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Fine Needle Aspiration Cytology of Lymphadenopathy in HIV-Infected Patients

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Abstract

To study the Fine needle aspiration cytology of lymphadenopathy in HIV-infected patients. Aspiration of lymph nodes was done with a 21-23 gauge fine needle in 74 HIV positive patients with lymphadenopathy. The smears were routinely stained with Papanicoloau, May Grünwald Giemsa, and Modified Ziehl-Neelson stains. Periodic acid Schiff and Grocott's methanamine stain were used wherever necessary. The most common cytological diagnosis was tubercular lymphadenitis (38 cases) followed by reactive hyperplasia (22 cases) and acute lymphadenitis/abscess (8 cases). There was one case each of Non Hodgkin lymphoma and metastatic carcinoma. 4 cases had unsatisfactory aspirates. The cytological diagnoses were concordant with the histological diagnoses in 19 out of 20 cases in which subsequent biopsy was available. FNAC is a very useful tool in the diagnosis of enlarged lymph nodes in HIV-infected patients. It is a quick, inexpensive, outdoor procedure and suitable for developing countries like India. The technique has high diagnostic accuracy.

Key Words

Lymphadenopathy, HIV, FNAC

Introduction

Acquired immunodeficiency syndrome (AIDS) was first recognized in United States in 1981. In 1983, human immunodeficiency virus (HIV) was isolated from a patient with lymphadenopathy, and by 1984 it was demonstrated to be the causative agent of AIDS (1). Lymph nodes, which form the bulk of lymphoid tissue, are the major anatomic site for establishing and propagation of HIV infection.

Lymphadenopathy is common in HIV- infected patients. The management of these patients requires evaluation of the cause of lymphadenopathy. Clinical examination and radiological investigations on their own have diagnostic limitations. Incision or excision biopsy for histological evaluation is time consuming and expensive (2). The present study was done to know the cytomorphologic smear patterns in lymphadenopathy in HIV positive patients and to determine the role of FNAC as a first line diagnostic procedure in the management of these patients.

Material and Methods

FNAC of lymph nodes of 74 HIV positive patients was done over a period of one year. In each case, a brief clinical history, general physical and local examination along with evaluation of the relevant investigations was carried out. The aspiration was done with a 21-23 gauge fine needle. The smears were routinely stained with Papanicolaou (PAP), May-Grünwald Giemsa (MGG) and Modified Ziehl-Neelson (ZN) stains. Special stains like

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Periodic Acid Schiff (PAS) and Grocott's silver methanamine(GMS) were used wherever necessary. The whole procedure was performed following specific safety recommendations (3,4). The cytological patterns of the stained smears were studied in detail. The results of cytology were correlated with histopathological diagnoses in cases where the subsequent biopsy was available. **Results**

A total of 74 HIV positive patients with lymphadenopathy were subjected to FNAC. These included 51 males and 23 females. Age of the patients ranged from 8 months to 57 years and the maximum number of cases was in the age group of 31-40 years. Most patients presented with cervical lymphadenopathy.

The cytological diagnoses included: tubercular lymphadenitis, reactive hyperplasia, acute lymphadenitis /abscess, lymphoma, metastatic carcinoma and unsatisfactory aspirate.(*Table 1*)

Tubercular Lymphadenitis: A diagnosis of Tubercular lymphadenitis was made in 38 cases. In these cases either the AFB were demonstrated on ZN stain irrespective of cytomorphology or there was presence of caseation necrosis and/or epithelioid cell granulomas in the absence of stainable organisms on special stains i.e. PAS and GMS (*Fig 1-3*). Four patterns of tubercular lymphadenitis were seen in the present study: necrotizing lymphadenitis, necrotizing granulomatous lymphadenitis, granulomatous lymphadenitis. (*Table 2*) AFB positivity was seen in 25 (68.78%) cases.

Reactive Hyperplasia: A diagnosis of reactive hyperplasia was given in 22 (29.72%) cases. In 20 of these cases, the cytological picture comprised of a polymorphic population of lymphoid cells comprising of lymphocytes, interspersed small and large cleaved cells, large non-cleaved cells, and immunoblasts along with plasma cells, monocytoid cells, tingible body macrophages and mitotic figures (*Fig 4*). In two cases there was paucity of normal nodal cellular components with only scattered lymphocytes and frequent plasma cells and macrophages (*Fig 5*).

Acute Lymphadenitis: The diagnosis of acute lymphadenitis was given in 8 cases (10.81%). It was characterized by predominant population of polymorphs along with lymphocytes and macrophages (*Fig 6*). No granulomas or caseous necrosis were found and all cases were negative for AFB and fungus on special stains.

Lymphoma: A single case of lymphoma was seen. Smears from the aspirated lymph node were highly cellular and composed of a monotonous population of lymphoid cells with high Nuclear:cytoplasmic ratio, large hyperchromatic nuclei with one or more prominent nucleoli and scanty basophilic cytoplasm (*Fig 7*). A cytological diagnosis of high grade Non Hodgkin's lymphoma was given.

Metastatic Carcinoma: There was one case of metastatic carcinoma. Smears of the lymph node aspirate depicted high cellularity with cells arranged in sheets and clusters as well as individually scattered in a background of lymphoid cells. The cells showed moderate pleomorphism, with high nuclear:cytoplasmic ratio, hyperchromatic nuclei, irregular nuclear membrane, prominent nucleoli and abundant cytoplasm (Fig 8). The cytological features were of Metastatic adenocarcinoma.

The cytological diagnoses were compared with the histological diagnoses in cases where subsequent histopathology was available. The histological diagnoses were consistent with the cytological diagnoses in 19 out of 20 cases (95% concordance rate).

Discussion

Tubercular lymphadenitis was the most common diagnosis in the present study, a finding is similar to that of Jayaram and Chew, (5) Shenoy *et al.*,(6) Nayak *et al.*,(7) and Vanisri *et al.*(8) In the present study, epithelioid granulomas were found in 19 (50%) cases. The granulomas were ill-defined in most of the cases as also reported by Llatjos *et al.*(9) and Satyanarayana *et al.*(10)

Among the four patterns of Tubercular lymphadenitis, Necrotizing granulomatous lymphadenitis characterized by the presence of granulomas and caseous necrosis was the predominant pattern. Necrotizing lymphadenitis was characterized by presence of caseous necrosis but absence of granulomas. Necrotizing suppurative lymphadenitis was characterized by fragmented and intact polymorphs in a necrotic background. There were no granulomas or giant cells and diagnosis was made on the basis of demonstration of AFB on ZN staining. Granulomatous lymphadenitis showing presence of epithelioid cell granulomas without areas of caseous necrosis was the least common pattern. In these cases, clinical features and investigations like ESR and tuberculin test and positive response to ATT provided supportive evidence to the diagnosis.

 Table 1. Cytological Diagnoses of Patients Involved in the

 Present Study

Cytological diagnosis	Number	Percentage
Tubercular lymphadenitis	38	51.35
Reactive hyperplasia	22	29.73
A cute lymphadenitis	8	10.81
Lymphoma	1	1.35
Metastatic carcinoma	1	1.35
Unsatisfactory	4	5.41
Total	74	100.0

Fig 1. Tubercular Lymphadenitis.Smear with Epithelioid Cell granuloma & Reactive lymphoid cells (MGG X 200)



Fig 3. Tubercular Lymphadenitis. Smear Showing Numerous Acid Fast Bacilli (ZN X 1000)



Fig 5. Reactive Hyperplasia of Lymph Node. Predominantly Mature Lymphocytes along with many Plasma cells and few Scattered Endothelial cells. (PAP X 400)



Table 2. Patterns of Tubercular Lymphadenitis Based on theCytomorphologic Features

Pattern	Number	Percentage
Necrotising lymph adenitis	10	26.32
Necrotising granulomatous lymphadenitis	14	36.84
Granulomatous lymphadenitis	5	13.16
Necrotising suppurative lymphadenitis	9	23.68
Total	38	100.0

Fig 2. Tubercular Lymphadenitis. Smear Showing Abundant Caseous Necrosis. (MGG X 200)



Fig 4. Reactive Hyperplasia of Lymph Node. Smear Showing Polymorphic Population of Lymphoid Cells (MGG X 400)



Fig 6. Acute Lymphadenitis/Abscess. Smear Showing Many Degenerated Polymorphs & Necrotic Debris.(MGG X 400)



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Fig 7. Non Hodgkin's Lymphoma. Monomorphic Population of Lymphoid Cells Depicting Large Hyperchromatic Nuclei & Scant Cytoplasm (MGG X 400)

A diagnosis of reactive hyperplasia was given in 22 cases. Reactive hyperplasia is the most common diagnosis in many western studies (2,11,12). It could represent Persistent generalized lymphadenopathy (PGL) due to direct effect of the HIV virus (HIV lymphadenopathy) or reactive hyperplasia to some other etiology. The histological appearance of HIV lymphadenopathy varies depending on the duration of the lesion. In the early stage, there is florid reactive hyperplasia characterized by greatly enlarged follicles with reactive germinal centers, intermediate stage is characterized by involution of germinal centers, depletion of lymphoid cells and some proliferation of blood vessels and the late stage is characterized by hyalinized burnt out germinal centers, depletion of lymphoid cells, excessive plasma cells and proliferation of blood vessels (13,14). FNA cytology though unable to differentiate between these histological stages definitely can establish in most instances a reactive lymphoid process. In 20 cases of reactive hyperplasia in our study, the cytological picture comprised of a polymorphic population of lymphoid cells along with tingible body macrophages and mitotic figures. These findings correspond well to the florid reactive hyperplasia of HIV lymphadenopathy but cannot be differentiated from reactive lymph nodes of different etiology as inferred by Martin-Bates et al. (2) and Vanisri et al.(8) Out of these two cases showed presence of atypical large lymphoid cells among the polymorphic population of lymphoid cells. These were kept under strict follow up and subjected to excision biopsy. Histopathological



Fig 8. Metastatic Carcinoma. Clusters of Epithelial cells with Hyperchromatic Nuclei & Prominent Nucleoli. Background Shows Lymphoid Cells & Necrosis. (PAP X 400)

examination confirmed the diagnosis of reactive hyperplasia in both these cases. Two cases showed paucity of normal nodal cellular components with only scattered lymphocytes and frequent plasma cells and macrophages. These cases may correspond to the late lymphocyte depletion stage of the HIV lymphadenopathy. Similar findings were also seen in studies done by Jayaram and Chew (5) and Nayak *et al.* (7)

The diagnosis of acute lymphadenitis was given in 8 cases (10.81%). Nayak *et al.* (7) reported 5 cases (15.62%) of acute lymphadenitis in their study. Martin-Bates *et al.*(2) reported 2 cases (7.4%) while Shenoy *et al.* [6] and Vanisri *et al.* [8] reported 1 case each.

We diagnosed a single case (1.35%) of lymphoma in our study. The percentage of cases with lymphoma in our study was less than that in many western studies (2,11,12). The cytological features were of high grade Non Hodgkin's Lymphoma.

A single case of metastatic carcinoma was seen in the present study. The features were of metastatic adenocarcinoma but the primary could not be ascertained as the case was lost to follow up. Saika *et al.*(15) and Nayak *et al.* (7) reported single cases of metastatic squamous cell carcinoma each while Shenoy *et al.* (6) reported metastatic poorly differentiated carcinoma.

The histological diagnoses correlated well with the cytological diagnoses in 19 out of 20 cases in which subsequent histopathological diagnoses giving a Concordance rate of 95%. In the only discrepant case, reactive lymphadenitis was diagnosed on FNAC, while caseating granulomas were seen on histopathology. The discrepancy might have been due to aspiration from a



non-representative area.

The diagnostic limitations of FNAC can be overcome in many cases by close communication between the cytopathologist and clinician. Repeat aspiration can be advised when there is a discrepancy between the cytological diagnosis and clinical impression and histopathology is required in difficult cases (3).

There were no major complications reported. The only complaints were pain and redness at the aspiration site which required no treatment. There were no incidences of needle stick, splash, or any other injury in the present study.

Conclusion

FNAC is a very useful tool in the diagnosis of enlarged lymph nodes in HIV- infected patients. It is a quick, inexpensive, outdoor procedure and suitable for developing countries like India. The technique has high diagnostic accuracy. The most important advantage is diagnosis of infective lymphadenitis enabling immediate

References

- Martin-Bates E, Tanner A, Suvarna SK, Glazer G, Coleman DV. Use of fine-needle aspiration cytology for investigating lymphadenopathy in HIV positive patients. *J Clin Pathol* 1993; 46 (6): 564-66.
- Cohen MB, Zaleski MS, Wenzel RP. AIDS-related safety issues for the cytology laboratory. *Diagn Cytopathol* 1991; 7 (5): 543-45.
- Cardo DM, Culver DH, Ciesielski CA, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. Centers for Disease Control and Prevention Needlestick Surveillance Group. N Engl J Med 1997; 337 (21): 1542-43.

- Jayaram G, Chew MT. Fine-needle aspiration cytology of lymph nodes in HIV-infected individuals. *Acta Cytol* 2000; 44 (6): 960-66.
- 6. Shenoy R, Kapadi SN, Pai KP, *et al*. Fine-needle aspiration diagnosis in HIV-related lymphadenopathy in Mangalore, India. *Acta Cytol* 2002; 46 (1) : 35-39.
- Nayak S, Mani R, Kavatkar AN, Puranik SC, Holla VV. Fine-needle aspiration cytology in lymphadenopathy of HIV-positive patients. *Diagn Cytopathol* 2003; 29 (3) : 146-48.
- Vanisri HR, Nandini NM, Sunila R. Fine-needle aspiration cytology findings in human immunodeficiency virus lymphadenopathy. *Indian J Pathol Microbiol* 2008; 51: 481-84.
- 9. Llatjos M, Romeu J, Clotet B, *et al*. A distinctive cytologic pattern for diagnosing tuberculous lymphadenitis in AIDS. *J Acquir Immun Deficien Synd* 1993; 6 (12) : 1335-38.
- Satyanarayana S, Kalghatgi AT, Muralidhar A, Prasad RS, Jawed KZ, Trehan A. Fine-needle aspiration cytology of lymph nodes in HIV-infected patients. *MJAFI* 2002; 58 (1) : 33-37.
- 11. Bottles K, McPhaul LW, Volberding P. Fine-needle aspiration biopsy of patients with acquired immunodeficiency syndrome (AIDS) : experience in an outpatient clinic. *Ann Intern Med* 1988; 108 (1) : 42-45.
- Reid AJC, Miller R, Kocjan GI. Diagnostic utility of fineneedle aspiration (FNA) cytology in HIV-infected patients with lymphadenopathy. *Cytopathology* 1998; 9 (4) : 230-39.
- Pallesen G, Gerstoft J, Mathiesen L. Stages in LAV/HTLV-III lymphadenitis. I. Histological and immunohistological classification. *Scand J Immunol* 1987; 25: 83-91.
- 14. Ioachim HL, Cronin W, Roy M, Maya M. Persistent lymphadenopathies in people at high risk for HIV infection. Clinicopathologic correlations and long-term follow-up in 79 cases. *Am J Clin Pathol* 1990; 93 : 208-18.
- 15. Saika UN, Dey P, Jindal B, Saika B. Fine-needle aspiration cytology in lymphadenopathy of HIV-positive cases. *Acta Cytol* 2001; 45 (4) : 589-92.