

Cancer Association of South Africa (CANSA)



Fact Sheet on Aids-related Lymphoma

Introduction

The term 'Aids-related lymphoma' describes those lymphomas occurring in individuals with Acquired Immune-deficiency Syndrome (Aids).

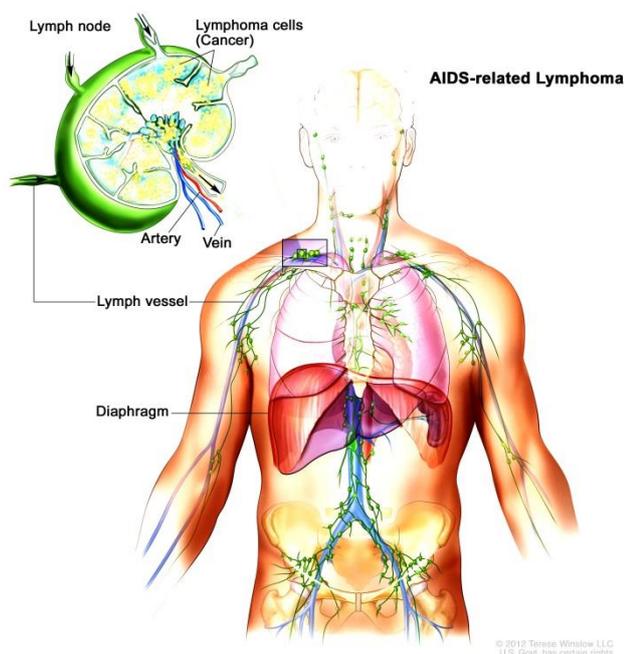
[Picture Credit: Aids-related Lymphoma]

A lymphoma is a type of cancer that arises from lymphoid cells. In Aids, the incidence of non-Hodgkin's lymphoma, primary cerebral lymphoma and Hodgkin's lymphoma are all increased.

There are three (3) different varieties of Aids-related lymphoma: Diffuse large B-cell lymphoma, B-cell immunoblastic lymphoma, and small non-cleaved cell lymphoma (Burkitt's lymphoma).

The lymph system is made up of thin tubes that branch, like blood vessels, into all parts of the body. Lymph vessels carry lymph, a colourless, watery fluid that contains white blood cells called lymphocytes back into the bloodstream. Along the network of vessels are groups of small, bean-shaped organs called lymph nodes through which the lymph travel on their way back into the bloodstream.

Clusters of lymph nodes make, and store, infection-fighting cells. The spleen is an organ in the left upper abdomen that makes lymphocytes and filters old blood cells from the blood. Other lymph tissue includes the thymus, a small organ beneath the breastbone, and the tonsils, organs in the throat. They are all part of the lymphatic system.



Because there is lymph tissue in many parts of the body, the cancer can spread to almost any of the body's organs or tissues including the liver, bone marrow (spongy tissue inside the large bones of the body that makes blood cells), spleen or brain.

PDQ Adult Treatment Editorial Board. 2020.

“Key points:

Aids-related lymphoma is a disease in which malignant (cancer) cells form in the lymph system of patients who have Acquired Immunodeficiency Syndrome (Aids).

There are different types of lymphoma.

Signs of Aids-related lymphoma include weight loss, fever, and drenching night sweats.

Tests tht examine the lymph system and other parts of the body are used to help diagnose Aids-related lymphoma.

Certain factors affect prognosis (chance of recovery) and treatment options.”

Kawakami, N., Namkoong, H., Shimoda, M., Kotani, H., Fujiwara, H. & Hasegawa, N. 2020.

“A 68-year-old man with past medical history of multiple cerebral infarctions presented to our hospital with subacute paresis. His vital signs on presentation were normal, and his physical examination, other than his neurological findings, was unremarkable. Neurological examinations suggested cerebellar ataxia. Laboratory testing confirmed positive for human immunodeficiency virus (HIV) infection. His CD4-positive lymphocyte count was 45/μL, and HIV-RNA was 2.3 × 10⁵ copies/mL. Brain computed tomography (CT) scan revealed multiple mass lesions and brain magnetic resonance imaging (MRI) with fluid-attenuated inversion-recovery (FLAIR) revealed periventricular hyperintensities, which suggested multiple malignant lymphoma and HIV encephalopathy. His state of consciousness had gradually worsened. Eventually, he died one month after admission. The autopsy unexpectedly showed disseminated Kaposi's sarcoma (KS). KS lesions were found in the stomach, small intestine, liver, spleen, mesentery and lungs. KS was not observed on his skin. Gross findings revealed multiple nodular lesions in each organ, and hematoxylin and eosin staining showed proliferation of spindle cells with vascular proliferation. Immunostaining was positive both for endothelial marker (CD31 and von Willebrand factor) and lymphatic endothelial marker (D2-40), which were consistent with KS. KS is the most common tumor in AIDS patients. It is caused by the human herpes-virus 8 infection. It manifests an indolent clinical course and mostly involves cutaneous lesions over the lower limbs, trunk and oral cavity. In this case, autopsy revealed disseminated KS pathologically, which was unrecognized before his death. This case highlights the possible existence of disseminated KS even without its cutaneous findings.”

Vangipuram, R. & Tyring, S.K. 2019.

“Malignancies were one of the earliest recognized manifestations that led to the description of the acquired immune deficiency syndrome (AIDS). The majority of cancers in AIDS patients are associated with coinfection with oncogenic viruses, such as Epstein-Barr virus, human herpesvirus 8, and human papillomavirus, with resulting malignancies occurring secondary to diminished immune surveillance against viruses and virus-infected tumor cells. Over 50% of AIDS lymphomas are associated with Epstein-Barr virus (EBV) and/or HHV8 infection. HHV8-associated diseases include Kaposi sarcoma (KS), primary effusion lymphoma (PEL), and multicentric Castleman disease (MCD). EBV is associated with several malignancies, including Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Coinfection with HIV and HPV is associated with an increased risk of various squamous cell carcinomas of epithelial tissues. HAART has significantly impacted the incidence, management, and prognosis of AIDS-related malignancies. In addition to changing the natural history of HIV infection in regard to incidence and survival, HAART has dramatically decreased the incidence of certain virally mediated HIV-associated malignancies such as KS and

primary CNS lymphoma. The beneficial effects of HAART on these tumors are attributed to drug-mediated HIV suppression and immune reconstitution. However, HAART has had a less favorable impact on EBV- and HPV-related malignancies. This chapter presents an overview of HIV-associated malignancies mediated by HHV-8, EBV, and HPV, and reviews the effect of HAART on the epidemiology, presentation, treatment, and outcomes of these cancers.”

Re, A., Cattaneo, C. & Rossi, G. 2019.

“Patients infected with human immunodeficiency virus (HIV) are at increased risk for developing both non-Hodgkin's lymphoma (NHL) and Hodgkin's lymphoma (HL). Even if this risk has decreased for NHL after the introduction of combination antiretroviral therapy (cART), they remain the most common acquired immune deficiency syndrome (AIDS)-related cancer in the developed world. They are almost always of B-cell origin, and some specific lymphoma types are more common than others. Some of these lymphoma types can occur in both HIV-uninfected and infected patients, while others preferentially develop in the context of AIDS. HIV-associated lymphoma differs from lymphoma in the HIV negative population in that they more often present with advanced disease, systemic symptoms, and extranodal involvement and are frequently associated with oncogenic viruses (Epstein-Barr virus and/or human herpesvirus-8). Before the introduction of cART, most of these patients could not tolerate the treatment strategies routinely employed in the HIV-negative population. The widespread use of cART has allowed for the delivery of full-dose and dose-intensive chemotherapy regimens with improved outcomes that nowadays can be compared to those seen in non-HIV infected patients. However, a great deal of attention should be paid to opportunistic infections and other infectious complications, cART-chemotherapy interactions, and potential cumulative toxicity. In the context of relatively sparse prospective and randomized trials, the optimal treatment of AIDS-related lymphomas remains a challenge, particularly in patients with severe immunosuppression. This paper will address epidemiology, pathogenesis, and therapeutic strategies in HIV-associated NHL and HL.”

Key Points Regarding Aids-related Lymphoma (ARL)

Important key points of Aids-related lymphoma (ARL) include:

- Aids-related lymphomas grow and spread rapidly
- It is a disease where malignant cells form within the lymphatic system in individuals who have acquired immunodeficiency syndrome (AIDS)
- There are different types of lymphoma
- Weight loss, fever, and night sweats are classic signs

Nganga, E.C. & Gitau, S. 2020.

“Lymphoma in HIV-infected patients is AIDS defining. This is the second most common AIDS defining malignancy after Kaposi's sarcoma. Development of lymphoma in HIV patients is related to immunosuppression and high viral load. Co-infection with other lymphotropic viruses especially EBV is also strongly associated with development of lymphoma in HIV patients. Despite advances in HAART therapy, incidence of diffuse large B cell lymphoma in HIV-infected patients remains significantly higher than in the general population. Early diagnosis is challenging due to presence of opportunistic infections and atypical presentation of the lymphoma in this subset of patients. Atypical imaging findings are not unusual, and the diagnosis of lymphoma on imaging is on many occasions unexpected as the patient would ideally be initially investigated for presumed opportunistic infection. Lymphoma treatment approaches in HIV patients are complicated by

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comorbidity with opportunistic infections and performance status of the patients. Treatment failure and early relapse are also common in AIDS-related lymphoma. This review article highlights the common and unusual multimodality imaging findings in HIV-associated lymphoma.”

Incidence of Aids-related Lymphoma in South Africa

The outdated National Cancer Registry (2017) does not provide any statistics regarding the incidence of Aids-related Lymphoma.

Symptoms of Aids-related Lymphoma (ARL)

The symptoms of Aids-related Lymphoma (ARL) is often similar to that of non-Hodgkin's lymphoma and is often vague. These are common symptoms:

- Fever with night sweats
- Weight loss
- Fatigue
- Swelling in lymph nodes in the neck, underarm, groin, or abdomen
- Skin rash or itchy skin
- Pain in the chest, abdomen, or bones

Diagnosis of Aids-related Lymphoma (ARL)

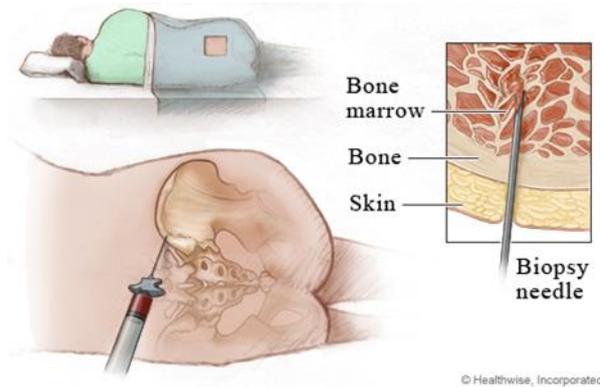
Various tests are used to diagnose Aids-related lymphoma, identify the type of lymphoma present, and determine how fast it is growing. These tests can also indicate whether the condition has spread, how well it may respond to therapy, and whether it is likely to return. One or more of the following tests may be used:

Blood Tests to Diagnose HIV - A basic HIV blood test determines whether the patient has developed antibodies to HIV. People with Aids-related lymphoma often have high levels of these antibodies in their blood at the time of diagnosis. Blood tests are also used to measure the patient's viral load and the number of CD4 cells.

Lymph Node Biopsy - a lymph node biopsy can confirm a diagnosis of Aids-related lymphoma and identify the type of lymphoma the patient has. Surgical biopsy is performed in the hospital using local anaesthesia.

Needle Biopsy - sometimes, a surgical biopsy is not possible because a swollen lymph node is difficult to reach without harming blood vessels or other structures. The doctor may then perform a needle biopsy, using fine needle aspiration or core needle biopsy, to obtain a tissue sample.

Bone Marrow Aspiration and Biopsy - the doctor may recommend a bone marrow aspiration and biopsy to determine if lymphoma has spread to the bone marrow.



[Picture Credit: Bone Marrow Aspiration and Biopsy]

Lumbar Puncture - doctors may perform a lumbar puncture, also known as a spinal tap. This test, performed on an outpatient basis in the hospital, which can reveal whether lymphoma has spread to the cerebrospinal fluid, a liquid that cushions the spine and brain.

Imaging Tests - doctors may also use imaging tests to determine how far the cancer has spread and how quickly it is growing.

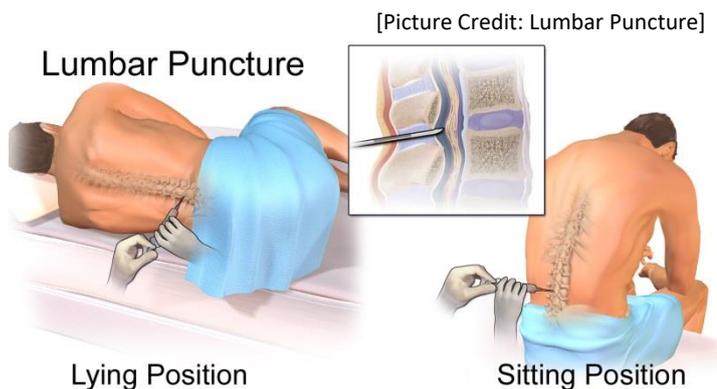
CT Scans - a CT scan uses X-rays and a computer to create three-dimensional, cross-sectional images of the body. This test can help the doctor identify the location of a tumour and measure its size.

PET Scans - the doctor may use a PET scan to look for smaller Aids-related non-Hodgkin's lymphoma tumours and to determine how active the disease is - that is, how quickly the cells are processing glucose, or sugar.

Additional Blood Tests - the doctor may order additional blood tests to determine if the patient has anaemia or a low number of platelets.

Another blood test measures the level of an enzyme called lactate dehydrogenase, which often increases as lymphoma advances.

Blood tests may also be used to look for infection with Epstein-Barr Virus. This virus causes mononucleosis and increases the risk of developing Hodgkin's lymphoma.



[Picture Credit: Lumbar Puncture]

Staging of Aids-related Lymphoma (ARL)

Staging of Aids-related lymphoma may be described as follows:

- E: "E" stands for extranodal and means the cancer is found in an area or organ other than the lymph nodes or has spread to tissues beyond, but near, the major lymphatic areas.
- S: "S" stands for spleen and means the cancer is found in the spleen.

Treatment of Aids-related Lymphoma (ARL)

Treating Aids-related lymphoma is usually a combination of treating the lymphoma as well as the Aids.

Different treatments and combinations of treatment may be used to treat Aids-related lymphoma:

HAART - highly active antiretroviral therapy (HAART) is used to slow down the progression of Aids.

Chemotherapy - combinations of chemotherapy drugs, which are used to treat other aggressive B-cell types of lymphoma, are often used to treat Aids-related lymphoma.

Biological therapy - the use of monoclonal antibodies is not well-defined in Aids-related lymphomas because of the increased risk of infection in people with Aids. However, it may be used in combination with chemotherapy in people with high enough CD4 counts.

Drugs to prevent and treat infections - drugs, such as antibiotics, are also used to prevent and treat infections.

Colony-stimulating factors - colony-stimulating factors (CSFs) are used to help reduce the risk of infection, anaemia and bleeding.

CNS prophylaxis - people with Aids-related lymphoma have a high risk of their lymphoma spreading to the central nervous system (CNS). CNS prophylaxis is used to try to prevent cancer cells from entering the tissue covering the brain and spinal cord.

PDQ Adult Treatment Editorial Board. 2020.

“Patients with Aids have weakened immune systems and treatment can cause the immune system to become even weaker. For this reason, treating patients who have AIDS-related lymphoma is difficult and some patients may be treated with lower doses of drugs than lymphoma patients who do not have AIDS.

“Highly active antiretroviral therapy (HAART) is used to lessen the damage to the immune system caused by HIV. Treatment with HAART may allow some patients with AIDS-related lymphoma to safely receive anticancer drugs in standard or higher doses. In these patients, treatment may work as well as it does in lymphoma patients who do not have AIDS. Medicines to prevent and treat infections, which can be serious, is also used.

“Four types of standard treatment are used:

Chemotherapy - is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. When chemotherapy is taken by mouth or injected into a vein or muscle, the drugs enter the bloodstream and can reach cancer cells throughout the body. When chemotherapy is placed directly into the cerebrospinal fluid (intrathecal chemotherapy), an organ, or a body cavity such as the abdomen, the drugs mainly affect cancer cells in those areas (regional chemotherapy). Combination chemotherapy is treatment using more than one anticancer drug.

“Intrathecal chemotherapy may be used in patients who are more likely to have lymphoma in the central nervous system (CNS).

“Chemotherapy is used in the treatment of AIDS-related peripheral/systemic lymphoma. It is not yet known whether it is best to give HAART at the same time as chemotherapy or after chemotherapy ends.

“Colony-stimulating factors are sometimes given together with chemotherapy. This helps lessen the side effects chemotherapy may have on the bone marrow.

“Radiation therapy - is a cancer treatment that uses high-energy X -rays or other types of radiation to kill cancer cells or keep them from growing. External radiation therapy uses a machine outside the body to send radiation toward the area of the body with cancer.

“High-dose chemotherapy with stem cell transplant - High doses of chemotherapy are given to kill cancer cells. Healthy cells, including blood-forming cells, are also destroyed by the cancer treatment. Stem cell transplant is a treatment to replace the blood-forming cells. Stem cells (immature blood cells) are removed from the blood or bone marrow of the patient and are frozen and stored. After the patient completes chemotherapy, the stored stem cells are thawed and given back to the patient through an infusion. These reinfused stem cells grow into (and restore) the body's blood cells.

“Targeted therapy - is a type of treatment that uses drugs or other substances to identify and attack specific cancer cells without harming normal cells.

“Monoclonal antibody therapy - this treatment uses antibodies made in the laboratory from a single type of immune system cell. These antibodies can identify substances on cancer cells or normal substances that may help cancer cells grow. The antibodies attach to the substances and kill the cancer cells, block their growth, or keep them from spreading. Monoclonal antibodies are given by infusion. These may be used alone or to carry drugs, toxins, or radioactive material directly to cancer cells. Rituximab is used in the treatment of AIDS-related peripheral/systemic lymphoma. New types of treatment are being tested in clinical trials.”

Noy, A. 2019.

“Cancer is the leading cause of death for HIV-infected persons in economically developed countries, even in the era of antiretroviral therapy (ART). Lymphomas remain a leading cause of cancer morbidity and mortality for HIV-infected patients and have increased incidence even in patients optimally treated with ART. Even limited interruptions of ART can lead to CD4 cell nadirs and HIV viremia, and increase the risk of lymphoma. The treatment of lymphoma is now similar for HIV-infected patients and the general population: patients with good HIV control can withstand intensive therapies appropriate to the lymphoma, including autologous and even allogeneic hematopoietic stem cell transplantation. Nonetheless, HIV-related lymphomas have unique aspects, including differences in lymphoma pathogenesis, driven by the presence of HIV, in addition to coinfection with oncogenic viruses. These differences might be exploited in the future to inform therapies. The relative incidences of lymphoma subtypes also differ in the HIV-infected population, and the propensity to advanced stage, aggressive presentation, and extranodal disease is higher. Other unique aspects include the need to avoid potential interactions between ART and chemotherapeutic agents, and the need for HIV-specific supportive care, such as infection prophylaxis. Despite these specific challenges for cancer treatment in the setting of HIV infection, the care of these patients has progressed sufficiently that recent guidelines from the American Society of Clinical Oncology advocate the inclusion of HIV-infected patients alongside HIV- patients in cancer clinical trials when appropriate.”

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About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The [South African National Clinical Trials Register](#) provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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