MD2B - Pediatric Oncology: Ewings Sarcoma

Overview

Ewings sarcoma is a cancerous tumor that arises in bone or soft tissue. Histologically, it is characterized as a neuroectodermal tumor, with small blue round cells, similar to lymphoma, rhabdomyosarcoma, retinoblastoma, and neuroblastoma. Approximately 200 new cases are diagnosed each year in the United States.

Ewings sarcoma occurs in children of all ages but is most common in adolescents, with a peak age of onset between 10-15 years. It is more common in males than females and is seen more frequently in Caucasians than in Asians, rarely occurring in African Americans.

As the second most common primary bone tumor in children (after osteosarcoma), it is the most lethal form of bone cancer in this age group. Ewings sarcoma most frequently occurs in the long bones of the extremities but can also arise in the pelvis, ribs, skull, scapula (shoulder blades), or extra-skeletal tissue. Unlike osteosarcoma, which usually arises from the metaphysis (the portion of the bone between the diaphysis and metaphysis containing the growth plate), Ewings sarcoma most commonly arises from the diaphysis (mid-shaft of the bone). While many patients (75%) present with localized disease at a single site, about 25% present with disease that has spread beyond the primary tumor, most commonly to the lungs, bone marrow, and other bones. Over 90% of tumors are associated with the (t (11,22)) and EWSR1-FLI1 translocation. Although patients may appear to have a localized tumor, most have micrometastatic disease (cancer cells that have spread beyond the primary tumor but are too small to be seen on imaging) at presentation. Therefore, chemotherapy is the backbone of treatment.

Symptoms

Ewings sarcoma most frequently presents with pain, swelling, or limited movement at the tumor site. Less frequently, a fracture can occur following minor trauma to the tumor site. Some children may also present with fever, fatigue, weight loss, or decreased appetite. If the tumor is located near the spinal cord or around a nerve fiber, symptoms such as weakness, numbness, tingling, paralysis, or bladder incontinence (loss of bladder control) may occur. In tumors of the chest, patients may present with shortness of breath or dyspnea.

- **Clinical Pearl:** Pain is often worse at night or with exertion and does not resolve with NSAIDs. This helps distinguish a potential diagnosis of malignancy from osteoid osteoma.

Differential Diagnosis

There may be a delay in the diagnosis of Ewings sarcoma, as the symptoms are often nonspecific, leading to multiple visits to the pediatrician. Pain caused by tumor may be attributed to growth pain, a sports injury, tendonitis (inflammation of a tendon), coxsitis (inflammation of the hip), or osteomyelitis (infection of a bone). In young children, neuroblastoma should also be considered in the differential diagnosis. A urinalysis can help distinguish between these two types of cancers, as urine catecholamines (specific hormones) are often elevated in neuroblastoma but not Ewings. Other childhood malignancies, including rhabdomyosarcoma, desmoplastic round cell tumor, and osteosarcoma, should also be considered.

Diagnosis

A physician will perform a careful physical examination and order the appropriate imaging and laboratory tests to help distinguish Ewings sarcoma from other benign or malignant bone conditions.

Imaging studies

- *X-rays:* A lytic bone lesion with surrounding periosteal reaction, known as Codman's triangle, is suggestive of Ewings.
    - **High yield:** This is often described as an "onion skin" appearance due to the periosteum lifting off the bone in layers in response to pressure of the tumor underneath it.
- *Bone scan or whole-body PET CT:* In general, a PET CT is preferred since extra-skeletal sites of cancer are not well visualized on a bone scan. A bone scan is still acceptable in the absence of a PET CT scan.
- Magnetic resonance imaging (MRI): The imaging modality of choice for diagnosis. The primary tumor will appear as a large soft tissue mass.
- *CT scan:* Ewings sarcoma appears as a large soft tissue mass.

Tissue samples

A biopsy of the primary tumor and the bone marrow are needed for diagnosis.

Treatment

Before the development of effective chemotherapy regimens, Ewings sarcoma was often treated with surgery alone. Unfortunately, with this approach, the 5-year survival rate was less than 20%, with many patients developing grossly metastatic disease within 2 years. With the advent of modern chemotherapy, the 5-year survival rate improved to 70% for those presenting with localized disease. While patients with metastatic disease have a lower survival rate (<10%), they are still considered curable.

Once a diagnosis of Ewings sarcoma is established, patients are treated with alternating cycles of VDC (vincristine + doxorubicin + cyclophosphamide) and IE (ifosfamide + etoposide). The goal of treatment is to shrink the primary tumor and treat sites of micrometastatic disease. After the sixth cycle of chemotherapy, patients undergo surgery to remove residual tumor.

In patients with unresectable disease (typically when the primary tumor is in the chest wall, pelvis, or head and neck region), radiotherapy is given instead. Chemotherapy continues during radiation, and patients go on to complete a total of 14 cycles of chemotherapy. After chemotherapy, patients may be eligible for additional radiation to address any remaining sites of metastatic disease.

Prognosis

Patients with small tumors that have not spread beyond their primary location have a 75% survival rate. Those with tumors located distally (at the far end of bones) have the best prognosis. Patients with pelvic tumors and those whose cancer has already spread at the time of diagnosis have poorer prognoses, with 5-year overall survival rates of 60% and 30%, respectively.

Patients who achieve long-term survival have a 24% chance of developing a secondary malignancy within 35 years, among other long-term side effects from treatment. Survivors of Ewings sarcoma should be followed long-term to manage late treatment toxicities.