

A Guide to Ewing Sarcoma

Written By Physicians
For Physicians





WHAT IS EWING SARCOMA (ES)?

ES is a malignant bone tumor that can evolve from any bone in the body (and occasionally soft tissue) and mostly affects adolescents and young adults (AYA), with a median age of diagnosis at 15 years. Sarcomas account for 1% of all cancers, with a predilection for Caucasians and males. The reported age standardized incidence rate per 1,000,000 in Canada, is higher for adolescents 15-19 years at 4.1¹ compared with children 0-14 years at 2.4.² The median delay from a patient's first symptoms to definitive sarcoma diagnosis has been reported as 3.2 months.³ We aim to increase awareness of this tumor to establish early diagnosis and prompt referral.

WHY EARLY DIAGNOSIS IS IMPORTANT

Early clinical suspicion is important to minimize distress for a patient and their family that may be linked to a delay in diagnosis. A patient may experience persistent, intractable pain and after a long journey within the health system to establish a diagnosis of cancer, with parents expressing feelings of regret and guilt.

Tumor size and metastases are significant prognostic factors.

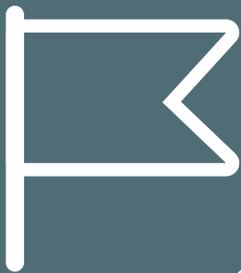
For every centimeter increase in soft tissue tumor size at diagnosis, the rate of survival is reduced by an estimated 3-5%.⁴ Metastatic disease is evident in 25% of patients at diagnosis, most often to the lungs, bone and bone marrow. Localized disease at one site has a superior 5-year disease free survival (DFS) of >70% compared to <30% in patients with metastases at diagnosis.⁵ Ewing sarcoma relapses in 30% of patients, mostly within the first two years from diagnosis and for patients with recurrent disease the 5-year overall survival rate is ~15%.^{6,7}



MEDICAL HISTORY, CLINICAL SIGNS & SYMPTOMS



Focus of history should be on duration of symptoms, trend or changes in size of lesion, intensity and timing of pain and constitutional symptoms. There is a wide spectrum of disease at presentation and clinical features depend on location of lesion. ES may involve any bone and less often, soft tissues. ES occurs mostly in bones, the most common sites been the pelvis (25%), extremities (50%), ribs, chest wall and vertebral column. Extraskkeletal ES (EES) or soft tissue tumors, favors an axial site outside of the pelvis and occurs at a higher mean age, 19.5 years, compared with 16.3 years in skeletal tumors.⁸



RED FLAGS:

- Pain that is persistent, continues at night (although can also subside at night), or associated with paraesthesia can help differentiate from a benign cause, such as 'growing pains'.
- Stiffness, swelling or unexplained restricted movement.
- Recent trauma/ injury can mask a malignant tumor and should not deter from investigation, especially if mechanism of injury inconsistent with degree of pain or other symptoms.
- Back pain can be deceptive and can often be attributed to a wide differential of conditions. A good history and thorough physical examination will help, along with a low threshold for spinal X-rays in the AYA population.
- Acknowledge if patient has sought help from multiple other providers for similar symptoms as repeated visits to the health care system for the same pain should be flagged; x-rays should be performed as a first step and with low index of suspicion in young people with persistent pain.
- Persisting constitutional symptoms - fevers, weight loss, night sweats – are in fact rare and their absence definitely does not exclude the presence of underlying disease.



PHYSICAL EXAM SHOULD FOCUS ON:

- Size, consistency and texture of mass, location, mobility, relation of mass to underlying bone.
- Presence and extent of palpable lymph nodes.
- Maintain a high suspicion for reproducible pathologic findings at the pelvis, mindful it is difficult to identify pelvic tumors on plain X-ray alone and they may require cross sectional imaging.

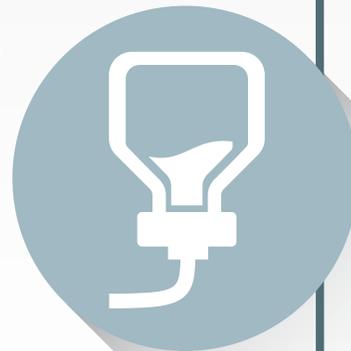
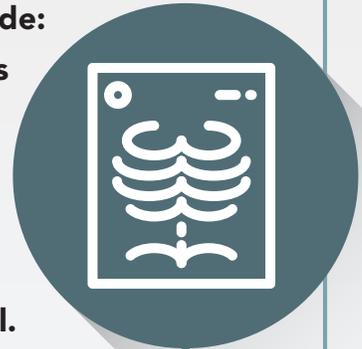
DIAGNOSIS

Plain x-rays can show features suspicious for ES; these include: moth eaten destructive lesions, often mixed sclerotic lytic lesions with cortical thickening and periosteal reaction creating 'onion peel appearance'. Soft tissue swelling with calcifications and pathological fracture can also be seen. There may be a potential need for cross sectional imaging if there are symptoms such as persistent pain, any aforementioned red flags and x-rays are normal.

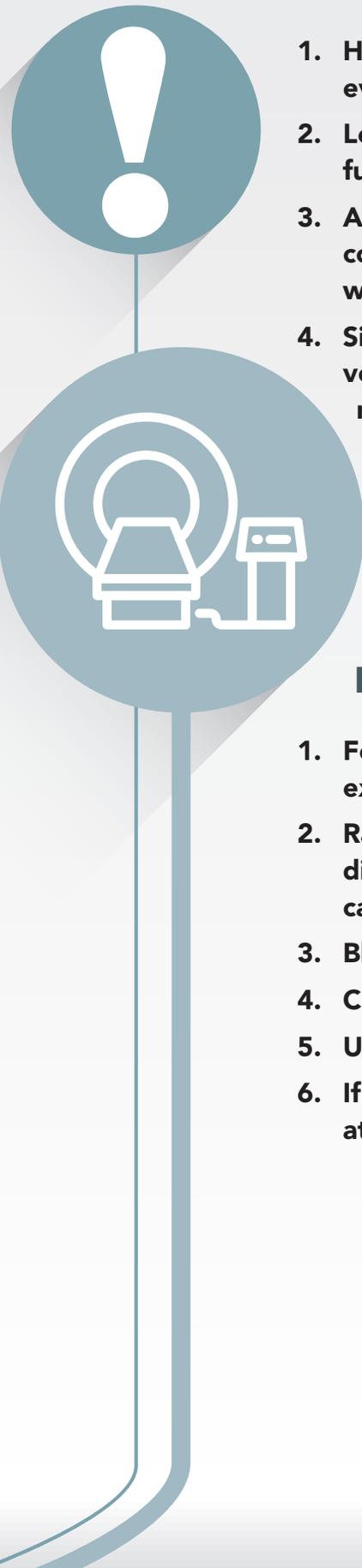
Histologically ES is a small round blue cell tumor diagnosed by biopsy. Almost all of these high-grade tumors involve the EWS gene on chromosome 22 in a reciprocal translocation, most often to FLI1. Biopsy should be well planned and carried out at the referral tertiary center by a specialized surgeon or interventional radiologist with expertise in sarcomas. This is for safety reasons, to collect enough tissue for diagnostic and prognostic analyses, for potential clinical trials and should be performed so that it does not interfere with future local control such as surgery.

Treatment

Treatment is multimodality; usually chemotherapy after biopsy, prior to and following local control. Complete surgical excision or definitive radiotherapy is important for local control. Both systemic and local therapies are necessary to ensure best chances of survival.



WHEN TO REFER TO TERTIARY CENTER^{3,4,9}

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1. Have a low threshold for referring to a sarcoma center – consider referral even if a biopsy is not done.
 2. Localized bone pain, constant or increasing intensity; decrease in functional limb capacity and/or unexplained limp.
 3. Any palpable mass, especially if >5cm and rapidly growing, should be considered for urgent investigations, that preferably, will be performed within a tertiary center.
 4. Signs of spinal cord compression by tumors close to or arising from the vertebral column require emergent investigation and attention. This is a medical emergency and requires urgent transport to a tertiary center. Multimodality treatment such as surgery, radiation and/ or steroids may be needed to relieve compression and prevent cord damage.

WHAT TO DO IF YOU SUSPECT A MALIGNANT BONE OR SOFT TISSUE TUMOR

1. Focused history, including family history and thorough physical examination
2. Radiographs or ultrasound if any concerning features as above (consider direct referral if high suspicion of malignancy and imaging in primary care setting may introduce delay)
3. Blood work- CBC, LDH
4. Chest X-Ray
5. Urgent referral to secondary or tertiary care facility
6. If in any doubt and just need to ask a friend, please call oncology on call at Sickkids, phone 416.813.7500

Author

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A Guide to Ewing Sarcoma is a helpful tool written by physicians, for physicians, that describes the history of the disease, signs, diagnosis and treatment options. It's an initiative of the Ewings Cancer Foundation of Canada (ECFC). ECFC was a registered charitable organization (2008-2018) run by a volunteer Board of Directors and founded by the Pernica family after the death of their 19-year-old son, Reid. In its 10 years in operation, the Foundation organized an annual, signature fundraiser in Toronto to raise money and awareness for Ewing sarcoma called Rally for The Cure. During the Foundation's tenure and through a partnership with the Children's Cancer and Blood Disorders group C17 Children's Cancer & Blood Disorders Council, it also funded four Canadian research grants and created and produced a professional documentary entitled, Make It Stop. Most recently, the ECFC passed the torch to SickKids Foundation where their good work under The Ewings Cancer Foundation Endowment Fund will continue indefinitely.

www.sickkidsfoundation.com/ewingscancerfoundation