UNDERSTANDING
Burkitt Lymphoma (BL)

LYMPHOMA CANADA

Overview

Lymphoma is the most common form of blood cancer. Lymphoma occurs when cells of the immune system called lymphocytes, a type of white blood cell, grow and multiply uncontrollably.

WHAT ARE LYMPHOCYTES?

Lymphocytes are a type of white blood cell and are a major part of the lymphatic system. Together with other cells of the immune system, they work to fight infection and prevent disease. Lymphocytes can be found in the blood and bone marrow; however, most of them are normally circulating in the lymphatic system.

There are two main types of lymphocytes that can develop into lymphomas: B lymphocytes and T lymphocytes. The types of cells that become cancerous in Burkitt lymphoma (BL) are B lymphocytes (B cells). B lymphocytes make antibodies to fight infections. They are called B cells because they mature in the bone marrow.

There are over 80 different subtypes of lymphoma. They fall into two main categories:

- Hodgkin lymphoma (HL)
- Non-Hodgkin lymphoma (NHL)

BL is a type of NHL. NHLs are approximately eight times more common than HL – 85% of all lymphomas are NHLs. The main difference between HL and NHL is the presence of Reed-Sternberg cells which are large abnormal lymphocytes that can be detected under a microscope. Reed-Sternberg cells are only present in Hodgkin lymphoma and are absent in Non-Hodgkin lymphoma.

NHLs are further sub-categorized by 'grade':

- Low-grade: indolent (or slow-growing) NHLs
- Intermediate or high-grade: aggressive (or fast-growing) NHLs

BL is an aggressive lymphoma. Aggressive lymphomas develop more rapidly than indolent lymphomas. Patients with aggressive lymphoma usually experience symptoms from the onset of their disease and may require immediate, intensive treatment. Indolent lymphomas however, develop more slowly and patients usually do not show symptoms until later, often as the disease progresses, and may not require immediate treatment.

BL can affect lymph nodes (nodal sites) as well as organs or tissues other than the lymph nodes (called extranodal sites) such as the spleen, liver, lungs, pancreas, kidney, and ovaries/testicles. It can also spread to the brain or spinal cord (called the central nervous system or CNS).

BL is caused by a type of genetic mutation called a translocation. This involves a switch in genetic material between a gene (units of heredity) located on chromosome 8 with a gene from another chromosome (14, 2 or 22). This leads to an abnormal increase in a protein (c-myc) that results in uncontrolled B cell growth. This an important finding to confirm the diagnosis of this type of lymphoma. However, this translocation may also occur in other types of lymphomas such as diffuse large B-cell lymphoma (DLBCL), which can make BL difficult to diagnose.

Who gets BL?

Burkitt lymphoma develops most often in children or young adults, accounting for 30% to 40% of all childhood lymphomas. However, it can also affect adults, typically between the ages of 30 and 50 years. Males are affected more frequently than females.

Viral infections that weaken the immune system, such as the Epstein-Barr virus (EBV) and human immunodeficiency virus (HIV), are risk factors for developing BL.

Types of BL

Burkitt lymphoma can be classified into three distinct subtypes:

ENDEMIC BURKITT LYMPHOMA

Endemic Burkitt lymphoma is the most common of the three types. It is also called African Burkitt lymphoma because it originated from and has the highest incidence rate (number of people affected) in Africa. It has been linked with the Epstein-Barr virus and malaria, both of which are common in this region. Outside of Africa, endemic BL is rare. It primarily affects children and is twice as common in boys than girls. It generally starts as a tumour on the jawbone or another bone in the face, and most commonly spreads to the CNS.

SPORADIC BURKITT LYMPHOMA

Sporadic Burkitt lymphoma is also called non-African or non-endemic BL. It is the most common type of BL in North American and European countries. It is sometimes linked with the Epstein-Barr virus, but many people with sporadic BL are not infected with this virus. Sporadic BL can affect both children and adults. This type of BL usually starts as a tumour in the abdomen, but it can also originate in other regions. It can spread to the CNS and bone marrow.

IMMUNODEFICIENCY-ASSOCIATED BURKITT LYMPHOMA

Immunodeficiency-associated Burkitt lymphoma tends to occur in people with weakened immune systems, typically in those with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS). It can also occur in people with conditions that cause immune deficiency or those taking immunosuppressive drugs. It is not linked to the Epstein-Barr virus. It is most likely to involve the lymph nodes, bone marrow and CNS at diagnosis.

Symptoms

Symptoms of Burkitt lymphoma usually develop quickly. The most common symptom is one or more lumps, which are often located in several parts of the body. These lumps are caused by lymphoma cells building up within the lymph nodes, causing them to enlarge (swell).

BL can cause a variety of symptoms depending on which subtype of BL you have and where it is growing. If BL is growing in the abdominal region, symptoms could include abdominal pain, back pain, abdominal swelling, gastrointestinal bleeding, nausea, and diarrhea. If it affects lymph nodes in the chest, neck and jaw regions, patients may experience breathlessness, difficulty swallowing and a sore throat. If the bone marrow is affected, symptoms associated with anemia (low red blood cell levels) or thrombocytopenia (low platelet levels) may develop.

BL can also affect other organs such as the eyes, ovaries, kidneys, and CNS. Lymphoma found in these organs may cause different symptoms.

Patients may also experience what are called **B symptoms**. In the case of lymphoma, B symptoms refer to a specific set of symptoms that may help to predict how your lymphoma will progress.

B SYMPTOMS ARE:

- Fever with temperatures above 38˚C (100.4˚F), without any sign of an infection;
- Night sweats, enough to drench your pajamas or bedding;
- Weight loss without trying (at least 10% of your body weight over 6 months).

Diagnosis

A diagnosis of Burkitt lymphoma is confirmed by a lymph node biopsy. This type of biopsy involves removing a sample of tissue (cells) from the lymph node. The removed tissue is then sent to a lab where it is examined under a microscope by a hematopathologist (a doctor who specializes in diagnosing diseases of the blood and bone marrow). This type of biopsy procedure can usually be performed under local anesthetic.

Other tests may also be performed to confirm your diagnosis. Because BL is a blood cancer, it is important to look at the entire body to find all of the lymphoma. This is usually done with blood tests and imaging scans which can include a whole-body computed tomography (CT) scan, positron emission tomography (PET) scan, and/or a magnetic resonance image (MRI) scan. Because of the fast tumor growth in BL, certain blood tests may show higher than normal test results, such as serum lactate dehydrogenase and uric acid. A bone marrow biopsy may also be performed to look for the presence of lymphoma cells in the bone, and sometimes a spinal tap (lumbar puncture) may be performed to determine if there are lymphoma cells in the brain and spinal cord.

Staging

Staging describes a cancer based on how much cancer is in the body and where it is located when first diagnosed. BL is staged based on the findings from your clinical examinations. Knowing the stage of your lymphoma helps your doctor determine the extent of your disease and monitor its progression over time.

Your BL may be staged using the Ann Arbor Staging System. The stage is determined by the number and location of lymph nodes affected, whether the affected lymph nodes are above, below or on both sides of the diaphragm (the large, dome-shaped muscle under the ribcage that separates the chest from the abdomen), and whether the disease has spread to the bone marrow or to other organs such as the liver.

THERE ARE FOUR MAIN STAGES:

- **Stage I** The lymphoma is in one group of lymph nodes or one extranodal site
- **Stage II** The lymphoma is in two or more groups of lymph nodes on the same side of the diaphragm
- **Stage III** The lymphoma is in nodes both above and below the diaphragm
- **Stage IV** The lymphoma is widespread and found in multiple areas throughout the body including nodal and extranodal sites

Stages I and II are considered early stages. Stages III and IV are considered advanced stages.

For children and adolescents with BL, another staging system called the Murphy Staging System (also sometimes called the St. Jude Staging System), is commonly used to define the stage of this lymphoma.

YOUR DOCTOR MAY ALSO ADD A SINGLE LETTER TO THE STAGE:

- **A** generally means the patient has not experienced any troublesome symptoms
- **B** means the patient has experienced B symptoms (fever, night sweats, weight loss)
- **X** means the patient has bulky disease (large tumours)
- **E** means the patient has extranodal disease (disease outside of the lymph nodes)

THERE ARE FOUR STAGES:

- **Stage I** The lymphoma is in a single nodal/extranodal site, excluding chest or abdomen.
- **Stage II** The lymphoma is not in the chest, but one of the following applies:
    - Lymphoma is in one nodal site and there is a tumour outside of the lymph nodes;
    - Lymphoma is in two or more nodal sites that are on the same side of the diaphragm;
    - There are two tumours outside of the lymph nodes that are on the same side of the diaphragm;
    - There is a tumour in the digestive tract, which can be removed by surgery;
    - The lymphoma may have also spread to nearby lymph nodes.
- **Stage III** One of the following applies:
    - There are two tumours outside of the lymph nodes;
    - One tumour is above the diaphragm and the other is below the diaphragm;
    - Lymphoma is in two or more nodal sites above and below the diaphragm;
    - Lymphoma is in the chest;
    - Lymphoma is in the abdomen and cannot be removed by surgery;
    - Lymphoma is in an area close to the spine.
- **Stage IV** The lymphoma is in the CNS or bone marrow, or both.

Prognosis

WHAT IS PROGNOSIS?

Prognosis is the medical term used to describe how the disease will progress, how well the patient will respond to treatment, and the likelihood of recovery. It is usually based on information gathered from thousands of other patients who have had the same disease and provides a general idea of what to expect when a patient is diagnosed with BL. However, it is important to remember that no two patients are alike and that it is not possible to accurately predict what will happen to a specific patient.

INTERNATIONAL PROGNOSTIC INDEX (IPI)

If you have BL, your doctor may give you a prognostic score using the International Prognostic Index (IPI). The IPI is a clinical tool developed by oncologists to aid in predicting the prognosis (outcome and survival) of patients with aggressive NHL.

One point is assigned for each of the following IPI risk factors:

- Age 60 years and over;
- Ann Arbor stage III/IV;
- More than one extranodal site;
- Serum lactate dehydrogenase (LDH) level above normal;
- Eastern Cooperative Oncology Group (ECOG) performance status ≥ 2 (looks at a patient's ability to care for themselves and their daily activity level).

These risk factors help identify if the patient is:

- Low-risk (0-1 factors);
- Low/intermediate-risk (2 factors);
- Intermediate/high-risk (3 factors);
- High-risk (4-5 factors).

Treatment Options

Although Burkitt lymphoma is an aggressive lymphoma, survival rates with treatment are high. The long-term survival rate for children is approximately 90% with treatment and can be up to approximately 70% for adults. Since BL develops quickly, it requires immediate treatment. The most common treatment for Burkitt lymphoma is intensive chemotherapy, which often involves the combination of multiple chemotherapy drugs. Chemotherapy is additionally used in combination with an antibody therapy, specifically with the monoclonal antibody rituximab, in many cases.

Some commonly used chemotherapy regimens include:

- **EPOCH** (etopisode, prednisone, vincristine [Oncovin], cyclophosphamide, doxorubicin [Hydroxydaunorubicin])
- **EPOCH-R** (EPOCH + rituximab [Rituxan])
- **R-CODOX-M** (rituximab [Rituxan], cyclophosphamide, doxorubicin, vincristine [Oncovin], methotrexate, cytarabine, leucovorin)
- **CODOX-M/IVAC** (cyclophosphamide, vincristine [Oncovin], doxorubicin, prednisone, methotrexate, ifosfamide, etoposide, high-dose cytarabine, leucovorin)
- **R-IVAC** (rituximab [Rituxan], ifosfamide, mesna, etoposide, cytarabine)
- **HyperCVAD** (cyclophosphamide, vincristine [Oncovin], doxorubicin, dexamethasone, methotrexate, leucovorin, cytarabine)

These drugs are typically administered intravenously (into a vein) which is performed in the hospital. A central-line, which is a catheter placed in a large vein, can be used to administer chemotherapy drugs and draw blood for testing. The chemotherapy is usually given in cycles of 2 to 4 weeks. A cycle includes treatment days followed by a period of rest and healing. The number of cycles you receive (called the 'course' or 'regimen') depends on your disease and the recommendation of your medical team based on your test results. Many patients will be able to receive their treatment as an out-patient, which means you will not have to stay in the hospital overnight.

If your BL is higher risk, your doctor may recommend additional intensive chemotherapy. If there is CNS involvement, intrathecal chemotherapy (therapy given directly to the brain and spinal cord through the cerebrospinal fluid (CSF) in your spine) may be used to treat or try to prevent the further spread of lymphoma cells. Intrathecal chemotherapy is injected directly into the CSF through a lumbar puncture (spinal tap).

For most patients with BL, the initial treatment may be effective at curing your lymphoma. However, for patients in whom the disease becomes refractory (does not respond to treatment) or relapses (returns after treatment), further therapies may be required. Additional chemotherapies or other drug treatments, autologous stem-cell transplantation (infusion of a patient's own stem-cells), radiation therapy or newer drugs available through a clinical trial, may be used as second-line or later line treatments. A patient may require multiple lines of therapy if their lymphoma relapses or is refractory to their previous treatment(s).

Patients with relapsed or refractory BL are often encouraged to participate in clinical trials so that they can receive newer treatments that are not yet on the market. Clinical trials are crucial for establishing more effective, less toxic treatments for patients. You should consult your medical team for more information on whether a clinical trial is an appropriate treatment option for you.

Treatment Side Effects

Many people may be frightened to learn that there can be side effects associated with the therapies they may take to treat their lymphoma. However, it is important to understand that:

- Not all patients who receive therapy experience side effects;
- Side effects are not always severe, they can be mild;
- Different therapies have different side effects;
- There are many effective treatments that can reduce side effects or prevent them from happening altogether.

Some of the most common side effects of chemotherapy include decreased blood cell production (myelosuppression), fatigue, vomiting, diarrhea, loss of appetite, change in taste, hair loss, "chemo-brain" (cognitive impairment(s) that cause difficulties with concentrating and remembering) and peripheral neuropathy (affects nerve endings causing tingling and numbness).

Most side effects are short-lived, but some can last for a few weeks or months after treatment has finished. Occasionally, side effects can be permanent. Some side effects can start long after treatment has finished. These are called late side effects. Your doctor will talk to you about any potential side effects before you start treatment.

Some BL patients may experience tumour lysis syndrome, which can happen spontaneously, but is often a side effect of chemotherapy. This condition occurs when tumor cells release their contents into the bloodstream. When cancer cells break down rapidly (usually as a result of intensive chemotherapy), the kidneys cannot remove all of these cells from the blood. This results in an electrolyte imbalance (such as high potassium) which can lead to renal failure and can be potentially life-threatening. However, if it is treated immediately, it can be managed with increased fluids and supportive medications.

Depending on the side effects you experience and how strongly you feel them, you might not be able to maintain your usual level of activity during and following treatment. You may need to set aside more time for rest and healing. Additionally, depending on the severity of your side effects related to a therapy, your doctor may suggest to stop your treatment, and can change your treatment to one that may not cause as many, or any, side effects.

Follow-Up Care

Once you have completed active treatment, you will likely be given a follow-up care plan to monitor your response to treatment and recovery, as well as to watch for late effects (side effects that develop months or years after treatment) or a potential recurrence. Follow-up care for your BL is often shared between your cancer specialists and your family doctor. Your medical team will work with you to decide on the correct follow-up care plan to meet your needs. Follow-up care after treatment is an important part of your cancer care. It is very important to go to all of your follow-up appointments. Your schedule of visits and the tests and procedures that you will undergo during your follow-up are tailored to your individual lymphoma.

Burkitt lymphoma usually stays in remission if treatment is successful. Relapse becomes less likely as time goes on and if it does occur, symptoms usually present within the first year after completion of treatment. Your doctor will tell you to watch for specific signs or symptoms of relapse or recurrence. It is important to watch for symptoms that can appear throughout your body, as relapse can occur at the site of your original diagnosis or it can occur in other regions of your body. Doctors may perform additional testing including blood tests and scans to check if your lymphoma has relapsed.

Use the time during your follow-up appointments to talk to your medical team about any changes or problems you notice and any questions or concerns you may have about your health after treatment. If you notice any change in your signs and symptoms between follow-up appointments, be sure to contact your medical team right away.

YOU DON'T HAVE TO FACE LYMPHOMA ALONE.

Lymphoma Canada connects patients, their family and friends, medical professionals, researchers, volunteers and donors, to build a strong lymphoma community.

For more information please visit lymphoma.ca or call 1-866-659-5556, or email us at info@lymphoma.ca.

LYMPHOMA CANADA