Hairy Cell Leukemia

It is called hairy cell leukemia because under a microscope, these malignant cells have short, thin hair-like projections on their surface.

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LEUKEMIA & LYMPHOMA SOCIETY OF CANADA®

Highlights

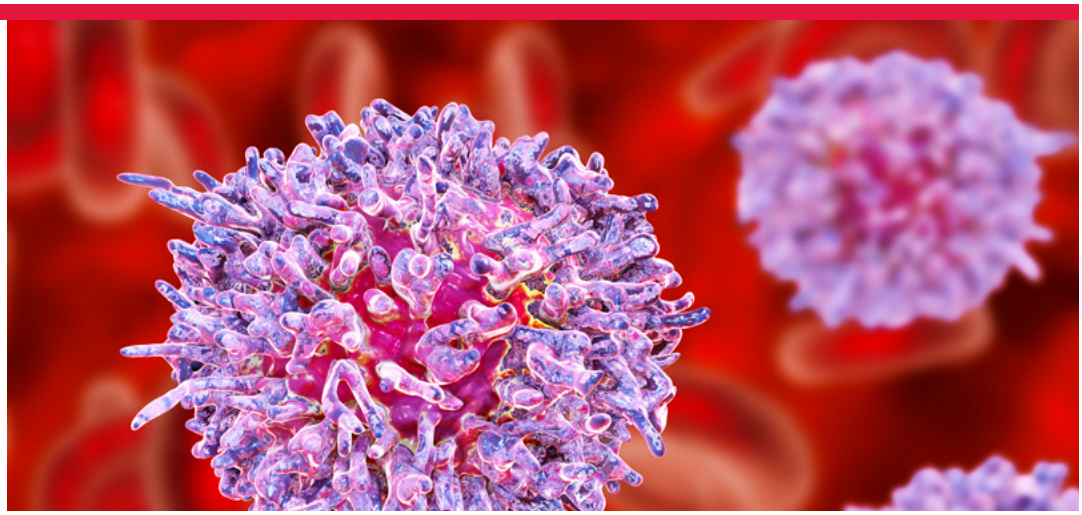
- Hairy cell leukemia (HCL) is a rare slow-growing type of cancer.
- A person with HCL usually has an enlarged spleen and a low blood cell count making them more prone to infections, bruising/bleeding and anemia.
- HCL cannot be cured but recent advances in treatment have made it possible for many HCL patients to survive longer than before.
- In most patients, the disease will return and require more treatment.

Introduction

Hairy cell leukemia is an uncommon cancer that starts in a B-cell (an important cellular component in your body's immune system). Changes in a B-cell gene cause the B-cell to become harmful or malignant, growing and multiplying uncontrollably. These harmful cells enter the bone marrow and spleen, and they may also attack the liver and occasionally the lymph nodes.

Once inside the bone marrow, these hairy cells reduce the development of red blood cells, platelets and white blood cells. When this happens, your normal blood cell count goes down making you more prone to infections, excessive bleeding and/or anemia.

HCL progresses slowly and is considered a chronic form of leukemia – a disease you will live with for a long period of time. Doctors will typically wait until symptoms appear or get worse before beginning treatment. The main treatment for HCL is chemotherapy,



and for many patients it is effective in extending survival that can last years. Even with a successful first treatment, however, the cancer will return in many patients and they will require additional therapy.

There is currently no cure for HCL.

Rarely, changes to the B-cell produce an unrelated hairy cell leukemia variant (HCL-V), which accounts for about 10% of all HCL cases. HCL-V cells are more aggressive than the classic HCL cells having their own cell characteristics and requiring different treatment.

Incidence and Risk Factors

HCL is an uncommon leukemia affecting more men than women. It is unknown what causes HCL, but there are known risk factors that may increase a person's chance of developing the disease. These risk factors include:

- Genetic mutation: having a BRAFV600E gene mutation.
- Age: the median age at diagnosis is about 58 years.
- Sex: more men than women are diagnosed with HCL.
- Exposure to chemicals: a strong presence of HCL among people who have been exposed to herbicides such as Agent Orange.

Signs and Symptoms

The signs and symptoms of HCL are not unique and may resemble those of other less serious illnesses. HCL patients often feel unwell as a result of low levels of normal blood cells.

You may experience these signs and symptoms:

Fatigue, paleness and shortness of breath

- when your red blood cell count is low (anemia)

Easy bleeding or bruising

- when the number of platelets in your bone marrow decrease (thrombocytopenia)

Higher risk of infection

- when you have a lower number of neutrophils and monocytes – types of white blood cells that fight infection (neutropenia and monocytopenia)

You may also experience:

- fever
- weakness
- unexplained weight loss
- pain below the ribs caused by an enlarged swollen spleen

Diagnosis

HCL can easily be confused with other blood diseases. For this reason, it is important that you obtain an accurate diagnosis in order to determine the best treatment option. Meeting with a hematologist-oncologist to undergo a thorough medical history and physical examination is your first step to reaching a diagnosis. During the examination, the doctor will look for signs of infection and disease, such as, enlarged lymph nodes.

Laboratory tests used to diagnose HCL include:

Complete blood count (CBC) with differential

- This test measures the number of red blood cells, platelets and white blood cells in a sample of your blood. The "differential" measures the different types of white blood cells. Usually, a person with HCL has low counts of white blood cells, red blood cells and platelets.

Peripheral blood smear

- In this test, a microscope is used to count your blood cells and to check if the blood cells appear normal. Cells that appear small to medium-sized with the presence of hair-like projections are HCL cells.

Bone marrow aspiration and biopsy

- These two procedures examine your bone cells for abnormalities. For a bone marrow aspiration, a special biopsy needle is inserted through the hip bone and into the marrow in order to extract a liquid sample of cells. For a bone marrow biopsy, a wider needle is used to remove a sample of solid bone that contains marrow.

Flow cytometry

- This test classifies cells according to their cell surface proteins. HCL cells have a characteristic cell surface protein pattern that is different from both healthy B-cells and other types of abnormal B-cells.

Molecular tests

- These are very sensitive DNA tests that check for specific genetic changes in cells. In almost all cases of HCL, the leukemia cells have a mutation of a specific gene, which helps to identify HCL from other B-cell leukemias and lymphomas.

Imaging

- A CT scan/or ultrasound may be used when there needs to be an examination for a possible enlarged spleen, liver and/or lymph nodes.

Treatment Planning

Your treatment depends on many factors. Test results help doctors predict how your HCL will likely progress and what your likely response to the treatment will be. Favourable risk factors are linked to a lower risk that HCL will return after treatment. Poor risk factors are associated with a higher risk that HCL will return after treatment.

The following poor risk factors are associated with a shorter remission after chemotherapy treatment using single agent purine analog (see Treatment below):

- enlarged spleen
- hairy cells in the blood
- unmutated IGHV gene

Risk factors give a general indication for what likely response you may

have to treatment, but every patient's medical situation is unique. Talk to your hematologist-oncologist about risk factors specific to you and ask your medical team about all treatment options including clinical trials. Visit LLSCanada.org for more information.

Treatment

The start of treatment will vary from one patient to another. If your blood count is stable and you have no symptoms at the time of your diagnosis, you may be treated with an active surveillance or watch-and-wait approach. A watch-and-wait approach means that treatment is delayed until signs and symptoms of HCL appear or get worse. Some HCL patients live many symptom-free years on the watch-and-wait approach without receiving any treatment. Frequent monitoring, including blood tests, will help doctors decide when treatment should be started if it shows the disease is beginning to advance.

On the other hand, your treatment will begin right away if you have blood counts below normal levels or show symptoms including unexplained weight loss, infections that keep coming back or physical discomfort due to an enlarged spleen or liver.

Most often HCL treatment involves chemotherapy with a purine analog. The choice between the drugs is usually determined by doctor experience, patient-related factors (i.e. drug allergy) and availability in your region. The drugs are effective in approximately 80 to 85 per cent of patients. Most patients receiving these drugs as first-line treatment achieve a complete remission that can last for several years.

A complete remission means:

- normal blood count level
- disappearance of hairy leukemia cells from the blood and bone marrow
- reduction in the size of the spleen
- absence of disease symptoms

Side Effects of Treatment

Before starting treatment, you may already have a low white blood cell count, resulting in a severe, active infection. Before starting chemotherapy you should consult with a HCL specialist since the treatment will reduce your white blood cell count even further. This can cause a condition called neutropenia where there is a lower than normal number of neutrophils, the white blood cells that help fight infection. While in treatment, you will be at greater risk of developing a serious infection. Doctors may prescribe an antibiotic to prevent infections or prescribe a treatment to help your body produce more white blood cells.

Treatment for Patients with Refractory or Relapsed HCL

Some patients do not respond to treatment while others respond at first, but over time, their disease returns and they require further treatment.

Refractory Disease

If you do not respond to primary treatment, it is called refractory disease. When this happens, you will be treated with a different drug or in combination with a monoclonal antibody.

Relapsed Disease

When the disease returns after treatment, it's called relapsed disease. The treatment options for relapsed disease depend on the quality and duration of your first remission. For a relapse after a long remission of over seven years, you may be given purine analog again. In other situations, you may receive a combination of purine analog and monoclonal antibody. Sometimes a monoclonal antibody is given alone if you are unable to receive a purine analog.

Treatments Under Investigation

Through research, scientists continue to find a cure for HCL and better therapies for patients with relapsed disease. Every new drug or treatment protocol goes through a series of clinical trials before it becomes a part of standard therapy.

Current clinical trials include:

BRAF Inhibitors

- Almost all HCL patients have a mutated gene, which makes the BRAF protein responsible for the production of HCL cancer cells. BRAF inhibitor stops production of the BRAF protein.

B-cell Receptor Inhibitors

- Bruton's tyrosine kinase (BTK) is an enzyme protein on the surface of B-cells that is responsible for the growth and survival of malignant B-cells. The BTK inhibitor stops the growth of these cancer cells by inactivating the BTK enzyme.

Immunotoxins

- Immunotoxins drugs link monoclonal antibodies and toxins in order for the monoclonal antibodies to attach to the leukemia cell surface and deliver the toxin to kill the cancer cell.

Long-Term Follow-Up

HCL is a chronic disease so expect to have regular checkups and blood tests while in remission. If your blood count starts to decline, you will need to discuss treatment options with your doctors once again.

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