

# **B Cell Lymphoma in HIV positive Patients Histopathological Perspective**

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### **Abstract :**

HIV has turned into a global epidemic and is a source of high morbidity as well as mortality. It has been observed that in HIV infections there is a profound depletion of the CD4 helper-inducer subset of lymphocytes. As these cells are most important for immunologic functioning, the clinical disease manifestations of immunosuppression and susceptibility to opportunistic infections and neoplasms are well documented in these patients. The immunologic deficits that are associated with HIV infection are very widespread and a thorough look out for the same needs to be done. The article provides an insight into associated B cell Lymphomas associated with HIV positive Patients .

### **Key Words:**

Transmembrane, Lymphocyte, suppressor, Lymphoma, Wiskott

### **Introduction:**

HIV Virus is an immunosuppressant virus and effects various levels of immune system. The clinical consequences of human immunodeficiency virus infection are due to the ability of this virus to

incapacitate the immune system of the host and rendering the host liable to develop immune deficiency diseases in the form of opportunistic infections and opportunistic cancers.

### **Text:**

AIDS is caused by HIV which is a human retrovirus belonging to the lentivirus family. The viral particle is covered by a lipid bilayer derived from the host cell and studded with viral glycoproteins gp41 and gp120. Like most retroviruses, the HIV-1 virion is

spherical and contains an electron-dense, cone-shaped core surrounded by a lipid envelope derived from the host cell membrane. The virus core contains: major capsid protein p24, nucleocapsid protein p7/p9, two copies of genomic RNA, and three viral enzymes (protease, reverse transcriptase, and integrase). p24 is the most readily detected viral antigen and is therefore the target for the antibodies used to diagnose HIV infection in blood screening. The viral core is surrounded by a matrix protein called p17, lying beneath the virion envelope. The viral envelope itself is studded by two viral glycoproteins (gp120 and gp41), critical for HIV infection of cells. The HIV-1 proviral genome contains the gag, pol, and env genes, which code for various viral proteins. In addition to these three standard retroviral genes, HIV contains several other genes (given three-letter names such as tat, rev, vif, nef, vpr, and vpu) that regulate the synthesis and assembly of infectious

viral particles.<sup>1,2,3</sup> The product of the tat (transactivator) gene, for example, is critical for virus replication. The nef protein activates intracellular kinase activity (affecting T-cell activation, viral replication, and viral infectivity) and reduces surface expression of CD4 and MHC molecules on infected cells. The two major targets of HIV infection are the immune system and the CNS. The life cycle of the virus is best understood in terms of its interactions with the immune system. The entry of HIV into cells requires the CD4 molecule, which acts as a high-affinity receptor for the virus. This explains the tropism of the virus for CD4+ T cells and its ability to infect other CD4+ cells, particularly macrophages and DCs. However, binding to CD4 is not sufficient for infection; the HIV envelope gp120 must also bind to other cell surface molecules (coreceptors) to facilitate cell entry. Two cell surface chemokine receptors, CCR5 and CXCR4, serve this role.<sup>4,5</sup>

**Structural genes of HIV Virus**

<b>Gag</b>	<b>Antigens</b>	<b>Proteins</b>
	<b>p 24</b>	<b>Capsid protein</b>
	<b>p 7p9</b>	<b>Core nucleocapsid protein</b>
	<b>p17</b>	<b>Matrix protein</b>
<b>Pol</b>	<b>Reverse transcriptase</b>	<b>Produces ds DNA pro virus</b>
	<b>Integrase</b>	<b>Produces ds DNA integration into host DNA</b>
	<b>Protease</b>	<b>cleaves poly protein</b>
<b>Envelop</b>	<b>gp 120</b>	<b><u>Surface protein</u> that binds to CD4 on host cell</b>
	<b>gp 41</b>	<b>Transmembrane protein for cell fusion</b>

**Regulatory genes of HIV virus:**

- |                |   |
|----------------|---|
| <b>1. Tat:</b> | <b>Transactivator protein : activator of transcription</b>            |
| <b>2. Rev:</b> | <b>Regulator Protein: regulator of transport of RNA to cytoplasm.</b> |
| <b>3. Nef:</b> | <b>Negative factor: Decrease MHC on infected T cells.</b>             |

Approximately 95% of lymphomas are considered to be B cell origin. Because cell surface expression of B cell antigens is seen .

It has been found that the Protein products of a number of retroviruses have been shown to have direct immunosuppressive properties independent of viral infection. Especially important is the role of a peptide in the HIV-1 gp41 transmembrane protein has been demonstrated in vitro to inhibit lymphocyte proliferative responses to mitogenic or antigenic stimuli. In addition the Protein products of a number of retroviruses have been shown to have direct immunosuppressive properties independent of viral infection. Lymphocyte abnormalities are also seen to be associated with HIV infection . The lymphocyte abnormalities observed with HIV infection include decreased lymphokine production, decreased expression of interleukin-2 (IL-2) receptors, decreased alloreactivity, and decreased ability to provide help to B cells.

The quantitative abnormality of T lymphocytes is the result of progressive depletion of the CD4+ helper T lymphocyte population .<sup>6,7,8</sup>

B-cell lymphoma frequently occurs in immunosuppressed individual sand specifically in HIV Positive Patients.<sup>6</sup>It has been noticed that the Genetic disorders of the immune system such as Wiskott-Aldrich syndrome, as well as immunosuppressive therapy used in organ transplantation, are associated with malignant transformation of B cells and an oligoclonal or monoclonal lymphoma. Non-Hodgkin's B-cell lymphoma is emerging as a recognized manifestation of HIV infection .Causative factors

operative in the development of lymphoma in AIDS are likely to be multifactorial . The Virus appears not be play a direct role but rather provides a permissive environment in which lymphoma develops. Lymphoma develops as an opportunistic neoplasm and is considered an AIDS-defining illness. Proliferative signals to B cells, whether from dysfunctional T cells, aberrant cytokine production, or infections may induce polyclonal expansion of the B-cell population .This expanded population may provide targets for genetic abnormalities that lead to malignant transformation and emergence of several dominant clones. The chromosomal abnormalities frequently seen in B-cell lymphoma involve translocation of loci encoding the immunoglobulin genes with the c-myc oncogene. Genetic evidence of Epstein-Barr virus is found in about one half of B-cell lymphomas in AIDS patients and virtually all primary CNS lymphomas in AIDS. A number of interacting factors are likely to be important in the pathogenesis of lymphoma in those patients with HIV infection united by the disorganization of immune function induced by HIV.

Usually the trend is that the B-cell lymphoma in AIDS patients tends to be of high-grade histologic pattern and follows an aggressive clinical course. Among the Histopathological subtypes it has been noticed that the Small, noncleaved or immunoblastic histologies are most frequent and account for nearly three fourths of all lymphomas in this setting. The remaining are usually a diffuse, large-cell type. The lower-grade lymphomas reported among HIV-infected individuals may represent background rather than neoplasm

directly associated with immunosuppression. Rarely, B-cell acute lymphoblastic leukemia or T-cell neoplasms have been reported.<sup>9,10,11,12,13</sup>

Most patients have extranodal disease involving the gastrointestinal tract, CNS, liver, other soft tissues, or tumors of the bone marrow. Lymphoma strictly confined to lymph nodes is uncommon. Mostly the Gastrointestinal lymphoma may occur anywhere from the esophagus to the anus. The cases of Primary CNS lymphoma are usually immunoblastic in histologic sub type . Such patients generally have solitary mass lesions in the parenchyma of the brain, whereas CNS involvement in conjunction with systemic lymphoma is more often meningeal in location. Most AIDS patients with B-cell lymphoma are classified as having stage III (involving both sides of the diaphragm without visceral involvement) or stage IV (visceral involvement). Systemic "B" symptoms are frequent, but fever should not be immediately ascribed to lymphoma in AIDS patients and secondary infectious causes need to be ruled out. Staging of patients should follow the approach used in other settings of non-Hodgkin's lymphoma, with particular attention to the gastrointestinal tract, bone marrow, and CNS. It is not clear that prognosis of lymphoma in AIDS is affected by stage.<sup>14</sup>

#### Conclusion:

B Cell Lymphomas represent a significant association of HIV Positive cases . A Thorough look out for the tumors should be taken and an aggressive protocol devised. All AIDS patients diagnosed with systemic non-Hodgkin's lymphoma should undergo careful CNS assessment with computed tomographic (CT) scan or magnetic resonance imaging (MRI) scan for ruling out Lymphomas.

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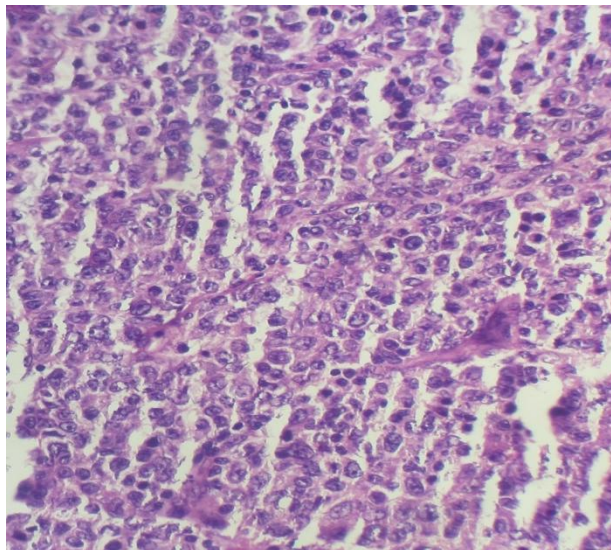
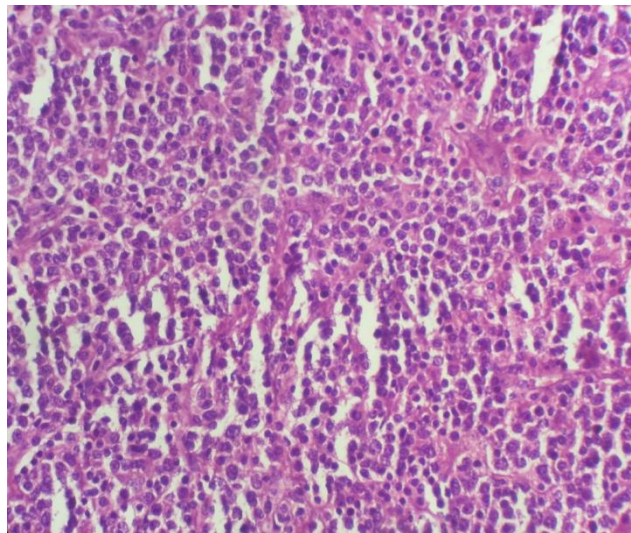


Fig: 1 NHL Lymphoma



**Fig: 2 NHL Lymphoma**



**Fig: 3 NHL Lymphoma**