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Case Report

Diffuse Large B-Cell Lymphoma Presenting As Cutaneous Nodules in AIDS Patient

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ABSTRACT

Non-Hodgkin's lymphoma (NHL) with cutaneous involvement is an uncommon presentation involving 5-10% of total extra nodal NHL. Incidence of NHL is 60-200 times higher in HIV positive patients. Diffuse large B cell lymphoma (DLBCL) accounts for 25-30% of HIV associated lymphomas. A 38 year old HIV-1 seropositive male patient presented with multiple swellings over abdominal wall of 3 months duration and pain in upper abdomen of 1 month duration. On examination multiple nodular swellings over abdominal and chest wall measuring 1x1 to 3x3 cms were seen, which were non-tender, immobile and firm in consistency. Per abdominal examination showed tenderness in epigastrium.
Laboratory investigations revealed anemia, neutrophilia and raised ESR. CD4 count was 33 cells/µl. USG abdomen revealed thickened stomach wall and abdominal wall lesions. Chest x-ray and bone marrow examination were unremarkable.
FNAC and histopathological examination of the nodular swelling showed features of cutaneous NHL and by immunohistochemistry a diagnosis of diffuse large B-cell lymphoma, Activated B-cell type (High grade) was made. However before any intervention could be started, the patient expired within four days. DLBCL though fatal, are potentially curable mandating early diagnosis followed by specific therapy.

Keywords: Cutaneous, lymphoma, NHL, DLBCL, AIDS

INTRODUCTION

Non-Hodgkin's lymphomas (NHL) are heterogeneous group of lymphoproliferative malignancies with differing patterns of behavior and responses to treatment. The incidence of NHL increases by 60-200 times in AIDS patients than in general population and the risk increases with progressive immunosuppression related with retrovirus. [1] AIDS associated lymphomas are second most common malignancies next to Kaposi's sarcoma. [2] Extranodal presentation is most frequent in HIV-seropositive patients than in general population but cutaneous involvement being an uncommon presentation involving only 5-10% of total extranodal NHL. [3] Diffuse large B-cell lymphoma (DLBCL) accounts for 25-30% of HIV associated lymphomas and in more than 60% of cases have extranodal presentation. [4]

CASE HISTORY

A 38 year old HIV-I seropositive male patient diagnosed 13 months back, not on any medications presented with multiple swellings over abdominal and chest wall gradually increasing in size from 3 months. There was history of loss of weight, difficulty in swallowing and pain in upper abdomen from 1 month.

On general physical examination multiple nodular swellings over abdominal and chest wall varying in size from 1x1 cm to 3x3 cms were seen. They were non-tender, immobile and firm in consistency. Skin over a swelling adjacent to umbilicus showed reddish discoloration (Figure1). There was no lymphadenopathy. Per abdominal examination showed tenderness in epigastrium. There was no hepatosplenomegaly.

Laboratory investigations revealed hemoglobin-10g/dl, total WBC count-8,000 cells/mm^3 with 85% neutrophils, platelet count -2.4 lakhs/mm^3 and ESR-70 mm at the end of one hour. CD4 count was 33 cells/µl. Sputum for AFB was positive (1+). Renal function tests were within normal limits.

Chest x-ray showed unremarkable lung parenchyma and mediastinal structures.USG abdomen and pelvis revealed thickened stomach wall (Figure 2a) with abdominal wall lesions which were predominantly hypoechoic with echoes and septations (Figure 2b). Few lesions eroding underlying ribs over chest wall were also noted (Figure 2b). There was moderate ascites. Other organs were unremarkable.

FNAC of the nodular swelling showed monomorphic population of large lymphoid cells having moderate to scanty deeply staining cytoplasm, large pleomorphic nuclei with vesicular chromatin and a prominent nucleoli. Features were suggestive of non-Hodgkin's lymphoma-abdominal wall (Figure 3) and biopsy was suggested.

Histopathological examination of the nodular swelling showed tumor cells arranged in the form of sheets. These cells had moderate to abundant cytoplasm with round nucleus and a prominent nucleoli. These tumor cells were admixed with mature lymphocytes, plasma cells and histiocytes. Tumor cells were seen infiltrating into adjacent adipose tissue (Figure4). Hence a diagnosis of cutaneous NHL was made. Bone marrow examination was unremarkable.

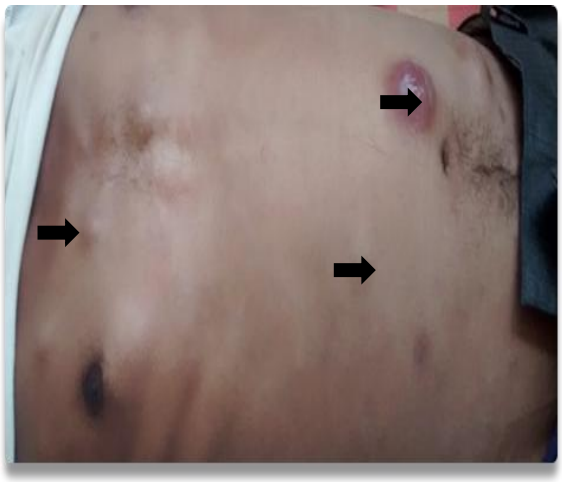

Figure 1: Multiple nodular swellings over abdominal and chest wall.

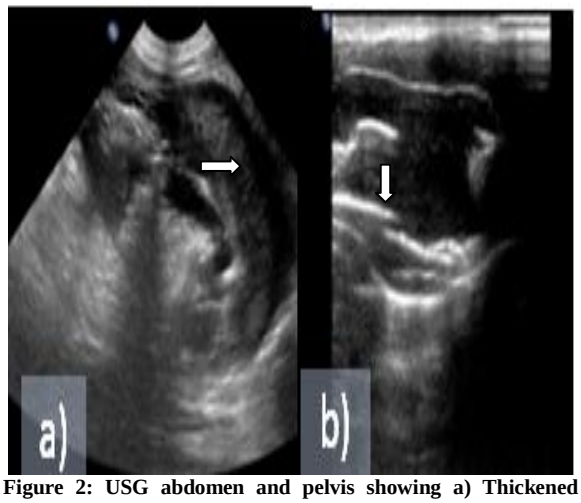

Figure 2: USG abdomen and pelvis showing a) Thickened stomach wall. b) Hypoechoic parietal wall lesion eroding underlying ribs over chest wall.

Immunohistochemistry revealed large lymphoid tumor cells immunoreactive for

CD20/MUM1/bcl2 (Figure 5) and immunonegative for CD10/Bcl6/CD3 with focal positivity for C-myc (Figure 6) and Ki67 proliferative index being more than 90% (Figure 5d).

Thus a diagnosis of Diffuse Large B-cell Lymphoma, Activated B-cell type (High grade) in Stage IV with B symptoms (Ann-arbor staging) was made. However before any intervention could be started, the patient expired within four days of taking discharge against medical advice.

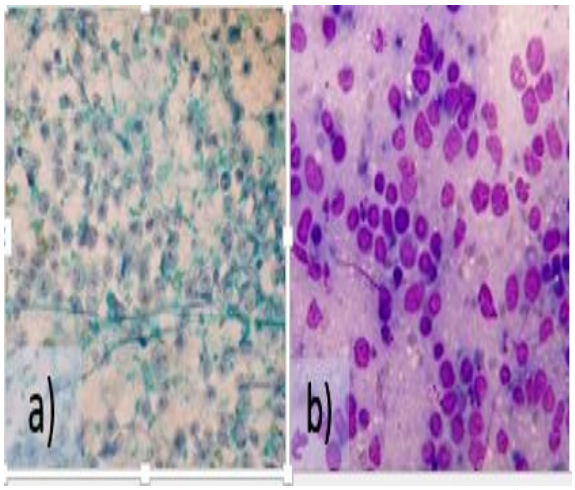

Figure 3: FNAC showing monomorphic population of large lymphoid cells with large pleomorphic nucleus and prominent nucleoli a)(PAP, x400). b)(Giemsa, x400)

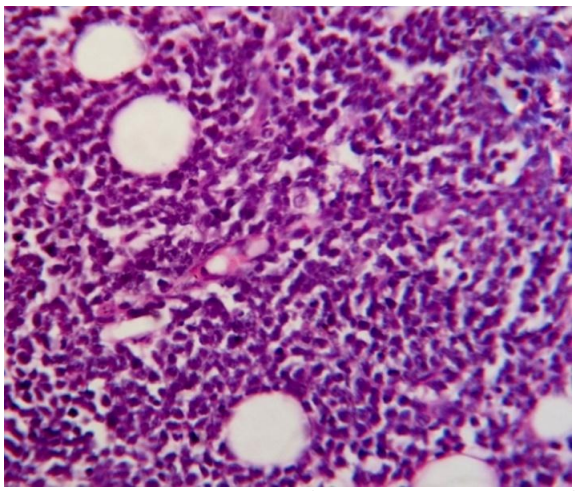

Figure 4: Biopsy showing sheets of monomorphic population of large lymphoid cells infiltrating into adjacent adipose tissue(H&E, X200)

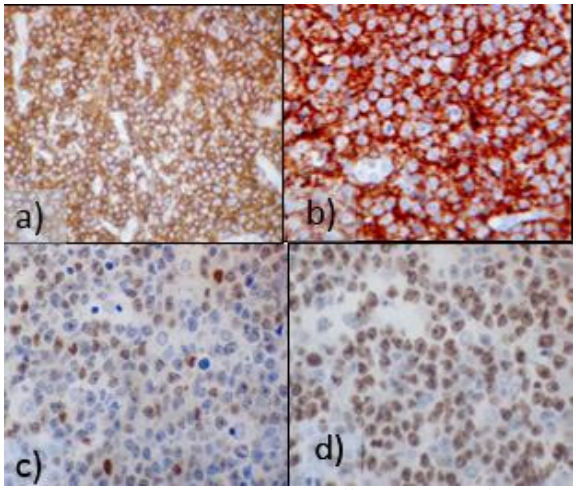

Figure 5: Immunopositivity for a)Diffuse positivity for CD20, b) bcl-2 c) MUM1, d) Ki67 proliferative index upto 90% is noted (IHC,x400)

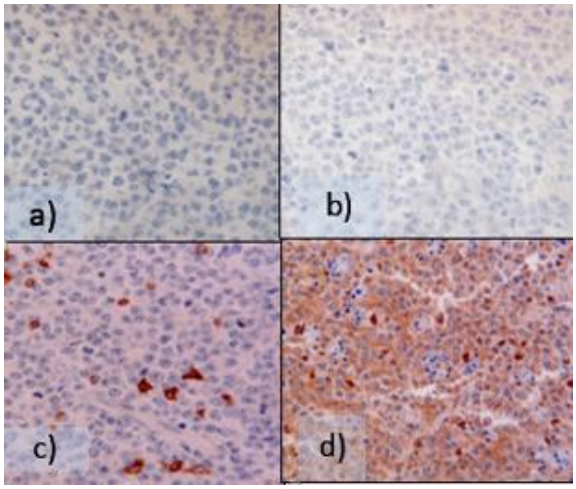

Figure 6: Immunonegativity for a)CD10, b) Bcl6 c)CD3 d) Focal C-myc positivity(IHC,x400)

DISCUSSION

NHL in HIV positive patients are aggressive, mostly of high grade, almost exclusively of B-cell origin and show commonly extranodal presentation. They are poorly responsive to therapy and appear late in HIV disease when the levels of CD4 count are low. [5]

DLBCL being more common subtypes of NHL is the most complex and heterogeneous of all NHL's [6] and is more common in immunodeficient individuals, particularly AIDS. [4]

DLBCL is classified under peripheral B-cell neoplasms in WHO classification, diffuse large B-cell lymphoma under REAL classification. It is classified as diffuse histiocytic lymphoma under Rappaport classification, centroblastic and immunoblastic under Kiel classification. [7]

DLBCL is more common in males with a peak incidence in seventh decade but can occur in children and young adults as well. It can arise as primary (or) secondary DLBCL. Primary DLBCL arises denovo in immunodeficient and in the setting of EBV infection. Secondary DLBCL follows indolent lymphomas like follicular lymphoma, B-cell chronic lymphocytic leukemia, lymphoplasmacytoid lymphoma, MALT and Hodgkin's lymphoma. [8]

DLBCL's grow rapidly and form bulky tumours in nodal (or) extranodal sites, the latter affected particularly often in cases of immunodeficiency. [8] The common extranodal sites are GIT, CNS, bone marrow, testis, liver, kidney and adrenals. [9]

In our case, patient was in third decade, as AIDS related NHL presents earlier than non-AIDS and with low CD4 count. Cutaneous nodules were the only presentation with GI symptoms. Though USG showed thickened stomach wall suggestive of lymphoma biopsy was not done. CSF analysis was also not possible.

DLBCL is classified as centroblastic, immunoblastic and anaplastic based on morphology. Molecular subtypes based on antigen profile are Germinal centre B-cell(GCB), Activated B-cell(ABC) and an Intermediate group seen in AIDS patients suggesting a unique pathophysiology.[1] In our case a predominant population of immunoblasts (>90%) were seen, with bcl-2, MUM1 positivity and CD10, bcl-6 negativity suggesting ABC subtype. Ki67 proliferative index was upto 90%, hence a close differential diagnosis Burkitt's lymphoma was ruled out as c-myc was focally positive andCD10 was negative. [10]

Prognosis is significantly influenced by age, staging, morphology and molecular subtypes with immunoblastic morphology and ABC molecular subtype having a poorer outcome[9]as in our case.

CONCLUSION

DLBCL though fatal and aggressive are potentially curable with multiagent chemotherapy and HAART. Immunity plays a significant role in the clinical outcome with reports showing spontaneous resolution when patient is started on HAART. [4]

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