ORIGINAL RESEARCH PAPER

Pathology

ROLE OF FNAC IN DIFFERENTIAL DIAGNOSIS OF HIV LYMPHADENOPATHY AND CORRELATION WITH CD4 COUNT

KEY WORDS: HIV, Fnac, Lymphnode, CD4 Count

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ABSTRACT

Background:-Lymphadenopathy is one of the earliest manifestation of HIV infection. It may be due to presence and effects of HIV, opportunistic infections, lymphoid malignancy etc. FNAC is a primary investigative procedure in the assessment of cause of lymphadenopathy. This study is performed to evaluate the role of FNAC in the differential diagnosis of HIV lymphadenopathy.

Materials and Methods :- This was a retrospective study consists of FNAC samples obtained from HIV patients having lymphadenopathy attending Cytology section of Department of Pathology, VIMSAR, Burla for a period of 2 years from April 2016 to March 2018.Smears were stained with Diff Quick, H&E, Z-N stain, India ink and CD4 correlation was done in each case.

Results:- Total 56 patients included in our study group among which 76.78% were male and rest were female. Cervical lymphadenopathy was the most common lesion (53.57%).Tubercular lymphadenitis was identified as the most common cause of lymphadenopathy in the present study.CD4 count in TB lymphadenitis ranged from 90-902/ µl. with a mean CD4 count 375 /microlit.CD4 count in Cryptoccoccal infection was <50/µl.

Conclusion:- The present study revealed the utility of lymph node cytology in the diagnosis and segregation of lymphadenpathy in HIV positive patients. It is simple, cost effective and valuable tool in the clinical management of AIDS patients

Introduction:

HIV Lymphadenopathy is the inflammation and enlargement of lymph nodes due to underlying HIV infection, which is caused by human immunodeficiency virus. The signs and symptoms of HIV lymphadenopathy include enlarged lymphnodes that are painless, seen in at least two areas of the body for a period of 3 months or more. In HIV infected individuals, lymphadenopathy occurs in the following manner. In 50% of the HIV –infected individuals, it is due to reaction of HIV, in 43% of them, it is HIV related lymphoid malignancy such as lymphoma, in the remaining 7%,it is due to HIV associated secondary infections.[1] Individuals who are immunedeficient, are at an increased risk for developing lymphofroliferative lesions and lymphomas.HIV infection is 1 of the 4 clinical settings associated with immunodeficiency recognized by (WHO) as having an increased incidence of lymphoma and other lympho proliferative disorder.[2] It is diagnosed through clinical examination or imaging of lymphnode and relevant etiology is confirmed through lymphnode cytopathology , histopathology, bacteriological and serological studies.[3]HIV positive persons can develop generalized lymphadenopathy which may be mistaken clinically for lymphoma , but is reactive based on morphology, phenotype and genotype.[4] Most lymphomas that arise in patients with HIV infection are diffuse aggressive B-cell lymphoma.[5] Persistent generalized lymphadenopathy (PGL) is a very common manifestation of HIV infection. Different opportunistic infections such as tuberculosis, toxoplasmosis, disseminated fungal infection, atypical mycobacterial infection,cytomegalovirus infection and malignancy such as Non – Hodgkin's lymphoma(NHL) may present with lymphadenopathy.[6] Lymphocytes are the target cells for HIV infection. Variable degree of lymph node involvement is seen in all stages of HIV.[7]

Fine-needle aspiration cytology (FNAC) offers a simple and effective modality for obtaining a representative sample of the material from lymphnodes, permitting cytological evaluation and other investigations.[8] Tuberculosis occurs when CD4 count has just started to decline and is 200-500cells/µl.[9] Mycobacterium avium complex(MAC) infection is most common with CD4 count ≤ 50/µl.[10]

Materials and Methods :

A total of 56 patients who had been diagnosed as HIV Positive, presented with lymphadenopathy were included in this study over a period of 2 years from April 2016 to March 2018 in VIMSAR Burla. The patients were diagnosed in ICTC centre after pretest Counseling and patients having lymphadenopathy were referred to Department of pathology (Cytology section) from ART centre for evaluation of cause of lymphadenopathy.CD4 count was done in ART centre by flow cytometry. FNAC from lymphnode was done with disposable 10ml syringe and 24 gauge needle. Smears were stained with H&E , Diff Quick, Zeihl-Neelsen , Gram stain and India ink stain. Histopathology study was done where ever necessary. CD4 Correlation was done in all cases.

Results :

During the period of 2yrs study, 56 cases were included in our study group among which 76.78% cases were male and rest were female. Youngest patient in our study group was a 7 yr mch presented as disseminated tuberculosis , other was 7 yr female child with reactive hyperplasia of lymphnode and oldest patient was 69yrs old presented with TB lymphadenitis. M:F ratio was 3.3:1 (**Table -1**). Cervical lymphadenopathy was the most common lesion 53.57% followed by axillary lymphadenopathy 26.78% (**Table-2**). The criteria followed for the diagnosis of TB lymphadenitis were AFB Positivity , culture positive irrespective of cytomorphology. FNAC smears revealed maximum number of cases presented with TB lymphadenitis (57.142%) followed by reactive hyperplasia (33.928%) , single patient having suppurative lymphadenitis ,2 cases showed lymphnode involvement with cryptococci and one case showed lymphadenitis by Mycobacterium avium intracellulare (MAI) (**Table 1**). Tubercular lymphadenitis (fig.1) was identified as most common cause of lymphadenopathy in the present study.CD4 count in TB lymphadenitis was ranged from 90-902/µl with a mean CD4 count of 375 /µl. TB lymphadenitis was further classified into three categories depending on the presence of necrosis and collection of epithelioid cells(granuloma). (a) Both caseous necrosis and granuloma,(b) only caseous necrosis and (c) only collection of epithelioid cells without necrosis. Z-N stain for AFB was positive in 28 cases out of 32 cases. Out of 4 AFB negative cases, 3 cases had only collection of epithelioid cells and one case had only necrosis and the AFB negative samples were sent for culture and it came out positive. One case of generalised lymphadenopathy was diagnosed as Non-Hodgkin Lymphoma in FNAC and confirmed by biopsy. Two patients presented with very small cervical lymphnode of size less than 0.5 cm with severe headache, were clinically

diagnosed as bacterial meningitis .But it was diagnosed as Cryptococcus neoformans on FNAC of cervical lymphnode. The patients were refered to ICTC (fig.2) centre for HIV test, and it came out positive . CSF study showed yeast form of Cryptococcus neoformans in India ink stain. CD4 count in our study varied from 33- 902 cells/ µl . In case of cryptococcal lymphadenitis CD4 count was 44 /µl in one case and 33/µl in other case. One case of MAI(Mycobacterium avium intracellulare) (fig.4) was presented as generalised lymphadenopathy and CD4 count was 77/µl. Maximum no. of cases with TB lymphadenitis had CD4 count between 499-200/µl . (**Table 3**).

DISCUSSION: In the present study, tubercular lymphadenitis (57.14%) was the most common cause of lymphadenopathy in HIV patients. Satyanarayan etal in their study, found reactive hyperplasia as the most common cause of lymphadenopathy. (11).Our study correlates with the study of HR Vanisri etal(12) ,khiste J etal.(13) and Shenoy et al (14). They found TB lymphadenitis as the most common cause of lymphadenopathy in their studies and it was 58.3%, 50% and 48% cases respectively. In the study of Nag Dipanwita et al they found 68% cases having TB lymphadenitis. (15) But in the study of A Shobhana et al they found reactive hyperplasia as the most common cause of lymphadenopathy, 55.5% cases with absolute CD4 count varies between411-945cells/ µl and TB lymphadenitis in 41% cases with CD4 count varies between 113 and 422cells/µl.(16).In the present study, we found the most common age group was 31-40yrs, followed by 21-30yrs . Our study correlates with the study of Azan Hadadi et al (17) they also found most common age group with lymphadenopathy was 31-40 yrs . In a study of Bottles et al (18) the age of HIV patient ranged from 18-52yrs and cervical lymphadenopathy was most common lymphadenopathy. In our study, we found cervical lymphnode as the most commonly affected group of lymphnode. Maximum no of patients were male (76.78%) in present study. In the study of Nag Dipanwita et al they found 76% male and 24% female.(15)Lymphnodes which forms the bulk of lymphoid tissue are the major anatomic sites for establishing and propagation of HIV infection. Lymphnodes are the filters of opportunistic pathogens. Some patients suffer progressive generalised lymphadenopathy (PGL) relatively early in the disease while others experience varying degree of transient lymphadenopathy. Lymph node involvement is a common presentation of virtually all patients with HIV infection(19)

In our study, we found 2 cases of cervical lymphadenopathy showing plenty of cryptococci in smear. Satyanarayan et al found one case of cryptococcal lymphadenitis in supraclavicular nodes. Alfanso et al reported 3 cases of cryptococcal infection in their study.(20) . Two cases of cryptococcal lymphadenitis had CD4 count < 50 cells/ µl and in case of NHL CD4 count was 72cells/µl,. J khiste et al found CD4 count of 68 cells/mcrolit. in case of lymphoma in their study. Sobhana et al found mean CD4 count of < 100/µl in HIV associated malignancies.

CONCLUSION: FNAC is an excellent tool for evalution of lymphadenopathy in HIV positive patients. It is useful in segregating lymphadenopathy cases for further management and it is also a valuable tool for identification of opportunistic infections . Correlation of Cd4+ T cells count provides information about immune status and stage of disease.

Table : 1 Age and Sex Distribution of cases

Type of Lesion	No. of cases	1 - 10		11 - 20		21 - 30		31 - 40		41 - 50		51- 60		61 -70	
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Reactive Hyperplasia	19	0	1	-	-	4	3	6	1	2	1	1	-	0	-
TB Lymphadenitis	32	1	0	0	0	8	2	10	2	3	3	2	0	1	0
Suppurative Lymphadenitis	01	-	-	-	-	-	-	1	-	-	-	-	-	-	-
Lymphoma (NHL)	1	-	-	-	-	-	-	-	-	-	-	1	-	-	-
MAI	01	-	-	-	-	-	-	-	-	1	-	-	-	-	-
Cryptococcosis	02	-	-	-	-	-	-	-	-	2	-	-	-	-	-

Table : 2 Distribution Of Sites Of Lymphadenopathy In Hiv Positive Patients N =56

	No. of cases	Percentage
Axillary	15	26.78
Cervical	30	53.57
Inguinal	04	7.14
Supraclavicular	01	1.78
Generalised	06	10.71

Table : 3 Correlation Of Cytological Pattern Of Lymphadeno pathy With Cd4 + T Cell Count

Type of lesion No. of cases	No.of cases	CD4 COUNT /µL			
		> 500	200 - 499	< 200	< 50
Reactive Lymphadenopathy	19	03	16	-	-
TB Lymphadenitis	32	03	22	07	-
NHL	01	-	-	-	01
Suppurative Lymphadenitis	01	-	-	01	-
MAI	01	-	-	01	02
Cryptococci	02	-	-	-	-

Table : 4 Comparision With Other Studies

DIAGNOSIS	DIFFERENT STUDIES		
	Shenoy et al (2002) n=48	Satyanarayan et al (2002) n = 196	vanisri et al (2008) n = 36
Mycobacterial Infection (TB)	48%	34.2%	58.3%
Reactive Lymphodenopathy	36	42.3%	36.1%
Lymphoma	10%	2.6%	2.7%

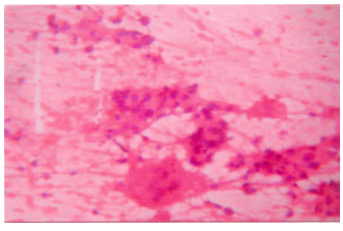

Figure: 1 Cytosmear of Tubercular Lymphadenitis (x 400, H&E)

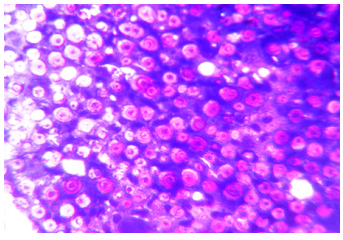

Figure: 2 Cytosmear shows cluster of cryptococci with thick capsule (x 400, diff quick)

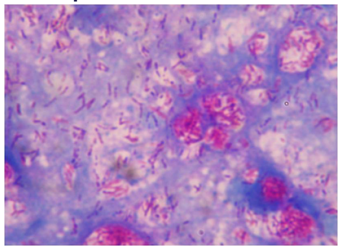

Figure: 3 Cytosmear showing acid fast bacilli both intracellular and extra cellular (x 1000, ZN stain)

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