Staging of Cytological Smears in HIV Lymphadenitis and Correlation with Histopathology

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ABSTRACT

BACKGROUND
Lymph nodes from HIV positive patients with progressive generalized lymphadenopathy undergo morphological changes associated with progression of disease. These changes can be categorized cytologically with correlation of histopathological findings. FNA cytology although unable to differentiate between the three histological stages, can establish in most instances a reactive lymphoid process. Lymphadenitis is a common finding which includes numerous infectious and noninfectious conditions. In this study I have included only patients who are confirmed and diagnosed as HIV positive, and presented with generalized lymphadenopathy.

METHODS
FNAC was performed smears were air dried, few preserved in 90% methanol simultaneously biopsy was done on these patients for histopathological examination. Smears are stained by pap and Leishman stains.

RESULTS
One hundred HIV positive patients were studied who presented with generalized lymphadenopathy. Cases of Reactive Lymphadenitis, which were diagnosed on Fine Needle aspiration, were studied and correlated with histopathological sections in following stages-
Type I pattern - Follicular hyperplasia with or without paracortical hyperplasia.
Type II pattern - Diffuse lymphoid hyperplasia with loss of Germinal centers.
Type III pattern - Marked lymphocytic depletion.

CONCLUSIONS
Patterns 1 & 2 are associated with persistent generalised lymphadenopathy type 11 is rarer. Hence one should be very cautious to study this staging, because it mimics various forms of lymphoma on FNA smears. Immunocytochemistry is helpful to confirm benign nature of the process by demonstrating polyclonality.

KEYWORDS
HIV, Lymph node, reactive process
Lymphadenopathy in HIV positive patient is a common occurrence where the spectrum of pathological changes ranges from the more common non lymphoid proliferations (HIV lymphadenitis) to involvement with non - Hodgkin’s and Hodgkin’s lymphoma, Kaposi’s sarcoma, and opportunistic infections. These changes are related to the HIV virus itself. FNA is a Powerful tool that may be used to differentiate to HIV lymphadenitis from these malignant conditions. Stage I is characterized by follicular hyperplasia. Stage II by follicular involution Stage III by depletion of follicles with development of a diffuse pattern. FNA cytology although unable to differentiate between the three, histologic stages can establish in most instances a reactive lymphoid process. FNA smears usually demonstrates polymorphous population of cells which predominates small lymphoid cells admixed with larger transformed lymphocytes (centroblasts) in a background of tingible body macrophages, plasma cells and mitotic figures. In some cases, corresponding to stage I HIV lymphadenitis large cells (centroblasts or transformed follicular center cells) may predominate in the smear. Care should be taken not to diagnose this appearance as large cell lymphoma.\(^1,2,3,4\)

**BACKGROUND**

Lymphadenopathy is common finding in patients with acquired immunodeficiency syndrome (AIDS) and related conditions which includes benign follicular hyperplasia, non Hodgkins lymphoma, Hodgkins disease, lymphadenopathic kaposi sarcoma, disseminated mycobacterial infection, and less commonly, metastatic tumor.\(^5\) The lymph node changes described in patients with AIDS and AIDS related complex (ARS) present three broad stages: the exuberant hyperplastic stage initially, the depleted phase at the other end of the spectrum, an intermediate phase between these two. The majority of investigators have described similar histological findings in the hyperplastic phase in lymph nodes in AIDS or ARC, with some emphasizing certain features that others have not considered important. Based on their studies and cases, one set of authors believe that only two features characterize this stage: florid reactive follicular hyperplasia and monocytic cells, associated with a small number of neutrophils, in the para follicular sinuses. O Murchadha et al confirm that the histologic changes alone are not diagnostic, they fail to recognize foci of mononuclear cells, associated with neutrophils in para follicular sinuses in many of their cases the failure to define the extent of follicular hyperplasia and failure to take into account the extent and duration of lymph node enlargement.

They say that these findings are characteristic and warrant testing for HIV infection. The sinusoidal mononuclear cells, also designated immature histiocytes, have been identified as monocytoid B cells. Why small number of neutrophils are found in association mononuclear cells, irrespective of etiology, is unclear.\(^6\) The known etiologic factors of florid reactive hyperplasia in lymph nodes include syphilis, rheumatoid arthritis, and plasma cell variant of angiofollicular hyperplasia (castlemans disease or giant lymph node hyperplasia) An example of this is toxoplasmosis which, in addition to reactive follicular hyperplasia, usually shows epithelioidiaclusters of histiocytes often impinging on reactive follicles, and clusters of mononuclear cells within nodal sinusoids. Cat scratch disease, lymphopatia venereum, and tularemia characteristically show necrotizing granulomatous lymphadenitis in addition to a component of reactive follicular hyperplasia. Similarly, the lymph nodes of rheumatoid arthritis and plasma cell variant of angiofollicular lymph node hyperplasia show marked interfollicular plasmacytosis in addition to reactive follicular hyperplasia. Reactive follicular hyperplasia extremely difficult to differentiate from follicular lymphoma. This processes is termed as giant follicular hyperplasia, usually results in painless enlargement of one or more lymph nodes of cervical chain, particularly in the parotid or submandibular location. The histological features of varying sized follicles set off by rim of small round lymphocytes, the presence of numerous tangible body macrophages, a high mitotic rate and the heterogeneous population of cells within the often serpentine giant follicles, and preservation of sinuses are all in favor of benign reactive processes. However there were some features present which generally are accepted as favoring a diagnosis of lymphoma. These are complete involvement of the lymph node surface area by these frequently coalescent giant follicles, the focal compression of sinuses and the capsular infiltration, although in all cases this was focal process with few small lymphocytes and plasma cells, without significant capsular thickening. Thus because of presence of contradictory features, it is reasonable to consider in the differential diagnosis both the etiologies of follicular hyperplasia and follicular lymphoma.\(^7,8\)

We wanted to study staging in reactive process in cytological smears and also to correlate with histopathology.
METHODS

One hundred HIV positive cases were selected aspiration done in OPD patients presented with generalized lymphadenopathy. All aseptic precautions was taken prior to aspiration and thereafter. This study was carried out in Dr. BRAMCH, KCG, T. B Sanitorium & Elbit diagnosis Bengaluru. Excision biopsy was done simultaneously for correlation with histopathology.

RESULTS

Cytomorphological features reveling reactive lymphadenitis were analysed in and tabulated as follows.

<table>
<thead>
<tr>
<th>Type</th>
<th>No.</th>
</tr>
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<tbody>
<tr>
<td>Type 1</td>
<td>50</td>
</tr>
<tr>
<td>Type 2</td>
<td>20</td>
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<td>Type 3</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 1

Type I & II patterns are associated with persistent generalised lymphadenopathy of the two patterns, type II is rarer and because of large number of immunoblasts in the paracortex can be mistaken for AILD. Type III pattern is seen with fully developed AIDS and is characterized by an absence of lymphoid follicles, a marked depletion of both T and B cells and prominent sinus histiocytosis. IHC and electron microscopic was performed in few cases where staging could not be made on both cyto and HPE.

DISCUSSION

Lymphadenopathy is a common finding in patients with acquired immunodeficiency syndrome. Which is probably of viral etiology is often preceded by a prodomal phase. This phase is characterized by superficial polyadenopathy either isolated, corresponding to the lymphadenopathic syndrome (LAS) or associated with other clinical and biological signs characterizing the AIDS related complex. Routine histological examination alone or preferably with immune labeling is often sufficient for the diagnosis of lymphadenopathic syndrome of AIDS; such an aspect associated with anti LAV and/or anti-HTLV III antibodies in serum, affirms the presence of a viral infection.

Although lymphadenopathy has limited differential diagnosis the precise cause of the enlarged lymph nodes is often difficult to establish by history physical examination radiographic studies and laboratory tests. Fine needle aspiration biopsy is a useful test to evaluate lymphadenopathy in the AIDS outpatient clinic. Follicular labyrinthine foci consisting of an expanded dendritic reticular (antigen trapping) cells has been described in lymph nodes from four immune deficient homosexual men with unexplained persistent lymphadenopathy. These findings support a role for routine electron microscopy as a aid to diagnostic evaluation of nodal tissue from patients with suspected AIDS. Viral non lymphoid cell tropism may be a significant factor in the pathogenesis of the disease. The histological finding of follicular lysis and hyperplasia with lymphocyte depletion in HIV infected group although not diagnostic, is a common finding in this disease and may be used as a marker for HIV infection. The fine needle aspiration is been evaluated in many studies, where adequate samples were obtained and very good correlation with excision biopsy was seen, indicating reliable microscopic interpretation. FNAC is a highly accurate, cost effective method of diagnosis. In our study staging could be done on FNA smears in known HIV positive cases, where
Cytomorphological features were well appreciated and clarity of the smears was excellent to interpret and well correlated with histological findings. Stage I and III was ease with clinical and microscopic findings. Stage II was done with further ancillary tests which included IHC and even electronic microscopy. Light microscopy revealed pronounced follicular hyperplasia with wide follicles composed of germinal centers. These findings were classical which was easily readable on cytology and it was evident on scanner view. In stage II discrete or semi-confluent aggregates of expanded non lymphoid dendritic reticular cells were a notable feature.

Germainal centre revealing dendritic cells, immunoblasts centrocytes and small lymphocytes which adhere to syncytial cytoplasm with pale grey violet granules.

CONCLUSIONS

This study concludes that aspiration smears can evaluate typing in HIV Lymphadenopathy. Although type II is rare or difficult to diagnosis, one can approach on cytomorphological features.

REFERENCES


