

Hairy Cell Leukemia

No. 16 in a series providing the latest information on blood cancers

Introduction

Hairy cell leukemia is a form of chronic lymphocytic leukemia (CLL). CLL is caused by an abnormal change in a B lymphocyte (a type of white 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 an estimated 500 to 800 cases of hairy cell leukemia in the United States each year. The cause of hairy cell leukemia is not known. Further, there is no established direct link between the disease and exposure to environmental toxins.

How is hairy cell leukemia diagnosed?

Symptoms and Signs

The symptoms of hairy cell leukemia are nonspecific and resemble those of some other illnesses. The two most important findings that lead to a diagnosis of hairy cell leukemia are:

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

Some patients first become aware of the disease because of fever, chills and 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.

Although the hairy cells are abnormal types of lymphocytes, lymph nodes do not usually become enlarged. Rather, hairy cells accumulate in the marrow, liver and spleen (probably where these cells grow or survive best).

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

- Anemia (a deficiency of red cells)
- Thrombocytopenia (a deficiency of platelets)
- Neutropenia and monocytopenia (a deficiency of neutrophils and monocytes, types of white cells that fight infection).

The deficiency of all three blood cell types is called “pancytopenia.” Patients with anemia may feel tired, pale or short of breath due to low red cell counts. Black and blue marks, as a result of the low concentration of blood platelets, may occur on the skin in the absence of injury or after a minor injury. Patients with low levels of white cells have an increased risk of infection.

Diagnosis

A doctor can make an accurate diagnosis by examining 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 cell count. However, neutrophil and monocyte counts (types of white cells) are still extremely low.

A bone marrow sample is often needed to confirm the disease. Obtaining a marrow sample from the hipbone can be done in a physician’s office. The skin over the area where the sample will be taken is first treated with an antiseptic and then numbed with a local anesthetic. Then a needle is inserted through the skin into the hipbone. A small amount of the marrow is removed through a syringe. This process is called marrow aspiration. Next, a tiny piece of the bone with its marrow is removed for evaluation. This procedure is called a marrow biopsy. The biopsy is performed with a larger, hollow needle to permit removal of very small pieces of marrow-containing bone. 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 are stained with dyes and examined under a lighted microscope to identify whether hairy cells are present. The marrow pattern is often very characteristic. However, a firm diagnosis requires “immunophenotyping,” a test to identify 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 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 therapy.

Abdominal, thoracic or superficial lymph node enlargement (lymphadenopathy) is not a common finding at the onset of the disease (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 computed tomography scanning (a CT scan) in the course of their disease management.

What is the treatment for hairy cell leukemia patients?

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

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

Treatment

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

Cladribine (Leustatin®) is the initial drug used to treat hairy cell leukemia. It is administered through a vein for seven consecutive days. About half of all patients treated with cladribine experience fevers of about 100°F during or immediately after treatment. The fevers occur when the number of hairy cells in the blood, marrow and other sites declines. These drug-related fevers are not associated with infections. The fevers usually disappear in three to 10 days. Patients may also feel tired for the first few weeks following the start of treatment. Blood cell counts may be lower as a result of treatment, but counts eventually improve and often return to normal. For more information, please see The Leukemia & Lymphoma Society's free publication, *Understanding Drug Therapy and Managing Side Effects*.

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.

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 hairy cell leukemia. It is administered by vein every other week for three to six months. Pentostatin administration takes about 20 minutes.

Patients who relapse after treatment with cladribine or pentostatin may be responsive to a second course of treatment with the same drug. 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. However, longer-term maintenance therapy with interferon may be necessary to hold the disease in check. Interferon may produce side effects that include fatigue, fever, bone pain and others.

Rituximab (Rituxan®), a monoclonal antibody that attaches to B lymphocytes, or the immunoconjugate BL22, can also be used if other agents are no longer effective. Please see the section *Clinical Trials* for information on rituximab and BL22.

Surgical removal of the spleen (called a splenectomy) was common before effective drugs for the treatment of hairy cell leukemia became available. Splenectomy is no longer a first-line treatment for the disease. Occasionally, it may be required for patients with very enlarged spleens, who have not responded to, or who relapse after treatment with cladribine, pentostatin, rituximab and BL22. Allogeneic stem cell transplantation may be considered for selected patients. This type of transplant uses stem cells obtained from the marrow or blood of a donor with an identical tissue type. 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 a complete discussion of this treatment, please see The Leukemia & Lymphoma Society's free publication, *Blood and Marrow Stem Cell Transplantation*.

Long-term follow-up

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. Patients with hairy cell leukemia may have increased risk of developing second cancers compared to age-sex matched comparison groups. Earlier diagnosis of a second cancer may be possible with surveillance.

Clinical Trials

The lives of many patients have been enhanced and extended as a result of the effective drug treatments that have been developed for hairy cell leukemia. Many patients may remain disease-free for years or decades after treatment with cladribine or pentostatin and may have a normal life expectancy. Interferon, splenectomy and, in younger patients, stem cell transplantation provide additional treatment options for people who do not respond to cladribine or pentostatin. New methods of therapy are under investigation to further improve the treatment of this disease.

Clinical trials are exploring the use of rituximab, which is being evaluated in clinical trials in combination with cladribine for the treatment of hairy cell leukemia. Study objectives are to evaluate complete response rates in patients treated with cladribine and rituximab to examine the efficacy of rituximab in eradicating minimal residual disease (MRD) after cladribine therapy, and to examine the effect of adding rituximab to cladribine on the long-term disease-free and overall survival status (compared to historical data for patients who have received cladribine alone). Rituximab is a monoclonal antibody that is approved by the U.S. Food and Drug Administration (FDA) for the treatment of CD20-positive follicular, low-grade and diffuse large B-cell non-Hodgkin lymphoma. It is a protein that binds to a component on B lymphocytes called the CD20 antigen. This binding stimulates the immune system to mount an attack against the cancer cells.

The immunoconjugate BL22 is a new agent developed at the National Cancer Institute that is now in clinical trials. It has been effective in the treatment of many patients with hairy cell leukemia 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.

The LMB-2 immunotoxin is another new agent that is now in clinical trials to study the response rate in patients with recurrent or refractory CD25-positive hairy cell leukemia. 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.

The hope is that these new therapies will increase the number of patients who achieve a complete remission and a cure from the disease.

Resources

The diagnosis of leukemia provokes a profound emotional response in patients, family members, and friends. It is best to speak directly with physicians regarding questions about chemotherapy and alternative methods of treatment. Patients, family members or loved ones should discuss any problems or reactions they may have with their healthcare professionals, who understand the complexity of emotions and the special ongoing needs of those living with leukemia. For more information about the social and emotional aspects of the disease, please request free copies of The Leukemia & Lymphoma Society's publications, *Each New Day: Ideas for Coping with Leukemia, Lymphoma or Myeloma* and *Coping: Support for People Living with Leukemia, Lymphoma or Myeloma*.

The Leukemia & Lymphoma Society is always here to assist you

The Leukemia & Lymphoma Society is a national voluntary health agency with 64 chapters in the United States and two chapters in Canada. The Society offers accurate, up-to-date information on blood cancers and coping strategies to the public and cancer treatment professionals. Support programs, patient financial aid and education programs are offered through the Society's local chapters. To find the Society chapter nearest you, visit our online chapter finder or contact:

The Leukemia & Lymphoma Society

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Information Resource Center (800) 955-4572

www.LLS.org

Information Specialists can answer general questions about diagnosis and treatment options, offer guidance and support, and assist with clinical trials information. Cancer clinical trials, sometimes called research studies, are conducted by physicians to improve the care and treatment of cancer patients. Clinical trials can be an important treatment option for leukemia, lymphoma or myeloma. They offer patients access to new therapies being tested to see if they can increase survival and/or improve quality of life. The IRC offers clinical trials information, including guidance on how patients can work with their physicians to find out if a specific study is an appropriate treatment option. Information specialists conduct individual clinical trial searches for patients, families and healthcare providers. This service is also available on our Web site, www.LLS.org.

The Society provides fact sheets and booklets that can be ordered via the 800 number or through the Free Materials section at www.LLS.org.

References

Flinn IW, Kopecky KJ, Foucar MK, et al. Long-term follow-up of remission duration, mortality, and second malignancies in hairy cell leukemia patients treated with pentostatin. *Blood*. 2000;96:2981-2986.

Goodman GR, Bethel KJ, Saven A. Hairy cell leukemia: an update. *Current Opinion in Hematology*. 2003;10(4):258-266.

Kreitman RJ, Wilson WH, Bergeron K, et al. Efficacy of the anti-CD22 recombinant immunotoxin BL22 in chemotherapy-resistant hairy-cell leukemia. *The New England Journal of Medicine*. 2001;345:241-247.

Saven A. Hairy cell leukemia. In: Lichtman MA, Beutler E, Kipps TJ, Seligsohn U, Kaushansky K, Prchal JT, eds. *Williams Hematology*. 7th ed. New York, NY: McGraw Hill; 2006:1385-1393.

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