



## Ewing Sarcoma Breakpoint Region 1

### Alternative Names

EWSR1  
EWS Gene  
EWS  
Ewing Sarcoma  
EWS  
ES  
Neuroepithelioma, Peripheral  
PNE  
Askin Tumor  
Esthesioneuroblastoma  
EWS/FEV Fusion Gene  
EWS/ZNF278 Fusion Gene  
EWS/FLI1 Fusion Gene  
EWS/ATF1 Fusion Gene  
EWS/ERG Fusion Gene  
EWS/WT1 Fusion Gene  
EWS/CREB1 Fusion Gene  
EWS/NR4A3 Fusion Gene  
EWS/POU5F1 Fusion Gene  
EWS/ETV1 Fusion Gene  
EWS/ETV4 Fusion Gene

### Record Category

Disease phenotype

### WHO-ICD

Neoplasms > Malignant neoplasms

### Incidence per 100,000 Live Births

0-1

### OMIM Number

133450

### Mode of Inheritance

Autosomal dominant

### Gene Map Locus

22q12

### Description

Ewing's sarcoma, named after the leading tumor pathologist James Ewing, who first described it, is a rare type of bone cancer, usually found in children and young adults between the ages of 5 and 30 years. The tumor consists of small round blue cells, and unlike osteosarcoma, is responsive to radiation therapy. ES can affect almost any bone, although the most commonly affected sites are the pelvis, thigh, lower leg, upper arm, and rib. In addition, occasionally, the tumor may affect only the soft tissues, in which case it is known as extrasosseous Ewing's sarcoma. If left untreated, the tumor may metastasize to other bones, and even to the lungs. Studies have indicated that Ewing type sarcomas cover a spectrum of tumors ranging from the classic Ewing's sarcoma to peripheral neuroectodermal tumors (PNET); all of which carry the same genetic defect: a t(11;22)chromosomal translocation.

Ewing's sarcoma is estimated to have an incidence of 0.6 per million people worldwide. X-rays of the sarcoma may show lytic or mixed lytic-sclerotic lesions in the long bones. Magnetic Resonance Imaging is the most preferred method of diagnosis. As in the case of other neoplasms, treatment involves chemotherapy, surgery, radiation therapy, or a combination of these. Surgery may involve amputation of the limbs, and in such cases, fitting prosthesis may be an option. The extrasosseous sarcoma has been shown to have a poorer prognosis with frequent development of local recurrences and distant metastases.

### Molecular Genetics

The EWS gene is a 32 Kb stretch of DNA on chromosome 11 that codes for a 64kDa protein. Almost 85% of incidences of Ewing's sarcoma have an underlying chromosomal translocation at the t(11;22)(q24;q12). This translocational event results in a fusion of the amino terminal end of the EWS gene to the carboxy-terminal domain of the FLI1 gene (Friend Leukemia Virus Integration 1). Tumor



formation is promoted by the formation of the resulting protein product (EWS Fusion Proteins or EFP), which is a chimeric transcription factor. One of the important genes that loses its transcription regulation due to this EWS-FLI1 fusion is the Transforming Growth Factor-Beta Receptor.

### **Epidemiology in the Arab World**

#### **Kuwait**

Alfeeli et al. (2005) presented the features of a Ewing sarcoma of the rib on a 3-phase bone scan in a child who was being investigated for rib fracture after trauma.

#### **Oman**

Sharma et al. (2000) were the first to report primary Ewing's sarcoma of the great wing of the sphenoid bone. The patient was a 16-year-old female who presented with one month history of progressive swelling (felt hot on touching) in the left temporal region, proptosis and diminished vision in the left eye. She also had a history of feeling warm at night and had a foreign body sensation in her throat. Clinically, she had a mildly tender non-pulsatile firm swelling (five cm in diameter), with no bruit at the left temporal region, along with left sided proptosis, left lateral rectus and left superior oblique palsies with impaired left nasal field of vision. Her blood investigations were normal other than mild anemia with leucocytosis. An interruption of the left oblique orbital line was detected on skull X-ray. CT scan of the brain revealed a large mixed attenuation mass with small cystic lesions in the left greater wing of the sphenoid bone, which extended to the left orbital cavity, middle cranial fossa, temporal and infra-temporal fossa, retromaxillary and parapharyngeal regions. No other abnormality was detected on skeletal survey, abdominal ultrasound and chest radiographs. Total excision of the mass (later confirmed by CT scan), which turned out to be a vascular tumor arising from the greater wing of the sphenoid bone with areas of hemorrhages and necrosis, was done through left trans-orbital-temporo-subtemporal approach, with intact dura mater of the middle fossa, the left periorbital, and temporalis muscle. Postoperatively, there was improvement of her vision as well as the extraorbital palsies and the foreign body sensation in the throat had gone. Intra-operative frozen section biopsy and paraffin sections had demonstrated malignant small cell neoplasm infiltrating the bone. The diagnosis of Ewing's sarcoma was made by detection of intra-cytoplasmic glycogen (PAS positive diastase labile granules) and immunohistochemistry results (negative reaction

against vimentin, desmin, NSE, myoglobin, S-100, LCA and GFAP). After the surgical excision, the patient received one course of local radiotherapy, followed by chemotherapy. The patient remained well with no clinical or radiological recurrence after one year of follow up.

#### **Saudi Arabia**

Jenkin et al. (2001) To evaluated the outcome and prognostic factors in Saudi Arabian patients with metastatic Ewing sarcoma and PNET of bone (PMES) at diagnosis. Of a total of 304 patients observed from 1975 to 1998, 99 (33%) consecutive patients with Ewing sarcoma and PNET of bone had metastatic disease at registration and 93 were available for analysis. The maximum x-axis diameter of the primary tumor was used as the measure of primary tumor size. Standard chemotherapy regimens were used in all treated patients. Forty-one (44%) patients did not receive radical local treatment due to an inadequate response to chemotherapy, or a decision not to undertake more than palliative treatment. Radical treatment of the primary site was radiation alone 41 (79%), resection alone 7 (13%), and resection and radiation 4 (8%). The 5-year survival rates were 9% for all 93 evaluable patients, 16% for 52 patients who received chemotherapy and radical local treatment, 0% for 41 patients who received lesser treatment, 19% for 43 patients with lung metastases alone, and 0% ( $P = 0.002$ ) for 50 patients with other sites involved. For 60 patients with imaging data, 5-year survivals were 34 and 0% when the maximum transverse diameter of the primary tumor was  $< 10$  cm ( $N = 20$ ) and  $\geq 10$  cm ( $N = 40$ ), respectively. Jenkin et al. (2002) further compared results related to localized Ewing Sarcoma/PNET bone in Saudi Arabia with results from countries with well developed health care systems. This retrospective analysis included 163 consecutive patients of all ages, treated with radical intent from 1975 to 1998. Standard chemotherapy was commenced in all patients. The local treatment modality was resection +/- radiation in 30% and radiation treatment alone in 67%. Three year survival significantly increased with the year of diagnosis, 1975-1988 45%; 1989-1993 55%; and 1993-1998 63% ( $P = 0.006$ ). Favorable prognostic factors were age  $\leq 14$  ( $P = 0.07$ ); site, distal extremity, and skull ( $P = 0.08$ ); and volume  $\leq 200$  ml ( $P = 0.06$ ). Secondary prognostic factors were response to induction chemotherapy, both histological, 100% necrosis, ( $P = 0.04$ ) and clinical CR+PR, ( $P = 0.02$ ). From 1994 to 1998, 3 year survival for tumors in the distal extremity and skull was 80% and for small



tumors, < 200 ml, at any site was 82%. In comparison, the 3 year survival for patients with tumors at any other sites was 60%, and for tumors >200 ml, 55%.

#### **United Arab Emirates**

Adams et al. (2006) reported the case of a 23-year-old man with malignant hyperthermia and a painful, swollen right shoulder. He sustained a traumatic fracture of the proximal right humerus 2 years previously. Examination revealed hot, tender swelling of the right shoulder with reduced range of movement. Radiographs showed features typical of Ewing sarcoma, and a 3-phase bone scan confirmed the presence of a primary bone tumor of the right humerus. Given the patient's high, unremitting fever, an Infecton scan was done to exclude a concomitant infection. The Infecton concentrated in the right shoulder. A biopsy of the humerus showed histopathologic features typical of Ewing sarcoma.

#### **References**

- Adams BK, Youssef I, Parkar S. Nonspecific infecton uptake in hyperemia secondary to a ewing sarcoma. Clin Nucl Med. 2006; 31(8):479-81. PMID: 16855437
- Alfeeli MA, Naddaf SY, Syed GM. Ewing sarcoma of the rib with normal blood flow and blood pool imagings on a 3-phase bone scan. Clin Nucl Med. 2005; 30(9):610-1. PMID: 16100480
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Jenkin RD, Al-Fawaz I, Al-Shabanah MO, Allam A, Ayas M, Memon M, Rifai S, Schultz HP. Metastatic Ewing sarcoma/PNET of bone at diagnosis: prognostic factors--a report from Saudi Arabia. Med Pediatr Oncol. 2001; 37(4):383-9. PMID: 11568903

Sharma RR, Netalkar A, Lad SD. Primary Ewing's sarcoma of the greater wing of the sphenoid bone. Br J Neurosurg. 2000; 14(1):53-6. PMID: 10884887.

#### **Related CTGA Records**

N/A

#### **External Links**

- <http://www.emedicine.com/RADIO/topic275.htm>
- <http://www.nlm.nih.gov/medlineplus/ency/article/001302.htm>
- [http://www.orpha.net/static/GB/ewing\\_sarcoma.html](http://www.orpha.net/static/GB/ewing_sarcoma.html)
- [http://www.rarediseases.org/search/rdbdetail\\_abstract.html?disname=Ewing%27s%20Sarcoma](http://www.rarediseases.org/search/rdbdetail_abstract.html?disname=Ewing%27s%20Sarcoma)

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