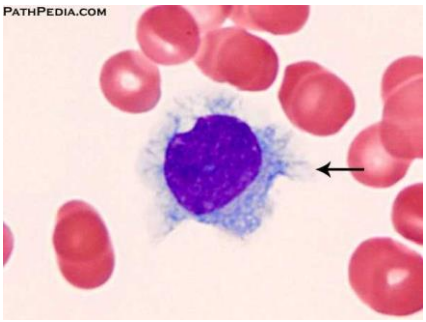
Cancer Association of South Africa (CANSA)

Fact Sheet on Adult Hairy Cell Leukaemia

Introduction

Leukaemia is a cancer of the blood forming system. Most types of leukaemia cause the bone marrow to make abnormal white blood cells. These abnormal cells can get into the bloodstream and circulate around the body.



[Picture Credit: Hairy Cell Leukaemia]

Adult Hairy Cell Leukaemia (HCL)

Hairy cell leukaemia is a rare, slow-growing cancer of the blood in which the bone marrow makes too many B cells (lymphocytes), a type of white blood cell that fights infection. These excess B cells are abnormal and look "hairy" under a microscope. As the number of leukaemia cells increases, fewer healthy white blood cells, red blood cells and platelets are produced.

This disease affects more men than women, and it occurs most commonly in middle-aged or older adults. It is considered a chronic disease because it may never completely disappear, although treatment can lead to remission for years.

Zheng, G., Chattopadhyay, S., Sud, A., Sundquist, K., Sundquist, J., Försti, A., Houlston, R., Hemminki, A. & Hemminki, K. 2019.

"Improvement of survival in lymphocytic leukaemia has been accompanied by the occurrence of second primary cancer (SPCs). Based on Swedish Family Cancer Database, we applied bi-directional analyses in which relative risks (RRs) were calculated for any SPCs in patients with chronic lymphocytic leukaemia (CLL), acute lymphoblastic leukaemia (ALL) and hairy cell leukaemia (HCL) and the risks of these leukaemias as SPCs. After CLL, RRs were significant for 20 SPCs, and high for skin squamous cell cancer (24·58 for in situ and 7·63 for invasive), Merkel cell carcinoma (14·36), Hodgkin lymphoma (7·16) and Kaposi sarcoma (6·76). Conversely, 15 CLL cancer pairs were reciprocally increased. The increased risks were reciprocal for ALL and four cancers. RR for ALL was 15·35 after myeloid neoplasia. HCL showed reciprocally increased RRs with non-Hodgkin lymphoma and melanoma. The concordance between RRs for bi-directional associations between CLL and different cancers, and HCL and different cancers was highly significant. For CLL (also for HCL), the bi-

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directional risks with skin cancers and other immune-related cancers suggest the probable involvement of immune dysfunction. For ALL, treatment may contribute to risks of multiple SPCs. Increased risk of ALL after haematological neoplasms may indicate bone marrow dysfunction. These findings may help guide treatment decisions and prognostic assessment."

Incidence of Adult Hairy Cell Leukaemia in South Africa

In providing the incidence figures of Leukaemia in South Africa, the outdated National Cancer Registry (2016) does not make provision for the reporting of the different types of Leukaemia – it also does not differentiate between acute and chronic Leukaemia - neither does it provide for different statistics for cases of adult and childhood Leukaemia - except in the 'Frequency of Histologically Diagnosed Cancer in South Africa' Section of the Registry .

According to the National Cancer Registry (2016) the following number of Leukaemia cases was histologically diagnosed in South Africa during 2016:

Group - Males 2016	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	264	1:801	0,68%
Asian males	10	1:659	1,02%
Black males	135	1:1 233	1,03%
Coloured males	17	1:1 105	0,33%
White males	102	1:354	0,48%

Group - Females 2016	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	227	1:1 107	0,54%
Asian females	9	1:798	0,72%
Black females	117	1:1 846	0,59%
Coloured females	21	1:844	0,41%
White females	80	1:465	0,49%

The frequency of histologically diagnosed cases of Leukaemia in South Africa for 2016 was as follows (National Cancer Registry, 2016):

Group - Males 2016	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	156	15	28	20	46	34	53	12
Asian males	1	0	1	1	1	3	2	0
Black males	45	11	22	10	18	15	13	1
Coloured males	1	1	2	3	4	2	4	0
White males	8	3	3	6	23	14	34	11

Group - Females 2016	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	38	26	17	26	31	37	37	15
Asian females	2	0	0	1	2	3	1	0
Black females	31	22	11	12	16	13	10	2
Coloured females	1	3	1	3	2	3	8	0
White females	4	1	5	10	11	18	18	13

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Signs and Symptoms of Adult Hairy Cell Leukaemia

The causes of Hairy Cell Leukaemia (HCL) are unknown. It is not infectious and cannot be passed on to other people. Because this disease usually develops slowly, it may not cause any symptoms for quite some time. It is sometimes discovered by chance when a blood test is taken for another reason, for example as part of a routine health check.

These and other signs and symptoms may be caused by adult hairy cell leukaemia or by other conditions:

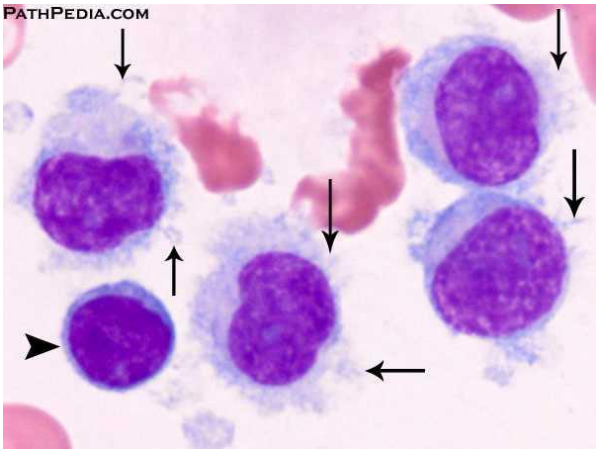
- Weakness
- Feeling tired
- Fever
- Frequent infections
- Easy bruising or bleeding
- Weight loss for no known reason.
- Pain or a feeling of fullness below the ribs.
- Painless lumps in the neck, underarm, stomach, or groin.

Streu, E. 2016.

Hairy cell leukemia is a relatively rare but distinct B-cell lympho-proliferative disorder of the blood, bone marrow, and spleen that accounts for only 2% of all adult leukemia cases. The median age at presentation is 50-55 years, with a 4:1 male to female predominance. Although considered uncommon, a number of unusual clinical presentations have been noted in the literature, including the presence of peripheral lymphadenopathy, lytic bone lesions, skin involvement, organ involvement, and central nervous system involvement. Unlike the clinical management of other hematologic malignancies, no current system is used to stage hairy cell leukemia.

Diagnosis of Adult Hairy Cell Leukaemia

The best approach to establishing the diagnosis of hairy cell leukaemia usually includes careful examination of blood and bone marrow biopsy specimens to identify cells with the morphologic features of hairy cells and to demonstrate that the neoplastic cells have an antigenic profile that is characteristic for hairy cell leukaemia.



[Picture Credit: Hairy Cell Leukaemia 2]

The cell is characterised by an eccentrically located nucleus with fine chromatin, indistinct nucleoli, and an abundant amount of grey-blue cytoplasm with shaggy margins.

The following tests and procedures may be used:

- Physical examination and history
- Complete blood count (CBC)
- Peripheral blood smear

- Blood chemistry studies
- Bone marrow aspiration
- Immunophenotyping
- Flow cytometry
- Cytogenetic analysis
- CT scan (CAT scan)

Treatment of Adult Hairy Cell Leukaemia

Not all patients will require treatment immediately after the diagnosis is made and can be monitored until it is needed. This 'watch and wait' surveillance approach can be difficult for patients and their families and may generate a lot of anxiety. However, unlike other types of cancer, leukaemias do not spread or metastasise and so waiting to start treatment until there are clear signs that it is indicated is usually perfectly safe and has the advantage of not exposing a patient to drugs, which may have side effects, earlier than is necessary.

Sarvaria, S., Topp, Z. & Saven, A. 2016.

"Hairy cell leukemia (HCL) is a chronic B-cell leukemia noted for an indolent course that ultimately results in cytopenias and massive splenomegaly. Whereas treatment with the nucleoside purine analogues cladribine and pentostatin results in lengthy remissions in nearly all patients with HCL, most patients will experience relapse while a small percentage of patients' disease fails to respond to therapy in the first place. Retreatment with a purine nucleoside analogue often leads to an effective but limited response. For decades, few other viable therapeutic options were available to these patients who required retreatment. Recently, new insights into the mechanism of disease of HCL have led to research in new potential treatment agents, either alone or with a purine nucleoside analogue. Clinical trials with rituximab, bendamustine, and conjugate immunotoxins will reveal what role these therapies will have in HCL treatment. A better understanding of the BRAF/MEK/ERK pathway and the B-cell signaling pathway has allowed further exploration into the novel drugs vemurafenib, dabrafenib, trametinib, and ibrutinib."

Kreitman, R.J., Dearden, C., Zinzani, P.L., Delgado, J., Karlin, L., Robak, T., Gladstone, D.E., le Coutre, P., Dietrich, S., Gotic, M., Larratt, L., Offner, F., Schiller, G., Swords, R., Bacon, L., Bocchia, M., Bouabdallah, K., Breems, D.A., Cortelezzi, A., Dinner, S., Doubek, M., Gjertsen, B.T., Gobbi, M., Hellmann, A., Lepretre, S., Maloisel, F., Ravandi, F., Rousselot, P., Rummel, M., Siddiqi, T., Tadmor, T., Troussard, X., Yi, C.A., Saglio, G., Roboz, G.J., Balic, K., Standifer, N., He, P., Marshall, S., Wilson, W., Pastan, I., Yao, N.S. & Giles, F. 2018.

"This is a pivotal, multicenter, open-label study of moxetumomab pasudotox, a recombinant CD22-targeting immunotoxin, in hairy cell leukemia (HCL), a rare B cell malignancy with high CD22 expression. The study enrolled patients with relapsed/refractory HCL who had ≥2 prior systemic therapies, including ≥1 purine nucleoside analog. Patients received moxetumomab pasudotox 40 μg/kg intravenously on days 1, 3, and 5 every 28 days for ≤6 cycles. Blinded independent central review determined disease response and minimal residual disease (MRD) status. Among 80 patients (79% males; median age, 60.0 years), durable complete response (CR) rate was 30%, CR rate was 41%, and objective response rate (CR and partial response) was 75%; 64 patients (80%) achieved hematologic remission. Among complete responders, 27 (85%) achieved MRD negativity by immunohistochemistry. The most frequent adverse events (AEs) were peripheral edema (39%), nausea (35%), fatigue (34%), and headache (33%). Treatment-related serious AEs of hemolytic uremic syndrome (7.5%) and capillary leak syndrome (5%) were reversible and generally manageable

with supportive care and treatment discontinuation (6 patients; 7.5%). Moxetumomab pasudotox treatment achieved a high rate of independently assessed durable response and MRD eradication in heavily pretreated patients with HCL, with acceptable tolerability."

PDQ Adult Treatment Editorial Board. PDQ Cancer Information Summaries [Internet]. Bethesda (MD): National Cancer Institute (US); 2002-2018 May 18.

Treatment of relapsed or refractory hairy cell leukaemia may include the following:

- Chemotherapy.
- Biologic therapy.
- Targeted therapy with a monoclonal antibody.
- High-dose chemotherapy.
- A clinical trial of a new biologic therapy.
- A clinical trial of a new targeted therapy.
- A clinical trial of chemotherapy and targeted therapy with a monoclonal antibody (rituximab).

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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