

Case Report

DIAGNOSTIC DILEMMA IN AIDS RELATED LYMPHADENOPATHY - A CASE REPORT WITH REVIEW OF LITERATURE

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ABSTRACT

Florid reactive hyperplasia (FRH) is encountered in a variety of clinical conditions. In AIDS related lymphadenopathy, it is accompanied by collection of monocytoid B-Cells in the sinuses, neutrophils and features of dermatopathic lymph-adenopathy. Our case is a 35 years old male patient with history of pain in the hypogastric region. Blood examination showed severe anemia, neutrophilic leucocytosis with relative lymphopenia. USG of abdomen revealed gross splenomegaly, mild hepatomegaly with fatty change and suspected secondaries in liver. On examination bilateral palpable lymph nodes were found in epitrochlear region with clinical suspicion of lymphoma. Histology showed the picture of FRH. Immunohistochemistry (IHC) for CD Marker study confirmed polyclonal nature of the lymphoid cells. Bilateral palpable epitrochlear lymphadenopathy in a diverse clinical background had raised a suspicion of HIV infection. Patient was sent to Integrated Counselling and Testing Center (ICTC) and was found to be HIV-1 positive. Subsequently CD4 cell count showed the level of 38 cell/ μ l of blood. The Characteristic picture of FRH in histology in a diverse clinical background is most helpful in excluding a lymphoma.

Keywords: HIV-1, Florid Reactive Hyperplasia (FRH), Immunohistochemistry (IHC)

INTRODUCTION

The first acquired immune deficiency syndrome (AIDS) case in India was detected in 1986. The 2012 estimates suggest that HIV prevalence (adult 15-49 years) in India at National level continues its steady decline from the estimated level of 0.41% in 2001 to 0.27% in 2011 (NACO, 2013-14). After sub-Saharan Africa and Nigeria, India has the third largest burden of HIV infection. The lymph node abnormalities in AIDS patients can be of various types, but the most common change is Florid reactive hyperplasia (FRH) (Baroni, 1993; Said, 1988). In AIDS related lymphadenopathy, it is characterized by collection of monocytoid B-Cells in the sinuses, presence of neutrophils and features of dermatopathic lymph-adenopathy. There are aggregates of small lymphocytes that can focally penetrate into the germinal centers and make their contribution to the follicle lysis with associated disruption of germinal center and distinctive clustering of large follicular center cells (Burns, 1985).

Besides FRH, the spectrum of AIDS related lymphadenopathy consists of granulomatous lymphadenitis (both tubercular and non-tubercular subtypes) pyogenic lymphadenitis, fungal lymphadenitis and also malignancies such as Kaposi sarcoma, malignant lymphoma of both Non-Hodgkin and Hodgkin type, carcinoma and metastasis. Therefore, systematic clinicopathological evaluation of lymphadenopathy is indispensable to arrive at a specific diagnosis. Here we present a case of HIV lymphadenopathy in a diverse clinical background with clinical suspicion of lymphoma.

CASES

A 35 years old male patient, reported in Medicine OPD with history of pain in the hypogastric region for last 2-weeks. The pain was insidious and slowly progressive. The patient was also complaining of low back-ache and reduces urine output. Patient was a known case of chronic alcoholic. On physical examination bilateral, multiple mobile firm non tender palpable lymph nodes of size 1.5 x 1.5 cm (approx.) were found in both sides of the epitrochlear regions (Figure 1). However, no other cutaneous cervical, axillary and inguinal lymph nodes were palpable. On Laboratory examination, complete

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hemogram showed severe anemia Hb-4.6 gm/dl, WBC Count was high i.e. 22,700 /cmm, Differential count showed neutrophilia - 92% with relative lymphopenia -4% and raised ESR -108 mm. Liver function test showed only mild elevation (AST -56u/L) and ALT - 48u/L Coagulation parameter (PT, APTT) were within normal limit.

Radiological findings: Chest X-ray did not reveal any abnormalities. X-ray of Lumber spine showed degenerative changes. Ultrasonography of abdomen revealed gross splenomegaly, mild hepatomegaly with fatty change and suspected secondaries in liver.

Microscopic findings: FNAC of the lymph node showed cellular elements comprising of mostly immature looking lymphoid cells admixed with mature lymphocytes and occasional tangible body macrophages (Figure 2). The Cellular picture was suggestive of Non-Hodgkin lymphoma. Ziehl-Neelsen stain did not reveal any acid fast bacilli. Though cellular picture of the node was suggestive of NHL, in our region Tuberculosis is very prevalent. So, we routinely screened all the lymphadenopathy cases for acid fast bacilli. Histological examination of multiple section of the node (hematoxylin & eosin stain) showed aggregates and invagination of mantle lymphocytes into the germinal center resulting in follicle lysis and disruption of germinal center. The inter follicular tissue showed prominent vascular proliferation (Figures 3 & 4). So the diagnosis was consistent with FRH. Further, IHC for CD Marker (CD3 and CD20) study confirmed polyclonal nature of the lymphoid cells (Figure 5).

Bilateral palpable epitrochlear lymphadenopathy in a diverse clinical background had raised a suspicion of HIV infection.

Further the Patient was sent to ICTC. He was tested for antibodies HIV-1 and HIV-2 using Enzyme Linked Immunosorbent Assay (ELISA) (3 kit tests – COMB AIDS (Span Diagnostic), AIDSCAN TRISPOT and PAREEKSHAK HIV Triline Card Test (Bhat Bio-tech India)) and the sera reactive by all these three test kits were considered as positive. The patient showed the presence of antibody to HIV-1. His CD-4 cell count was done which showed the level of 38 cell/ μ l of blood (Flow cytometry).

Finally, the case diagnosed as AIDS. The patient was advised to take highly active anti-retro viral therapy (HARTT). However, he left the hospital against medical advice and was lost to follow up.

DISCUSSION

Lymphadenopathy is classically described as enlargement of node larger than 1 cm and this symptom must be present for at least 3 months duration at 2 or more lymph node. It is normally classified as generalized (occurring in multiple nodal basins throughout the body) or localised (occurring in a single nodal basin). However, the term lymphadenopathy refers to the lymph node that are abnormal not only in size but also in consistency, location and mobility. The generalized lymphadenopathy can be stated when the lymph nodes are enlarged in two or more noncontiguous area. It is an indication of systemic diseases so further investigation is therefore necessary. However, the gold standard for diagnosing the cause of Lymphadenopathy is still remains the open biopsy, when the reason for lymphadenopathy is not clear after initial evaluation (Jacobs, 2010).

Persistent generalized lymphadenopathy (PGL) is a common condition in-patient with HIV infection. PGL is characterized by unexplained, non-painful enlargement of more than one group of lymph node (other than in the groin) in two or more noncontiguous sites and persists for more than 3 months. The HIV virus has a strong tropism for lymphoid tissues. It infects primarily the CD4⁺T lymphocytes (T helper cell) therefore the lymph nodes are commonly involved during the all stages of infection. The virus attaches itself to CD4 receptor and co-receptor (CCR5) and then penetrates the cell. The cells that have such CD4 receptors on their surface are T-lymphocytes, Monocytes, dendritic cells and microglia. HIV targets a pool of activated CD4 + T cells and this may lead to exhaustion of the immune system. The depletion of lymphocytes results in the drop of the amount of CD4 cells from normal level of 1000 to 1400 cells / μ l to several hundreds. WHO staging system of AIDS (2007) included Stage-I asymptomatic with CD4⁺ T cell count > 500/ μ l. Stage-II, mild symptoms with CD4⁺ T cell count < 500 / μ l , Stage-III, systematic HIV infection < 350 / μ l of blood. When the number of CD4⁺ T cell count drops under the level of 200 cells / μ l, there is progression from HIV to AIDS (clinical stage IV).

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Figure 1: Epitrochlear lymph node

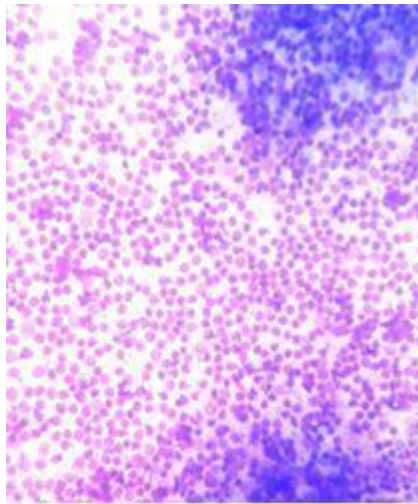


Figure 2: FNAC

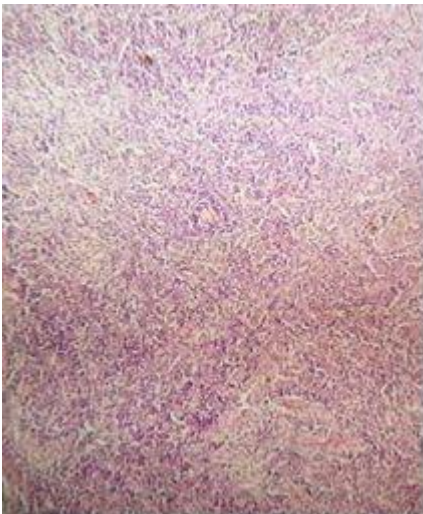


Figure 3: Histology – H and E, x100

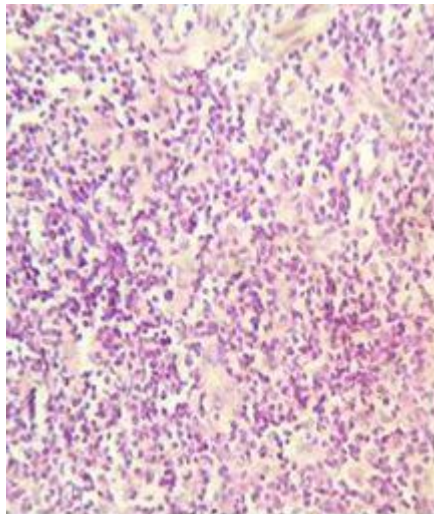


Figure 4: Histology H and E, x400

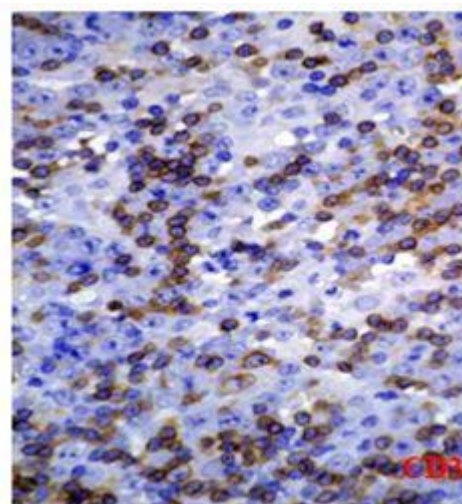
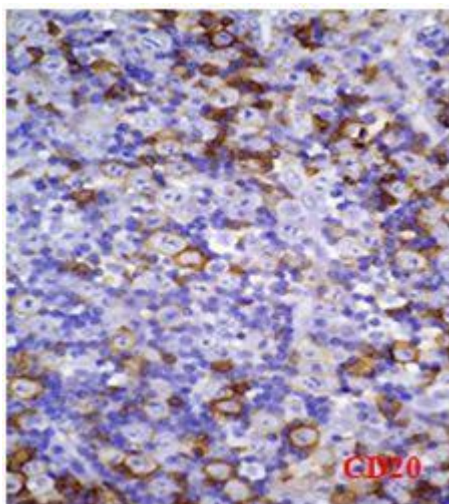


Figure 5: Immunohistochemistry (IHC) showing Lymphoid cell positive for CD20 and CD3

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Though the association of lymphadenopathy and HIV infection has been well described (Abrams, 1984) but both the size and distribution of the enlarged lymph nodes have been poorly characterized. Palpable supraclavicular, iliac, or popliteal nodes of any size and epitrochlear nodes larger than 5 mm are considered abnormal. In a hospital based study in sub-Saharan Africa, palpable epitrochlear lymph nodes were a good marker of early HIV disease where the prevalence of HIV infection was 56% (Malin, 1994). Our study also shows epitrochlear lymphadenopathy is a good marker of HIV infection.

In our case USG findings of abdomen showed suspected metastatic lesion in liver. As we could not follow up the patient, we are still in dilemma whether truly metastatic lesion was present or not.

Conclusion

Generalised lymphadenopathy, although suggestive of HIV infection, does not exclude other diagnoses such as viral infections, tuberculosis, and haematological malignancy. FRH is likely to be misdiagnosed as malignant lymphoma clinically, radiologically as well as cytologically. Characteristic picture of FRH in histology in a diverse clinical background is most helpful in excluding a lymphoma. So it can be reinforced that epitrochlear lymphadenopathy should alert a clinician or a pathologist to check HIV status of the patient. Knowledge of the rate of occurrence of enlarged lymph nodes and variations in their size and distribution could help identify useful diagnostic markers.

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