Cancer Association of South Africa (CANSA)

Fact Sheet
on
Angioimmunoblastic
T-Cell Lymphoma

Introduction

Lymphoma is a type of cancer involving cells of the immune system, called lymphocytes. Just as cancer represents many different diseases, lymphoma represents many different cancers of lymphocytes -- about 35 different subtypes, Lymphoma is a group of cancers that affect the cells that play a role in the immune system and primarily represents cells involved in the lymphatic system of the body.

[Picture Credit: Lymphatic System]

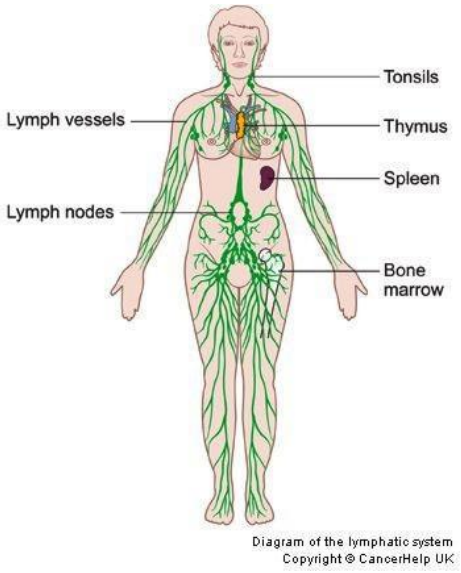

Diagram of the lymphatic system

Types of Lymphoma

Lymphomas fall into one of two major categories:

- Hodgkin's lymphoma (HL, previously called Hodgkin's disease)
- Non-Hodgkin's Lymphoma (NHL, all other lymphomas)

These two types occur in the same places, may be associated with the same symptoms, and often have similar appearance on physical examination. However, they are readily distinguishable via microscopic examination.

Angioimmunoblastic T-Cell Lymphoma (AITL)

Angioimmunoblastic T-cell lymphoma (AITL) is a rare, aggressive (fast-growing) T-cell lymphoma that accounts for approximately one to two percent of all non-Hodgkin's Lymphoma cases. Elderly patients are more likely to have AITL, and it occurs more often in men than women. The majority of patients with AITL are diagnosed with advanced-stage disease.

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Moskowitz, A.J. 2019.
"Patients with angioimmunoblastic T-cell lymphoma (AITL), one of the most common types of peripheral T-cell lymphoma (PTCL), typically present with advanced disease, systemic symptoms, and immune deregulation. Treatment can be challenging owing to frequent relapses after initial and subsequent therapy."

Yabe, M., Dogan, A., Horwitz, S.M. & Moskowitz, A.J. 2019.
"Angioimmunoblastic T-cell lymphoma (AITL) is one of the most common types of T-cell lymphoma, representing about 15-20% of cases of peripheral T-cell lymphoma (PTCL). It is characterized by a unique clinical presentation and distinct pathologic and molecular features. Classes of drugs particularly active in AITL are emerging; however, treatment of relapsed and refractory disease remains a challenge. "

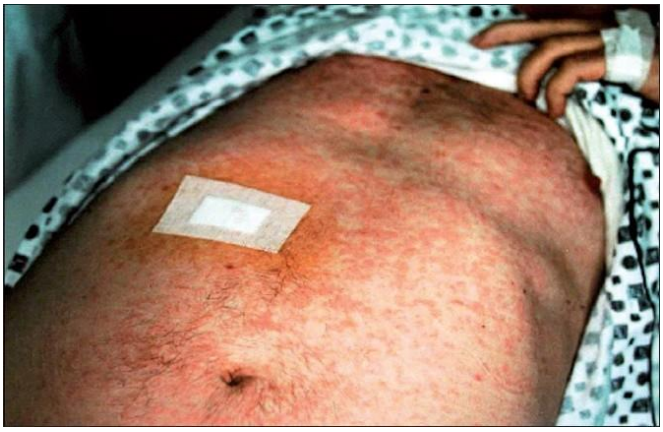
Incidence of Angioimmunoblastic T-Cell Lymphoma in South Africa (AITL)
The out dated National Cancer Registry (2016), known for under reporting, does not provide information regarding the incidence of Angioimmunoblastic T-Cell Lymphoma.

Causes of Angioimmunoblastic T-Cell Lymphoma (AITL)
It has been noticed that many people with this lymphoma show signs of having had an infection with a virus called the Epstein–Barr virus (EBV). It is not clear, however, whether this virus is causing the genetic changes in the lymphocytes – which then grow out of control to form a lymphoma – or whether an EBV infection has just been reawakened in the body because the immune system is not working as well as it should because of the lymphoma.

Signs and Symptoms of Angioimmunoblastic T-Cell Lymphoma (AITL)
Angioimmunoblastic T-Cell Lymphoma (AITL) causes a wide range of possible symptoms:

- Lumps, which are swollen lymph nodes (glands) found in the groin, armpits and neck
- Feeling generally unwell
- Unexplained fever
- Weight loss without trying to lose weight
- Night sweats
- Itching
- Lymph nodes that are abnormal in size, number or consistency
- Oedema
- Abdominal discomfort and sometimes distension (swelling) caused by cancerous lymphocytes in the spleen and/or the liver or by a collection of fluid in the abdomen (this is called 'ascites')
- Difficulty with breathing due to collection of fluid around the lungs (a pleural effusion)

- Maculopapular rashes (these can resemble a viral rash)



[Picture Credit:
Typical Rash Associated with AITL]

- Joint pains
- Tiredness or shortness of breath due to a type of anaemia called 'haemolytic anaemia', which is caused by an autoimmune reaction against red blood cells
- Symptoms of infections – infections are more likely to occur and to be more severe if there is AITL in the bone marrow.

Diagnosis of Angioimmunoblastic T-Cell Lymphoma (AITL)
The patient will have a physical examination and may have some or all of the following tests:

- blood tests – to measure the numbers of different blood cells in the sample (the blood counts
- bone marrow biopsy, a test in which a small sample is taken from the bone marrow in the hip bone to see if the lymphoma is affecting the bone marrow
- scans – computed tomography (a CT scan) of the chest, abdomen and
- positron-emission tomography (a PET scan)

Szablewski V, Dereure O, René C, Tempier A, Durand L, Alame M, Cacheux V, Costes-Martineau V. 2019.
BACKGROUND: We report the cases of three patients presenting skin lesions whose biopsies showed nodular polymorphic infiltrates consisting of lymphocytes, plasma cells, histiocytes, eosinophils, B blasts, and Hodgkin Reed-Sternberg (HRS)-like cells. Two of them were initially diagnosed as classical Hodgkin lymphoma (cHL), on the other hand, the last one as a B-cell lymphoma. All patients have been treated for angioimmunoblastic T-cell lymphoma (AITL).
METHODS: We performed a second review of the skin biopsies with further immunophenotypic molecular analyses. Scrupulous observation revealed, in the background of the three cases, atypical small to medium-sized lymphocytes carrying a CD3+, CD4+ T-cell phenotype and expressing PD1 and CXCL13 follicular helper T-cell markers. The two lesions initially diagnosed as cHL showed scattered HRS-like cells with CD30+, CD15+, PAX5+, CD20-, Epstein Barr Virus (EBV) + classical phenotype. The case initially diagnosed as B-cell lymphoma showed a diffuse B-cell proliferation associated with small B-cell and medium to large-sized B blasts that were positive for EBV.
CONCLUSION: Those cases highlighted that atypical T-cells may be obscured by B-cell proliferation mimicking cHL or B-cell lymphoma in cutaneous localization of AITL and confirmed the requirement of collecting clinical information before performing a diagnosis.

Staging of Angioimmunoblastic T-Cell Lymphoma (AITL)
Once the test results of all the tests are back the medical team will be able to tell what stage the lymphoma is at.

Treatment of Angioimmunoblastic T-Cell Lymphoma (AITL)
A few people can be treated with steroid tablets alone, but Angioimmunoblastic T-Cell Lymphoma (AITL) is usually treated with:

- Chemotherapy - chemotherapy is treatment with drugs that kill the lymphoma cells or stop them from dividing.
- Stem cell transplantation

Yamasaki, S., Yoshida, S., Kato, K., Choi, I., Imamura, Y., Kohno, K., Henzan, J., Tanimoto, K., Oqawa, R., Suehiro, Y., Miyamoto, T., Eto, T., Ohshima, K., Iwasaki, H., & Jukuoka Blood and Marrow Transplantation Group. 2020.
"The effects of stem cell transplantation (SCT) in patients with peripheral T-cell lymphoma not otherwise specified (PTCL-NOS) and angioimmunoblastic T-cell lymphoma (AITL) remain controversial. We analyzed the feasibility of SCT and risk factors associated with outcomes of PTCL-NOS and AITL patients to identify the potential clinical efficacy of SCT. We retrospectively analyzed the data of PTCL-NOS (n = 83) and AITL (n = 112) patients who received autologous (n = 10 and 16, respectively) or allogeneic (n = 12 and 4, respectively) SCT, or no SCT (n = 61 and 92, respectively) between 2008 and 2018. All PTCL-NOS and AITL diagnoses were reconfirmed by an experienced hematopathologist. Median age at PTCL-NOS and AITL diagnoses in the SCT group was younger than that in the no SCT group. Significant risk factors for lower overall survival were intermediate-high and high-risk international prognostic indexes in PTCL-NOS patients (P = 0.0052), and a > 2 modified prognostic index for T-cell lymphoma (P = 0.0079) and no SCT (P = 0.028) in AITL patients. Autologous or allogeneic SCT compared with no SCT in AITL patients resulted in 3-year overall survival of 68.6% and 100% vs. 57.2% (P = 0.018). Strategies should be developed to improve selection of PTCL-NOS and AITL patients suitable for SCT and/or additional novel therapies."

Epperla, N., Ahn, K.W., Litovich, C., Ahmed, S., Battiwalla, M., Cohen, J.B., Dahi, P., Farhadfar, N., Farooq, U., Freytes, C.O., Ghosh, N., Haverkos, B., Herrera, A., Hertzberg, M., Hildebrandt, G., Inwards, D., Kharfan-Dabaja, M.A., Khimani, F., Lazarus, H., Lazaryan, A., Lekakis, L., Murthy, H., Nathan, S., Nishihori, T., Pawarode, A., Prestidge, T., Ramakrishnan, P., Rezvani, A.R., Romee, R., Shah, N.N., Sureda, A., Fenske, T.S. & Hamadani, M. 2019.
BACKGROUND: There is a paucity of data on the role of allogeneic hematopoietic cell transplantation (allo-HCT) in patients with angioimmunoblastic T-cell lymphoma (AITL). Using the CIBMTR registry, we report here the outcomes of AITL patients undergoing an allo-HCT.
METHODS: We evaluated 249 adult AITL patients who received their first allo-HCT during 2000-2016.
RESULTS: The median patient age was 56 years (range = 21-77). Majority of the patients were Caucasians (86%), with a male predominance (60%). Graft-versus-host disease (GVHD) prophylaxis was predominantly calcineurin inhibitor-based approaches while the most common graft source was peripheral blood (97%). Median follow-up of survivors was 49 months (range = 4-170 months). The cumulative incidence of grade 2-4 and grade 3-4 acute GVHD at day 180 were 36% (95% CI = 30-42) and 12 (95% CI = 8-17), respectively. The cumulative incidence of chronic GVHD at 1 year was 49% (95%CI 43-56). The 1-year non-relapse mortality (NRM) was 19% (95% CI = 14-24), while the 4-

year relapse/progression, progression-free survival (PFS), and overall survival (OS) were 21% (95% CI = 16-27), 49% (95% CI = 42-56), and 56% (95% CI = 49-63), respectively. On multivariate analysis, chemoresistant status at the time of allo-HCT was associated with a significantly higher risk for therapy failure (inverse of PFS) (RR = 1.73 95% CI = 1.08-2.77), while KPS < 90% was associated with a significantly higher risk of mortality (inverse of OS) (RR = 3.46 95% CI = 1.75-6.87).
CONCLUSION: Our analysis shows that allo-HCT provides durable disease control even in AITL patients who failed a prior auto-HCT and in those subjects with refractory disease at the time of allografting.

- Supportive Treatments:
- Supportive treatments are treatments the patient is given to help with the symptoms of the lymphoma and the side effects of the chemotherapy.

Moskowitz, A.J. 2019.
"Patients with angioimmunoblastic T-cell lymphoma (AITL), one of the most common types of peripheral T-cell lymphoma (PTCL), typically present with advanced disease, systemic symptoms, and immune deregulation. Treatment can be challenging owing to frequent relapses after initial and subsequent therapy. The front-line treatment approach currently mirrors the approach used for other nodal PTCLs with cyclophosphamide, doxorubicin, vincristine, and prednisone chemotherapy and consideration for autologous stem-cell transplant (SCT). In the relapsed and refractory settings, allogeneic SCT offers the chance for long-term remission. Choice of treatment of relapsed or refractory disease depends on whether an allogeneic SCT is planned. Agents with preferential activity in relapsed or refractory AITL include epigenetic modifiers such as histone deacetylase inhibitors and hypomethylating agents. Other targeted agents show promise in AITL, including brentuximab vedotin and phosphoinositide-3-kinase inhibitors. Ongoing studies are evaluating new potential targets for AITL, with particular focus on identifying markers of response and resistance. Additional studies are assessing incorporation of novel agents into the front-line treatment of AITL. These studies will lead to more individualized treatment approaches and, ultimately, improved outcomes for patients with AITL."

Xu, L.M., Li, N.N., Wang, Z., Wu, X.X., Dng, Y.J., Fu, X.R., Liu, Y., Hu, L.D., Li, X.F., Wang, Y.N., Wu, Y.M., Ren, H.Y., Zhang, M.Z., Wang, M.H., Li, Y.H. & Huang, W.R. 2019.
Objective: To evaluate clinical outcomes of autologous (auto-HSCT) and allogeneic hematopoietic stem cell transplantation (allo-HSCT) for angioimmunoblastic T-cell lymphoma (AITL) .
Methods: From June 2007 to June 2017, clinical data of AITL patients who underwent HSCT in eight hospitals were assessed retrospectively.
Results: Of 19 patients, 13 male and 6 female with a median age of 50 (32-60) years old, 12 auto-HSCT and 7 allo-HSCT recipients were enrolled in this study, all donors were HLA-identical siblings. Two of allo-HSCT recipients were relapsed auto-HSCT ones. There were 5 patients (5/12) in complete response (CR) status and 7 (7/12) in partial remission (PR) status before transplantation in auto-HSCT group, and 2 (2/7) in PR status and 3 (3/7) in progression disease (PD) status before transplantation in allo-HSCT group. The median follow-up for the surviving patients was 46.5 months (range, 1-100 months) for the whole series, two patients lost in auto-HSCT group. Three patients developed acute graft-versus-host disease (aGVHD) and 5 chronic graft-versus-host disease (cGVHD) after allo-HSCT. Three patients died of primary disease and 1bleeding in auto-HSCT group. One patient died of primary disease and 2 transplantation-related mortality in allo-HSCT group. The 3-year cumulative overall survival (OS) were 56% (95%*CI* 32%-100%) and 57% (95%*CI* 30%-100%) for auto-HSCT and allo-HSCT, respectively (*P*=0.979) . The 3-year cumulative progression-free survival (PFS) were 34% (95%*CI* 14%-85%) and 57% (95%*CI* 30%-100%) for auto-HSCT and allo-HSCT, respectively (*P*=0.451).

Conclusion: Both auto-HSCT and allo-HSCT were optimal choices for AITL. In clinical practice, which HSCT was better for AITL patients should be based on comprehensive factors including sensitivity to chemotherapy, risk stratification and disease status at transplantation.

Follow-up Care and Support

Once treatment is completed and AITL is in remission, physicians will continue to monitor the health and status of each patient. Patients in remission should have regular visits (at least 6-monthly in the beginning) with their physician who is familiar with their medical history as well as with the treatments they have received.

Disease relapse and infections are common with this cancer. It is important to seek medical attention for fever or other symptoms related to improper functioning of the immune system.

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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Lymphatic System

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