MD2B - Pediatric Oncology: Acute Lymphoblastic Leukemia (ALL)

Overview

Acute lymphoblastic leukemia, also known as acute lymphocytic leukemia or ALL, is a cancer arising from the bone marrow. Specifically, it is a type of cancer that affects the white blood cells, those cells in our body responsible for fighting off infection. In ALL, too many immature white blood cells (lymphoblasts) are produced, and they begin to replace the normal blood cells in the bone marrow. ALL is the most common cancer to occur in children and it accounts for over one-fourth of all cases of pediatric cancer. In the United States, approximately 4,500 new cases of ALL are diagnosed each year in people less than 25 years of age. The peak incidence occurs between 2 and 5 years of age. ALL occurs more commonly in males than females and more frequently in Caucasians than African Americans. Children with certain genetic conditions, including Down's Syndrome and immunodeficiencies are at greater risk for developing ALL. Advances in treatment have greatly increased the survival rates for pediatric ALL patients, and over 80% of children obtain 5-year survival.

Symptoms

The presenting symptoms of ALL result from bone marrow infiltration and disease spread. ALL primarily affects the white blood cells which are cells responsible for fighting off infection. Therefore, children with ALL often present with a repeated series of infections. The abnormal white cells take over the bone marrow resulting in lower numbers of normal red blood cells (which are responsible for carrying oxygen) and platelets (which are responsible for helping to stop bleeding after injury). As a result, children with ALL can be pale and tired, and often experience bruising and bleeding. In addition, children with ALL can present with fever, bone and joint pain, weight loss, difficulty breathing, swollen lymph nodes, or enlargement of the liver and spleen. In children with disease present in the central nervous system, headache and vomiting can be the initial symptoms. In boys with testicular ALL, a unilateral painless swollen testicle may be the presenting symptom.

Diagnosis

A careful history and physical examination, along with laboratory tests will help determine if a child has ALL.

- CBC (complete blood count) with differential: a blood sample is taken to look at the number and shape of the various blood cells, including red blood cells, white blood cells, and platelets. A pathologist (doctor who specializes in looking at cells under the microscope) can recognize cancerous cells present in the blood and can identify the specific type of cancer. Specific genetic studies and staining procedures can be performed to identify different molecular characteristics of certain cancerous cells.
- Chemistry panel: a blood sample is taken to evaluate liver and spleen function and to look at the levels of various salts and chemicals in the blood.
- Bone marrow aspirate: a small sample of bone marrow fluid will be removed from the hip bone via a needle. A pathologist will examine the bone marrow under the microscope to see if there are cancerous cells in the marrow.
- Lumbar puncture (also referred to as spinal tap): a small sample of cerebral spinal fluid or CSF (the fluid that surrounds the brain and spinal cord) will be removed from the child's back using a needle. A pathologist will examine the fluid to see if there are leukemic cells in the CSF.

- Chest x-ray: A chest x-ray will be performed after diagnosis to rule out a mass in the chest cavity which can lead to breathing difficulties.
- Testicular ultrasonography: Rarely, ALL can travel to the testes and a child may initially present with one enlarged testicle. If so, an ultrasound (a diagnostic test using sound waves) will be performed to evaluate the cause of the swollen testicles.

Treatment

ALL is a systemic disease, as the cancer has traveled all over the body and is not localized to one specific spot. Therefore, chemotherapy is the main form of treatment. Successful treatment involves administration of multiple different chemotherapy drugs, divided into several phases that occur over two to three years. The four stages of treatment are: induction, consolidation, intensification, and maintenance. The aim of induction therapy is to get the child into remission, defined as less than 5% blasts in the marrow. After remission has been achieved, consolidation, intensification, and maintenance therapy occur to keep the cancer in remission and prevent emergence of drug resistance. Successful treatment of ALL also involves the delivery of chemotherapy into the central nervous system. Irradiation of the central nervous system may be utilized to additionally target any cancer cells that might be present in the brain or spinal cord

Relapses most frequently occur in the bone marrow; however, relapse can also occur in the central nervous system, the testis, the ovary, and the eye. Most relapsed leukemias retain their original molecular characteristics, but sometimes cellular changes can occur known as a "lineage switch." Relapse protocols include more intense chemotherapy, bone marrow transplantation, or localized radiation.

Prognosis

Although survival rates for children with ALL were not always high, advances in finding effective chemotherapy agents have increased the 5-year survival rate to around 80%. Important factors influencing prognosis include white blood cell (WBC) count at the time of diagnosis, patient age and sex, initial response to induction therapy, and certain molecular features of the cancer cells. WBC count less than 50,000, age between one and ten years, hyperdiploid cells, female gender, and good response to induction therapy are all factors equated with a better prognosis.

Syndromes associated with ALL

Although no specific risk factors have been shown to cause ALL, children who have Down's syndrome, Neurofibromatosis type 1, Bloom syndrome, and ataxia telangiectasia experience ALL at higher rates than the general population.