RESEARCH BRIEF

Ewing Sarcoma of the Clavicle: A Case Series

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Clavicle is a rare primary site for Ewing sarcoma (ES). We analyzed 4 patients with clavicular ES under our follow up and reviewed the literature on management of this rare tumor. All our patients were females with a median age of 16 years and were non metastatic at presentation. After a median follow-up of 21.5 months, 3 out of 4 patients are in complete remission. Clavicular ES in contrast to ES of other sites seems to have a female preponderance and outcomes are similar to non metastatic ES of other common sites.

Key words: *Clavicle;Ewing Sarcoma, Malignancy.*

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Ewing Sarcoma (ES) is a small round cell tumor arising most commonly from pelvic bones, femur, humerus and the ribs in children and adolescents [1]. At the molecular level ES results from the translocation of *EWS* gene in chromosome 11 to the *FLI* gene in chromosome 22 [1]. Pathologically ES is characterized by positivity for mic-2 (CD99). Clavicle is the only long bone to arise from membranous ossification [2]. Malignant tumors of clavicle are very rare and comprise less than 0.5% of all malignant bone tumors [3] and 1.4% of all ES [1].

METHODS

We identified 4 patients with primary clavicular ES at our center from June 2003-June 2009. Baseline workup included core needle biopsy of the tumor for confirmation of ES, CT scan or MRI of neck and chest, bone scan, and bone marrow biopsy. The patients received Neoadjuvant chemotherapy (NACT) with vincristine, actinomycin-D, doxorubicin and cyclophosphamide, alternating every 3 weekly with ifosfamide and etoposide [4]. Response to NACT was assessed clinically and by imaging (CT or MRI scan). The patients who responded to NACT underwent total clavicular excision after 9-12 weeks of initiation of NACT. Patients with residual tumor post operatively or positive surgical margins received radiotherapy to the local site. Adjuvant chemotherapy with drugs as used for NACT was administered for 48 weeks.

RESULTS

All 4 patients were non-metastatic at presentation and were females (median age 16 years, range 5-18 years). Pain and swelling were the predominant presenting manifestations with median duration of 4.2 months (range: 2-6 months). Two patients had received anti-tubercular therapy for presumed bone tuberculosis prior to presentation. There was no predilection for any site or side of clavicle. Biopsy in all four patients was morphologically consistent with a small round blue cell tumor which showed positivity for mic-2 (CD99) on immunohistochemistry. Reciprocal chromosomal translocation t(11;22) (q24;q12), could not be studied. All patients responded clinically and radiologically to NACT and underwent total clavicular excision (TCE) after 9-12

WHAT THIS STUDY ADDS?

- Functional outcomes of clavicular Ewing sarcoma are excellent and with multi-modality treatment, survival is similar to non-metastatic Ewing sarcoma of other common sites.

weeks of NACT. One of the 4 patients had a positive surgical margin and was administered local radiotherapy. After a median follow up of 21.5 months (range 10-37 months), 3 of our patients are in complete remission. One patient with negative surgical margin relapsed locally in the neck while on adjuvant chemotherapy and thereafter received palliative radiotherapy. Post TCE none of our patients had significant restriction of movement and did not require any reconstructive procedures.

DISCUSSION

We could identify only one earlier published cases series on clavicular ES [5]; three case series on clavicular tumors which also included ES patients [6-8] and two case reports describing clavicular ES [9, 10].

The reported male to female ratio for ES is 1.6:1; an interesting observation was that all our patients were females and overall 16/25 (64%) patients of non-metastatic ES of clavicle reported in the literature including ours were females. The median age of presentation of clavicular ES in reported literature including ours is 15 years (range: 10 months-33 years), this is similar to what has been reported for ES arising from all other sites [1]. Data on long-term outcomes and details related to chemotherapy are lacking amongst the published cases of clavicular ES.

Successful outcome in ES is dependent on prompt initiation of NACT followed by surgery and adjuvant chemotherapy with addition of radio-therapy if required. Patients with non-metastatic ES have an overall survival of 70-75% [1], currently 3/4 of our patients are alive and disease free. Survival in patients with metastatic ES is dismal and is less than 15-20% [1]. Good functional outcomes can be maintained after clavicular excision for clavicular tumors and reconstruction procedures are rarely required [5,7]. The majority of clavicular tumors in children and adolescents are malignant. Differential diagnosis of clavicular tumors in children and adolescents include osteosarcoma, chondrosarcoma Langerhans cell histiocytosis, lymphoma, malignant fibrous histiocytoma, osteomyelitis, osteochon-droma and aneurysmal bone cysts [6-8].

Patients with clavicular ES present late to the oncologist, due to the fact that ES is not suspected at this rare site. Most patients receive therapy for unrelated conditions like tuberculosis as was seen in two of our patients. Medical personnel need to be aware that ES does occur in the clavicle.

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REFERENCES

1. Bernstein M, Kovar H, Paulussen M, Randall R, Schuck A, Teot L, *et al*. Ewing's sarcoma family of tumors: Ewing sarcoma of bone and soft tissue and the peripheral primitive neuroectodermal tumors. *In*: Pizzo PA, Poplack DG, editors. Principles and Practice of Pediatric Oncology. 5th ed. Philadelphia Pa: Lippincott Williams & Wilkins; 2006. p.1002-32.
2. Ellis H, Johnson D. Pectoral girdle, shoulder and axilla. *In*: Standring S, editor. Gray's Anatomy: The Anatomical Basis of Clinical Practice. 39th edn. Edinburgh: Elsevier Churchill Livingstone; 2005. p.817-49.
3. Waller DA, Newman RJ. Primary bone tumours of the thoracic skeleton: an audit of the Leeds Regional Bone Tumour Registry. Thorax.1990;45:850-5.
4. Grier HE, Krailo MD, Tarbell NJ, Link MP, Fryer CJ, Pritchard DJ, *et al*. Addition of ifosfamide and etoposide to standard chemotherapy for Ewing's sarcoma and primitive neuroectodermal tumor of bone. N Engl J Med.2003;348: 694-701.
5. Rodriguez Martin J, Pretell Mazzini J, Viña Fernandez R, Marti Ciruelos R, Curto de la Mano A. Ewing sarcoma of clavicle in children: report of 5 cases. J Pediatr Hematol Oncol. 2009;31:820-4.
6. Kapoor S, Tiwari A, Kapoor S. Primary tumours and tumorous lesions of clavicle. Int Orthop. 2008;32:829-4.
7. Natarajan M, Meller I, Malawer MM. Claviculectomy for bone tumors. Ind J Orthop. 2006;40:115-8.
8. Smith J, Yuppa F, Watson RC. Primary tumors and tumor-like lesions of the clavicle. Skeletal Radiol. 1988;17:235-6.
9. Weber KL, Makimato A, Raymond AK, Pearson MG, Jaffe N. Ewing sarcoma of the clavicle in a 10-month-old patient. Med Pediatr Oncol. 2000;34:445-7.
10. Desai NJ, Upadhyay SB, Mengar B, Bhanvadia V. Ewing's sarcoma/primitive neuro-ectodermal tumour: a case report. J Indian Med Assoc. 2009;107:107.