

Highlights

- Hairy cell leukemia (HCL) is a chronic leukemia caused by an abnormal change in a B lymphocyte.
- Two symptoms of HCL that lead to a diagnosis include an enlarged spleen and an unexpected decrease in normal blood cell counts.
- Most individuals with HCL receive treatment at the time of diagnosis or at some point during the course of the disease. In a small percentage of cases, people do not require immediate treatment and may prefer to wait until signs and symptoms of the disease arise.
- Cladribine (Leustatin®), given intravenously (IV), is the initial drug used to treat HCL.
- Allogeneic stem cell transplantation may be considered for selected patients.
- Periodic medical examinations for patients in complete remission are important because some patients will relapse and successful retreatment is possible. Identifying relapses early may reduce infections.

About Hairy Cell Leukemia

Hairy cell leukemia (HCL) is a chronic leukemia. It is caused by an abnormal change in a B lymphocyte (a type of white blood cell). The disease is called hairy cell leukemia because the leukemic lymphocytes have short, thin projections on their surfaces that look like hairs when examined under a microscope.

There are about 950 new cases of HCL in the United States each year. More men than women are diagnosed with HCL. The median age at diagnosis is 52. The cause of HCL is not known. There is no established direct link between the disease and exposure to pollutants or poisons (toxins) in the environment.

Signs and Symptoms

The symptoms of HCL are not specific and might resemble those of other illnesses. Hairy cells accumulate in the marrow, liver and spleen (probably where these cells grow or survive best) and there is very little involvement of the lymph nodes.

The two most important findings that lead to a diagnosis of HCL are:

- An enlarged spleen
- An unexpected decrease in normal blood cell counts

In the course of the disease, normal blood cell production is disrupted by the accumulation of hairy cells in the bone marrow. Patients may have:

- Anemia (a decrease in the number of red blood cells)
- Thrombocytopenia (a decrease in the number of platelets)
- Neutropenia and monocytopenia (a decrease in the number of neutrophils and monocytes, types of white blood cells that fight infection)

The decreased number of all three blood cell types is called “pancytopenia.” Patients with anemia may feel tired, pale or short of breath due to low red blood cell counts. With low concentration of blood platelets, a patient may get black and blue marks on the skin from just a minor injury or no injury at all. Patients with low levels of white blood cells have an increased risk of infection.

Some patients first become aware of HCL because of fever, chills or other signs of infection. Patients may also have:

- Discomfort or fullness in the upper left side of the abdomen as the result of an enlarged spleen
- Unexplained weight loss

Diagnosis

A hematopathologist (a doctor who specializes in examining tissue and diagnosing disease) can make an accurate diagnosis by examining a patient's blood and marrow cells. Hairy cells may be hard to find in the blood, but often can be identified with careful searching. Occasionally, there are many hairy cells in the blood, which increases the total white blood cell count. However, neutrophil and monocyte counts (types of white blood cells) are still extremely low.

A bone marrow aspiration (a liquid sample of cells removed from the marrow through a fine needle) and biopsy (a very small amount of bone filled with marrow cells is removed using a special hollow needle) are often needed to confirm the hairy cell leukemia diagnosis. The biopsy is particularly important because hairy cells are often difficult to obtain by aspiration and may be identified more easily in a biopsy.

The dried marrow cells from the biopsy are stained with dyes and examined under a lighted microscope to identify whether hairy cells are present. A firm diagnosis requires a test called "immunophenotyping," which identifies the pattern of surface proteins on the cells. (Hairy cells can have a characteristic surface protein pattern.) Immunophenotyping can be performed on the blood or marrow cells.

Imaging studies use special machines that produce pictures, shadows, and other images that show inside the body. Imaging may be used to measure the extent of disease. An ultrasound might be used to confirm the precise size of the spleen. Subsequent imaging studies may be performed to identify a decrease in spleen, liver and lymph node size as a measure of the response to treatment.

Abdominal, thoracic or superficial lymph node enlargement (lymphadenopathy) is not common when a patient is first diagnosed. In fact, this condition is found in only about 5-10 percent of patients. Patients who relapse or those late in the course of the disease have a relatively high frequency of abdominal lymphadenopathy and might have a computed tomography (CT) scan in the course of their disease management.

Treatment Planning

Every patient's medical situation is different and should be evaluated individually by an oncologist who specializes in treating HCL. It is important for you and members of your medical team to discuss all treatment options, including treatments being studied in clinical trials, to see if you might be eligible to participate in a trial.

For more information about choosing a doctor or a treatment center, see the free LLS publication *Choosing a Blood Cancer Specialist or Treatment Center*.

Treatment

The goal of treatment for HCL is to achieve a complete remission. A complete remission means that:

- Hairy cells cannot be identified in the blood and marrow
- The liver, lymph nodes and spleen are of normal size
- Blood cell and marrow cell counts have returned to normal

Most individuals with HCL receive treatment at the time of diagnosis or at some point during the course of the disease. In a small percentage of cases, people do not require immediate treatment and may prefer to wait until signs and symptoms of the disease arise.

Cladribine (Leustatin®) is usually the first drug used to treat HCL. It is administered using a needle into a vein, or intravenously (IV), for five to seven days in a row. About half of all patients treated with cladribine experience a fever of about 100°F during or immediately after treatment. The fever may occur when the number of hairy cells in the blood, marrow and other sites declines. This drug-related fever is not associated with an infection. It usually stops after three to ten days following the first injection. Patients may also feel tired for the first few weeks after the start of treatment. Blood cell counts may be lower as a result of treatment, but counts eventually improve and often return to normal.

About 85 percent of patients treated with cladribine have a complete remission and 10 percent have a partial response. Although minimal residual hairy cell disease can be found with very sensitive techniques in most patients who have an apparent complete remission, long-term remissions are common.

Patients are advised to consult with a doctor who specializes in treating leukemia and to discuss the most appropriate treatment options, including whether or not participation in a clinical trial is recommended.

Talk to Your Doctor About Side Effects of Treatment.

Management of side effects is important. If you are having any concerns about your side effects, talk to your doctor to get help. Most side effects can be managed with a separate medication that will not interfere with the treatment you are taking for your disease. In addition, most side effects are temporary and resolve when treatment is completed.

Some of the side effects of specific drugs are discussed on this page and page 2. For additional drug information, see the free LLS publication *Understanding Side Effects of Drug Therapy* or visit www.LLS.org/drugs. Visit the U.S. Food and Drug Administration (FDA) drug information webpage at www.fda.gov/drugs/resourcesforyou/consumers/default.htm.

Treatment for Refractory or Relapsed Patients

Patients who do not respond to cladribine or who relapse after achieving remission are usually treated with pentostatin (Nipent®). Pentostatin has yielded very high response rates in patients with HCL. It is given intravenously (IV) every other week for three to six months. Pentostatin administration takes about 20 minutes. Some of the potential side effects include fever, chills, weakness, fatigue and lack of coordination especially in walking.

A patient might relapse after treatment with cladribine or pentostatin. But sometimes that same patient might be responsive to a second course of treatment with that same drug. Another drug called interferon-alfa (Roferon-A® or Intron® A) is also capable of killing hairy cells and may be used if neither cladribine nor pentostatin produces a satisfactory response. Interferon can be given three times a week by injection for as long as one year. Longer-term maintenance therapy with interferon may be necessary to hold the disease in check. Interferon may produce side effects that include fatigue, fever and bone pain.

Surgical removal of the spleen (called a splenectomy) was common before effective drugs for the treatment of HCL became available. Splenectomy is no longer a first treatment for the disease. Occasionally, a splenectomy may be required for patients with enlarged spleens who have not responded to, or who relapse after, treatment with drug therapy.

Allogeneic stem cell transplantation uses stem cells obtained from the marrow or blood of a donor with an identical tissue type. This kind of treatment is considered for selected patients. First, the patient is treated with intensive chemotherapy, sometimes combined with radiation, in an effort to eradicate the leukemic cells. Normal blood cell development in the marrow, which is also severely impaired

by this treatment, is restored by the transplantation of donor stem cells. This procedure may be useful in younger individuals who have a compatible donor and who do not respond to chemotherapy. For more information, see the free LLS publication *Blood and Marrow Stem Cell Transplantation*.

Treatments currently in clinical trials may be used if other agents are no longer effective. Please see the section *Treatments Under Investigation* below for more information.

Treatments Under Investigation

Research for HCL over the last several years has resulted in many new and emerging therapies, offering better treatment options for patients. Patients may have the opportunity to take part in clinical trials. These trials, conducted under rigorous guidelines, help clinicians and researchers determine the beneficial and adverse effects of potential new treatments. Studies are also conducted to evaluate new indications for therapies that are already approved for other diseases.

For more information about clinical trials, see the free LLS publication *Understanding Clinical Trials for Blood Cancers*, visit www.LLS.org/clinicaltrials or call our Information Specialists.

Some drugs under investigation include:

- **Moxetumomab Pasudotox (HA-22).** The immunoconjugate HA-22 is an agent that was developed at the National Cancer Institute and is currently in clinical trials. It has been effective in the treatment of many patients with HCL who are or who have become resistant to current therapy. This agent is an antibody that targets a feature (surface antigen) of hairy cells known as CD22. A potent bacterial toxin that kills hairy cells is attached to the antibody.
- **Ibrutinib.** The oral Bruton's tyrosine kinase inhibitor PCI-32765 (ibrutinib) is being studied in clinical trials as a single agent for the treatment of relapsed HCL. Ibrutinib may stop the growth of cancer cells by blocking some of the enzymes needed for cell growth.
- **LMB-2.** The LMB-2 immunotoxin is in clinical trials to study the response rate in patients with recurrent or refractory CD25-positive HCL. LMB-2 is made up of two parts: a genetically engineered monoclonal antibody that binds to cancer cells with CD25 on their surface, and a toxin produced by bacteria that kill the cancer cells to which LMB-2 binds.
- **Rituximab (Rituxan®).** Clinical trials are exploring the use of Rituxan in combination with cladribine for the treatment of HCL. Rituxan is a monoclonal antibody that is approved by the FDA for the treatment of CD20-positive follicular, low-grade and diffuse large B-cell

non-Hodgkin lymphoma. Studies are looking to evaluate complete response rates in patients treated with cladribine and Rituxan and to examine the effectiveness of Rituxan in eradicating minimal residual disease (MRD) after cladribine therapy. Studies are also examining the effect of adding Rituxan to cladribine on long-term, disease-free and overall-survival status (compared to historical data for patients who have received cladribine alone).

- **Vemurafenib (Zelboraf®)**. Recent data have shown that almost all patients with HCL have BRAF mutations. Vemurafenib, given by mouth and approved by the FDA for the treatment of melanoma, targets BRAF and is now being used in clinical trials in patients with relapsed and refractory HCL.

Long-Term Follow-Up

Periodic medical examinations for patients in complete remission are important. Some patients will relapse and successful retreatment is possible. Identifying relapses early may reduce infections. Patients with HCL may have increased risk of developing second cancers compared to age- and sex-matched comparison groups. Earlier diagnosis of a second cancer may be possible with surveillance.

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We're Here to Help

LLS is the world's largest voluntary health organization dedicated to funding blood cancer research, education and patient services. LLS has chapters throughout the country and in Canada. To find the chapter nearest you, enter your ZIP code into "Find Your Chapter" at www.LLS.org or contact

The Leukemia & Lymphoma Society

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Callers may speak directly with an Information Specialist Monday through Friday, from 9 a.m. to 6 p.m. ET. You may also contact an Information Specialist between 10 a.m. and 5 p.m. ET by clicking on "Live Chat" at www.LLS.org or by sending an email to infocenter@LLS.org. Information Specialists can answer general questions about diagnosis and treatment options, offer guidance and support and assist with clinical-trial searches for leukemia, lymphoma, myeloma, myelodysplastic syndromes and myeloproliferative neoplasms. The LLS website has information about how to find a clinical trial, including a link to our free online clinical-trial search service at www.LLS.org/clinicaltrials.

LLS also provides free publications that can be ordered via the (800) 955-4572 number or through the "Free Education Materials" option at www.LLS.org/resourcecenter.

Resources

Hairy Cell Leukemia Foundation

www.hairycellleukemia.org
(224) 355-7201

The Foundation is dedicated to improving outcomes for patients by advancing research into the causes and treatment of HCL, as well as by providing educational resources and comfort to all those affected by HCL. The website includes a list of centers of excellence and access to publications from experts.

Information for Veterans

www.publichealth.va.gov/exposures/agentorange
(800) 749-8387

Veterans with certain blood cancer diagnoses, including HCL, who were exposed to Agent Orange while serving in Vietnam may be able to get help from the United States Department of Veterans Affairs.

Information for World Trade Center Survivors

www.cdc.gov/wtc
(888) 982-4748

People who were involved in the aftermath of the attacks of Sept. 11, 2001, may be eligible for help from the World Trade Center Health Program. These include: responders, workers and volunteers who helped with rescue, recovery and cleanup at the World Trade Center and related sites in New York City; survivors who were in the New York City disaster area, lived, worked or were in school in the area; and responders to the Pentagon and the Shanksville, PA crash who have been diagnosed with a blood cancer.

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