



DIAGNOSIS AND TREATMENT OF EWING'S SARCOMA: REVIEW ARTICLE

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ABSTRACT

Ewing sarcoma (ES) is an aggressive sarcoma of bone and soft tissue occurring at any age with a peak incidence in adolescents and young adults. The treatment of ES relies on a multidisciplinary approach, coupling risk-adapted intensive neoadjuvant and adjuvant chemotherapies with surgery and/or radiotherapy for control of the primary site and possible metastatic disease. In addition, the preferred method of tumour resection has changed; limb salvage has nearly replaced amputation of the affected limb. Limb salvage procedures can be performed in place of amputation without compromising patient survival rates. Depending on the obtained surgical margin, postoperative radiation might also be performed. If preoperative radiological examinations indicate that surgical excision would be difficult, preoperative radiation can be administered. As the treatment outcomes of ES have improved, late complications and secondary malignancies have become a problem. After treatment, patients with ES require very long-term follow-up in order to detect secondary malignancies and growth-related musculoskeletal complications.

Key words: Ewing sarcoma, neoadjuvant, chemotherapies, salvage

INTRODUCTION

Ewing sarcoma is highly malignant tumour occurring between the age of 10-20 years, sometimes up to 30 years. [1]. Since a common genetic locus is responsible for a large percentage of Ewing sarcoma and primitive neuroectodermal tumours, these are sometimes grouped together in a category known as the Ewing family of tumours. [2]. Although usually classified as a bone tumour, Ewing's sarcoma can have characteristics of both mesodermal and ectodermal origin, making it difficult to classify. [3]. It can occur anywhere in the body, but most commonly in the pelvis and proximal long tubular bones, especially around the growth plates. The diaphyses of the femur are the most common sites, followed by the tibia and the humerus. Thirty percent are overtly metastatic at presentation. Patients usually experience extreme bone pain. Rarely, it can develop in the vagina. [4].

According to the Bone Cancer Research Trust (BCRT), the most common symptoms are: localized pain, swelling, and sporadic bone pain with variable intensity. The swelling is most likely to be visible if the sarcoma is located on a bone near the surface of the body, but when it occurs in other places deeper in the body, like on the pelvis, it may not be visible. [5].

Diagnostic imaging:

Plain radiograph:

The initial imaging investigation of a suspected bone tumour is a radiograph in two planes. Tumour-related osteolysis and periosteal reactions suggest a diagnosis of primary malignant tumour. Periosteal reactions, the reactive osteogenesis of the periosteum, are caused by extra-osseous extension of the tumour. Several types of periosteal reactions have been observed: (i) an 'onion skin' or 'onion-peel appearance' is a prominent multi-layered reaction, (ii) a 'sunburst' or 'spiculae' pattern is a perpendicular reaction, while (iii) 'Codman's triangle' is a triangular lifting of the periosteum from the bone at the site of detachment. Typically, Ewing's sarcoma appears as an ill-defined, permeative, or focally moth-eaten, destructive intramedullary lesion accompanied by a periosteal reaction ('onion skin') that affects the diaphyses of long bones.



Figure 1: X-ray (lateral view) of an Ewing's sarcoma (marked by white arrow) in the tibia of a child.

MRI:

MRI is particularly important in the imaging of Ewing's sarcoma as this tumour is ill-defined on plain radiographs or by computed tomography (CT). MRI typically demonstrates lesions that involve large segments of the intramedullary cavity, which extend beyond the area indicated by plain radiographs. MRI is widely used to assess responses to neoadjuvant chemotherapy or irradiation, because regression of the extra-skeletal tumour mass can be precisely defined. Currently, MRI is the standard imaging method for such evaluation. Recent studies have demonstrated, however, that PET, thallium-201 scintigraphy and dynamic MRI provide more valuable information than MRI for assessment of therapeutic responses. [6].



Figure 2: MRI showing Ewing's sarcoma of the left hip. White areas shown in right.

PATHOLOGY

The definitive diagnostic method is biopsy. Histologically, Ewing's sarcoma is composed of a homogeneous population of small round cells with high nuclear to cytoplasmic ratios.

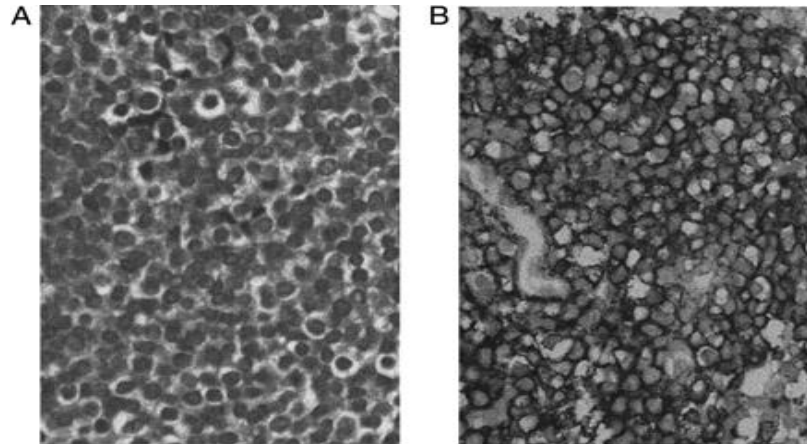


Figure 3: Microscopic features of Ewing's sarcoma. (A) Hematoxylin-eosin specimens demonstrate a uniform population of small round cells with a high nuclear to cytoplasmic ratio. (B) Immunohistochemical staining for the MIC2 is positive.

PROGNOSTIC FACTORS:

The most unfavourable prognostic factor in Ewing's sarcoma is the presence of distant metastasis at diagnosis. Even with aggressive treatment, patients with metastases have only an approximately 20% chance of long-term survival. Other unfavourable prognostic factors include an age older than 10 years, a size larger than 200 ml, more central lesions (as in the pelvis or spine), and poor response to chemotherapy. Patients with such lesions have a reduced chance of survival. [7].

Management:

Almost all patients require multidrug chemotherapy (often including ifosfamide and etoposide) [8] as well as local disease control with surgery and/or radiation [9] An aggressive approach is necessary because almost all patients with apparently localized disease at the time of diagnosis actually have asymptomatic metastatic disease.

Chemotherapy:

Treatment of Ewing's sarcoma should include chemotherapy to treat distant metastases regardless of

their identification at initial staging. Prior to the use of multi-agent chemotherapy, the long-term survival of Ewing's sarcoma was less than 10%. Currently, most clinical centres performing intensive chemotherapy are reporting long-term survival rates between 60 and 70%, suggesting that Ewing's sarcoma is sensitive to anti-cancer agents. Current anti-cancer drugs proven effective for the treatment of Ewing's sarcomas are doxorubicin (DXR), cyclophosphamide (CPA), vincristine (VCR), actinomycin-D (ACT), ifosfamide (IFM), and etoposide (VP16).

LOCAL TREATMENT; SURGERY AND/OR IRRADIATION

Local treatment of the primary lesion remains controversial. Previous reports demonstrated a decrease in the rate of local recurrence (<10%) and an increase in the rate of overall survival with wide resection of the primary tumour. In addition, retrospective analyses by several groups provide the impression that local control is preferable when surgery is possible.[10]

If pre-operative imaging suggests that it will likely be possible to resect the lesion with wide margins, wide resection without irradiation is the treatment of choice for primary lesions. If the possibility of achievement of adequate surgical margins is uncertain, pre-operative radiotherapy should be added. As Ewing's sarcomas are sensitive to both chemotherapy and irradiation, even questionable candidates for limb salvage may be eligible after neoadjuvant chemotherapy with or without irradiation. If the surgical margins are found to be inadequate after surgery, postoperative radiotherapy may also be added. When surgical margins are certain to be inadequate at preoperative imaging, amputation may be the only surgical option available. Central, large, unresectable primary tumours are sometimes treated with radiation alone. A debulking intralesional procedure does not improve local control; in the CESS and EICESS trials, patients who had an intralesional resection followed by radiotherapy displayed the same local control rate as those who were treated with radiotherapy alone[11]

SURGICAL MARGIN:

The current standard treatment schedules for resectable Ewing's sarcoma begin with neoadjuvant chemotherapy, followed by limb salvage procedure and post-operative adjuvant chemotherapy. Although amputation had been the only surgical method for several decades, limb salvage procedures, which include local resection and reconstruction, are currently performed in almost all the cases of Ewing's sarcomas. Limb salvage procedures can be performed without compromising survival rates.[12]

Reconstruction:

After resection of Ewing's sarcomas, large bone defects should be reconstructed to restore the function of the affected limbs. The main options for reconstruction include Autogeneous bone grafts may be

vascularized; vascularized bone autograft operations are now performed widely as a result of the development of microsurgery. As blood flow can be preserved and the cells in the grafted bone remain alive, bone formation and bone fusion are vigorous. This technique has generated remarkable improvement in therapeutic success rates [13]. Because of the limited amounts of bone that can be collected, however, it is sometimes difficult to repair large bone defects; in such cases, allogeneic bone grafts or endoprosthesis is indicated.

CONCLUSION

Ewing sarcoma (ES) is an aggressive sarcoma of bone and soft tissue occurring at any age with a peak incidence in adolescents and young adults. In this article we have described about how to diagnose and treat the case of ewing sarcoma.

REFERENCES

1. Iwamoto Y (February 2007). "Diagnosis and treatment of Ewing's sarcoma". *Jpn. J. Clin. Oncol.* 37 (2): 79–89. doi:10.1093/jjco/hyl142. PMID 17272319.
2. Iwamoto Y (February 2007). "Diagnosis and treatment of Ewing's sarcoma". *Jpn. J. Clin. Oncol.* 37 (2): 79–89. doi:10.1093/jjco/hyl142. PMID 17272319.
3. Longtin R (November 2003). "Ewing sarcoma: a miracle drug waiting to happen?". *J. Natl. Cancer Inst.* 95 (21): 1574–6. doi:10.1093/jnci/95.21.1574. PMID 14600088.
4. "Vulva and Vagina tumors: an overview". *atlasgeneticsoncology.org*. Retrieved 2018-03-14.
5. "Symptoms of Ewing's Sarcoma - Bone Cancer Research Trust". *Bcrt.org.uk*. Archived from the original on 2013-01-30. Retrieved 2012-11-05
6. Van der Woude HJ, Bloem JL, Hogendoorn PC. Preoperative evaluation and monitoring chemotherapy in patients with high-grade osteogenic and Ewing's sarcoma : review of current imaging modalities, *Skeletal Radiol*, 1998, vol. 27 AND (pg. 57-71)
7. Localized Ewing tumor of bone: final results of the cooperative Ewing's Sarcoma Study CESS 86.
8. Lahl M, Fisher VL, Laschinger K (February 2008). "Ewing sarcoma family of tumours: an overview from diagnosis to survivorship". *Clin J Oncol Nurs.* 12 (1): 89–97. doi:10.1188/08.CJON.89-97. PMID 18258578. Archived from the original on 2013-01-28.
9. Randall, RL (2005). "Ewing's Sarcoma Family of Tumours (ESFT)". *ESUN*. Retrieved 2009-04-15.
10. Local therapy in localized Ewing tumors: results of 1058 patients treated in the CESS 81, CESS 86, and EICESS 92 trials.
11. Local therapy in localized Ewing tumors: results of 1058 patients treated in the CESS 81, CESS 86, and EICESS 92 trials.
12. Paulussen, M, Ahrens, S, Braun-Munzinger, G et al, EICESS 92 (European Intergroup Cooperative Ewing's

Sarcoma Study)—Preliminary results. *Klin Pädiatr.* 1999;211:276–283.

13. Reconstruction and limb salvage after resection for malignant bone tumour of the proximal humerus. A sling procedure using a free vascularised fibular graft.