalised lymphadenopathy in 1.84 %(n=4) cases each. Amongst cervical lymph nodes 59.80% (n==122) had single palpable lymph node, 26.47% (n=54) had multiple unilateral cervical lymph nodes while 13.72 %(n=28) cases had bilateral cervical lymphadenopathy. Constitutional symptoms like pyrexia, night sweats and weight loss were present in 13.82% (n=30) cases. Grossly aspirates ranged from blood tinged material and cheesy to purulent material. Epithelioid cells on FNAC were seen as elongated polygonal cells with pale cytoplasm and indistinct cytoplasmic borders. Nuclei have elliptical sometimes comma shaped with finely granular chromatin. These cells may form loose aggregates or cohesive clusters that are reminiscent of granuloma. Based on presence of epithelioid cells and other cytological features, cases were grouped into 5 groups. Group 1 (n=44) cases showed epithelioid grnulomas without necrosis with lymphocytes / reactive lymphoid cells.[**Figure 1**] Group 2 (n =80) cases showed epithelioid granuloma with necrosis.[**Figure 2**] Group 3 (n = 51) cases showed mainly necrosis with few scattered epithelioid cells. Group 4 (n=40) cases showed polymorphs, necrosis, and few scattered epithelioid cell.[**Figure 3**] Group 5 (n=2) cases showed epithelioid cells with numerous atypical lymphoid cell(NHL) on the background.[**Figure 4**]

Table 1 show age and sex distribution

Age group(years)	Male	Female	Total no: of cases
0-20	19	20	39
21-40	73	75	148
41-30	08	12	20
61-80	05	05	10

Table 2 show cytomorphological features , AFB and Culture Positivity

Group	Cytology Features	No of cases	AFB positive cases	Culture positive cases No of cases done/positive cases
Group1	Epithelioid granuloma with lymphocytes/reactive lymphoid cells without necrosis	44	13	7/1
Group 2	Epithelioid granuloma with necrosis	80	45	15/5
Group 3	Necrosis with scattered epithelioid cells	51	30	14/8
Group4	Few epithilioid cells polymorphs and necrosis	40	24	10/4
Group 5	Epithelioid cells with atypical lymphoid cells (NHL)	02	0	0
Total		**217**	**112**	**46/18**

Figure 1: FNA smear shows epithelioid granuloma (Leishman, X400)

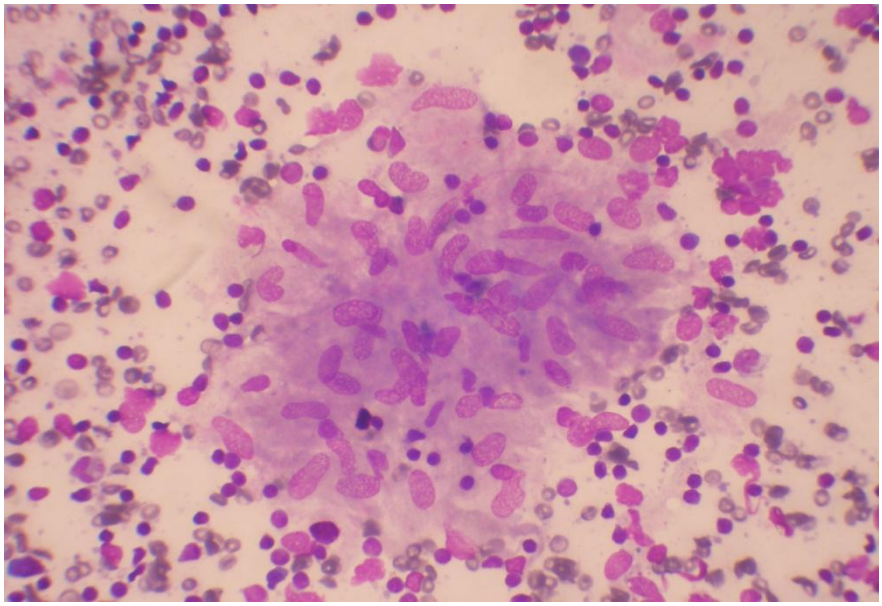


Figure 2: FNA smear shows epithelioid granuloma(thin arrow) with necrosis (thick arrow) (Leishman, X400)

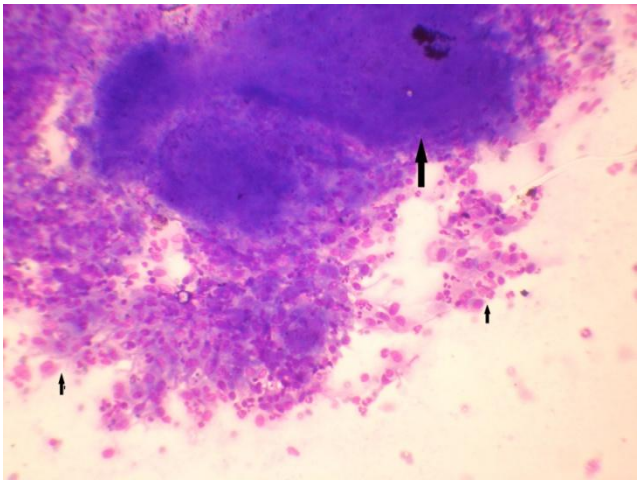


Figure 3: FNA smear show polymorphs, necrosis and scattered epithelioid cells (arrow) (Leishman, X400)

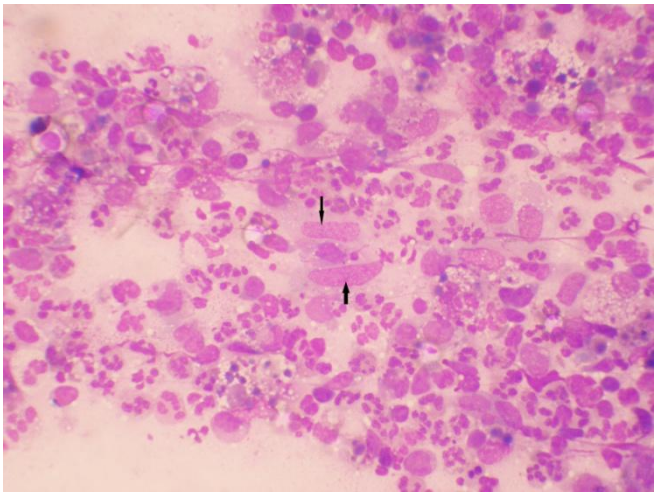


Figure 4: FNA smear shows scattered epithelioid cells (arrow) and large atypical lymphoid cells of NHL (Leishman, X400)

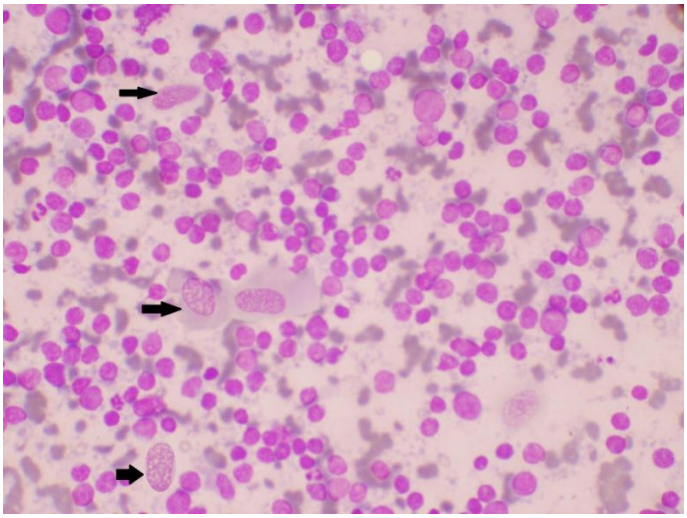
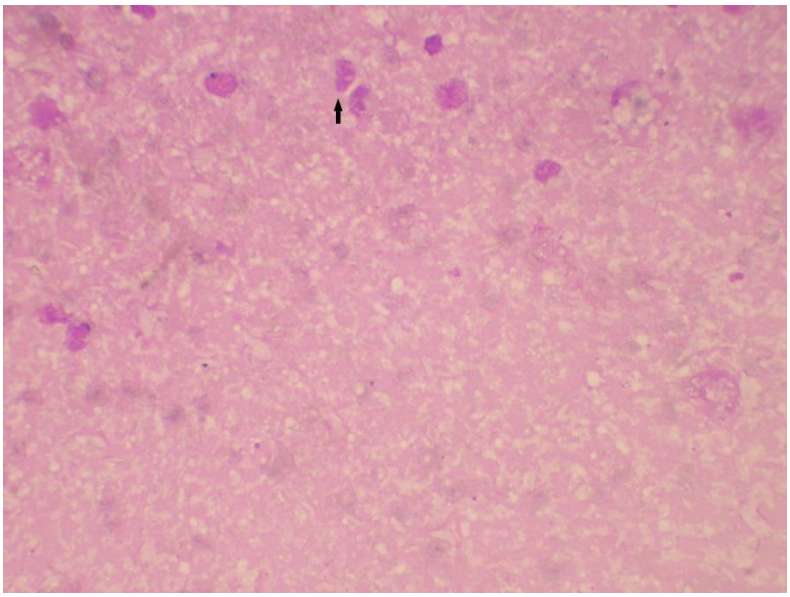


Figure 5: FNA smear shows acellular eosinophilic caseous necrosis with scattered epithelioid cells (arrow) (Leishman, X400)



Out of 171 cases in which necrosis was seen, caseous necrosis could be identified in 35.67 %(n=61) cases which included 24 Group 2, 31 Group3 and 6 Group 4 cases. It was seen as amorphous to granular eosinophilic acellular material. **Table 2** show cytomorphology features, AFB positivity and culture positivity in all 5 groups. AFB positivity in our study was 51.61% (n=112) with highest positivity in group 4 (60%) cases. Forty AFB negative cases in which culture for AFB was done, 39.13% (n=18) cases showed culture positivity with maximum (57.4%) in group 3 cases. Histopathology examination of 12 lymph nodes confirmed diagnosis of tuberculous lymphadenitis in 10 cases and non-hodgkin's lymphoma in 2 cases. No fungi were detected on fungal stains which was carried out in 22 cases on FNAC.

DISCUSSION:

Lymphadenopathy is one of the commonest clinical presentation of patients attending outdoor clinics in most hospitals. Well defined role of FNA in the investigation of lymphadenopathy has previously been studied in number of studies [7-11] and has become an integral part of initial diagnosis and management. In the context of granulomatous disorders the possible aetiology is wide. FNA with other ancillary tests such as microbiological, immunohistochemical , additional biochemical and special staining techniques are useful for obtaining a definitive diagnosis. Evaluation of granuloma is a complex problem in developed countries. Typically tuberculous lymphadenitis show epithelioid cell granuloma, caseation necrosis, and/or AFB on FNA smears. But they may not be found in several cases in cytology smears that are ultimately proved to be tuberculoses in aetiology. Clinical signs and symptoms of tuberculous lymphadenitis are nonspecific. Early diagnosis and treatment is the cornerstone of tuberculosis control strategies which reduce morbidity and mortality.[1, 5, 6, 12] Some authors believe in regions where tuberculosis is very common, morphologic findings of granulomatous inflammation are consistent with tuberculosis.[13,14]

In our study maximum cases (68.20%) were in the age group of 21 to 40 years of age. Similar age distribution was seen in studies conducted by Natraj G et al.[15]; Rajaskaran S et al.[16] and Purohit M et al.[17]. A slight female predominance with male to female ratio of 1:1.06 was seen in our study. Paliwal N et al.[6] and Natraj G et al.[15]

also noted female predominance. In contrast Rajaskaran S[16] et al. and Ahmad S[18] et al. noted male predominance. Cervical lymph nodes were most commonly involved (96.72%). In our study these findings were in concordance with Bezabih M[1] et al, Gupta AK[12] et al, Metre MS[19] et al and Sharma S[20] et al. Maximum cases (59.80%) in our study presented with a single cervical lymph node enlargement. In study conducted by Paliwal N[6] et al., 63.3% of cases presented with single lymph node enlargement while Ahmad S[17] et al observed matted cervical lymph nodes in majority of cases (60%).

The most common cytomorphological pattern (36.86%) in our study was group 2 cases which showed epithelioid granuloma with necrosis. Similar observation was made by Gupta AK [12] et al. In his study 50.35% cases showed epithelioid granulomas with necrosis. Out of total 171 cases in which necrosis was seen, caseous necrosis could be identified in 35.67 % (n=61) cases. Commonest cause of caseation in developing countries like India is tuberculosis. Detection of caseous material on FNA smears depends on the experience of pathologists.[21] It is seen as amorphous acellular to granular eosinophilic material with loss of cellular details[**Figure 5**] which enabled us to give definitive diagnosis of Tubercular lymphadenitis. Total AFB positivity in our study was 51.61% (n=112) with highest positivity (60%) in group 4 cases. Frequency of AFB positivity in various study ranges from 10-70%.[22, 23, 13,14] Low AFB positivity can be explained by the facts that-1) many cases of extra pulmonary tuberculosis are paucibacillary 2) Early stage of the disease and immunologic status of the patients. 3) Number of AFB has to be 1000 to 1000000/ml of the material to be detected by light microscopy. Demonstration of AFB is diagnostic of tuberculosis. A definitive diagnosis of tubercular lymphadenitis was offered in these cases. Out of 46 AFB negative cases in which culture examination for AFB was done using Lowenstein Jensen medium showed positivity of 39.13% (n=18) cases which enabled us to give definitive diagnosis of tuberculosis. So we observed though it takes several weeks for culture examination, it is the gold standard for diagnosis for tuberculosis.

Thus out of 217 cases definitive diagnosis of tuberculosis was made in total of 151 cases on FNA based on epithelioid granulomas with caseous necrosis, and/or AFB on Z.N. stain and AFB culture positivity. They were advised standard anti tubercular treatment (ATT) for 6 month as per Revised National Tuberculosis Control Program. (RNTCP) Out of the remaining 66 cases Grocot- Gomeri Methaneamine Silver stain was carried on FNA smears of 22 cases to rule out the fungal aetiology of granulomatous lymphadenitis. No fungi were detected. Two cases in group 5 which showed epithelioid granuloma with numerous atypical large lymphoid cell on the background. A diagnosis of Non-Hodgkin's lymphoma was suggested and subsequently confirmed on histology. Thus in remaining 64 cases there were no clinical signs and symptoms which pointed the other specific aetiology of granulomatous lymphadenitis. Out of 64 cases, 19 cases came for treatment after FNA diagnosis of granulomatous lymphadenitis. In these cases there were no definitive cytological features of tuberculosis described above were present on cytology features. Culture for AFB was also negative. These cases were given therapeutic trial of standard anti tubercular drugs for 2 months based on clinical signs and symptoms. Follow up of the cases was possible in total 41 cases, which included 31 cases in which definitive diagnosis of tuberculosis was given and 10 cases in which therapeutic trial of ATT was given. Duration of follow up ranged from 1 to 4 months. All the cases showed improvement clinically viz- reduction in size of lymph node and improvement in constitutional symptoms if present.

Other diagnostic modalities are used to improve to the diagnostic accuracy. Results of serology tests are highly variable with respect to sensitivity (0 to 100%) and specificity (59 to 100%).[24, 25] PCR and molecular methods are rapid and specific but are costly and unavailable in resource poor countries at many places.

Conclusion:

Any case of lymphadenopathy in which epithelioid cells are seen, tuberculosis must be suspected. Definitive diagnosis of tuberculosis on FNA requires epithelioid cells, caseation necrosis and/or AFB on smear. Culture examination for AFB is gold standard for diagnosis of tuberculosis. If definitive diagnostic features of tuberculosis are not seen in FNA or culture examination coupled with clinical signs and symptoms such cases should be given therapeutic trial of ATT in the regions where incidence of tuberculosis is very high.

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