Primary Ewing's Sarcoma of the Temporal Bone: A Rare Case Report and Literature Review

Divya Gupta^{1,2} · Achal Gulati¹ · Purnima¹

Received: 14 February 2015 / Accepted: 7 December 2015 / Published online: 14 December 2015
© Association of Otolaryngologists of India 2015

Abstract Ewing's sarcoma is a malignant, round cell tumor arising from the bones and primarily affecting children and adolescent, accounting for 3 % of all childhood malignancies. Although the long bones and the trunk are typically affected, rare cases of it involving isolated bones throughout the body have been reported. Involvement of the skull bones is rare, constituting 1–6 % of the total Ewing's sarcoma cases but those affecting the cranial bones are rarer still, constituting only 1 %. We describe an 8 months old infant having Ewing sarcoma, of the petrous and mastoid parts of temporal bone along with the occipital bone, whose clinical presentation mimicked mastoiditis with facial nerve palsy. We discuss the clinical and therapeutic course of an extensive primary Ewing sarcoma of the temporal bone, which was treated without performing surgery and review this entity's literature in detail.

Keywords Ewing's sarcoma · Temporal bone · Facial palsy

Introduction

Ewing's Sarcoma (ES) is the second most common primary malignant tumor after osteosarcoma, accounting for 3 % of all childhood malignancies [1], typically affecting the trunk

and long bones. Only 1–6 % of the total ES cases affect the skull (i.e., maxilla, frontal, parietal, ethmoid, or temporal bones) [2]. We present a case report of ES of temporal bone in an 8 months old female which will be an addition to the 28 cases reported so far in the searched indexed literature of last 50 years. We discuss the clinical and therapeutic course of the case, clinical presentation of which mimicked mastoiditis with facial nerve palsy. The patient was treated without performing surgery, by chemotherapy and with placement of a ventriculoperitoneal shunt to tide over the emergency posed by raised intracranial pressure, thus, unfolding a different line of acute management for such cases.

Case Report

An eight-month old female presented to ENT OPD with complaints of swelling behind the right ear for 7 days and facial asymmetry for 4 days. There was no history of aural discharge or fever/vomiting/seizures/loss of consciousness/swelling elsewhere. The patient was conscious and alert. A 3 × 2.5 cm erythematous and tender swelling was present with raised local temperature behind right pinna. Though pinna and external auditory canal were normal in appearance, tympanic membrane on the right side appeared congested and the patient had mastoid tenderness. The patient had right lower motor neuron type facial nerve palsy with no other clinical correlation of neurological dysfunction (Fig. 1a, b). The child was admitted and started on antibiotics after making a provisional diagnosis of right acute otitis media with mastoiditis causing facial nerve palsy.

An initial array of investigations showed only mild leukocytosis with unrecordable functioning facial nerve

---

✉ Divya Gupta
divyagupta.leo@gmail.com
Achal Gulati
achalgulati@rediffmail.com

¹ Department of Otorhinolaryngology and Head and Neck Surgery, Maulana Azad Medical College and Associated Lok Nayak Hospital, New Delhi 110002, India

² 66, Raj Nagar, Pitam Pura, Delhi 110034, India

Fig. 1 Photograph at initial presentation showing **a** swelling behind the ear in temporo-occipital region and **b** absent nasolabial fold on the right side and slight deviation of mouth towards left, suggesting right facial nerve weakness

Fig. 2 **a** CT scan showing large heterogeneous extra-axial lesion in the posterior fossa and right middle cranial fossa with destruction of mastoid region of temporal bone and adjacent occipital bone. **b** MRI showing large well margined extra axial lesion in the right temporo-parieto-occipital region with multiple cystic areas within with intense heterogeneous enhancement with mass effect cerebellum

fibres on electroneuronography on right side. Deterioration of the general condition of the child, development of papilledema and symptoms like vomiting, alarmed us and further investigations were carried out. Computed tomographic (CT) scan of head and MRI T2W axial and coronal cuts revealed a large heterogeneous extra-axial lesion in the right temporo-parietal-occipital region with destruction of mastoid part of temporal bone and adjacent areas of occipital bone with evidence of compression on the brain stem, cerebellum and 4th ventricle with consequent obstructive hydrocephalus (Fig. 2a, b). MR Venogram showed displacement and attenuation of the right occipital and transverse sinus along with thrombosis of the right internal jugular vein. Cerebrospinal fluid analysis was however normal.

Fine needle aspiration cytology study done from postaural swelling came suggestive of Ewing's Sarcoma with small round cells arranged in pseudorosette pattern.

Fig. 3 CT scan of the head of the patient after completion of chemotherapy

Cells were positive to periodic acid-Schiff (PAS) and negative to desmin and leucocyte common antigen. Bone scans of the infant did not reveal any metastatic deposits elsewhere in the body.

An urgent surgical intervention to lower the intracranial tension was warranted as the infant was not responding adequately to medical management. Hence, a ventriculo-peritoneal shunt was placed to lower the intracranial tension. Subsequently, the patient was given 12 cycles of chemotherapy over 36 weeks which consisted of alternate cycles of vincristine, actinomycin-D, cyclophosphamide and etoposide, ifosfamide respectively at 3 week intervals with an excellent response. There was complete recovery of facial palsy and external swelling. Her CT after 1 year of completion of therapy did not show any evidence of disease (Fig. 3). On her most recent hospital visit after 4 years of completion of treatment of ES, she is well and leading a normal life.

Discussion

First described by James Ewing in 1921 as a diffuse endothelioma of bone, ES is a malignant tumour of bones, primarily arising in the diaphyseal region of tubular bones and pelvis in the first two decades of age. Males are affected more than females, the male to female ratio being 1.6:1 [3]. Our case is the second youngest reported case so far, the only exception being a 5 months old male [4]. The disease most frequently involves diaphyses of long bones (47 %) followed by pelvis (29 %), ribs and vertebrae (12 %) and jaw and cranium (9 %) [3]. Only 1–6 % of the ES cases have been found to be involving the skull bones and even rarer, the membranous bones [2]. A brief summary of the cases of Primary Cranial Ewing's Sarcoma

involving the temporal bone in the past 50 years as gathered from the referenced indexed literature is given in Table 1 [2–24].

In contrast to 40 % cases of ES throwing metastasis during treatment and 73 % within 1 year after ES diagnosis, only one reported case of cranial ES displayed distant metastasis during follow up period [10]. Hence, most researchers claim a better prognosis for ES of the head and neck region, more so for cranium as compared to that arising in other anatomic locations due to infrequent metastasis and prolonged survival, although it needs to be substantiated by accumulation of further cases [25]. Our case has been followed up for 4 years and does not show any residual, recurrent or metastatic disease evidence.

ES is one of the differential diagnoses of pediatric small round blue cell tumours. Immunohistochemical findings (positive for CD99 but negative for lymphocytic markers) and genetic/molecular genetic characteristics of (11; 22) translocation and identification of typical fusion transcripts help to recognize and differentiate ES from other lesions. The origin of ES is a subject of much debate. The precise origin of ES continues to dodge investigators and the relationship between classic ES of bone and primitive neuroectodermal tumor of bone remains contentious. Once believed to be originating from primitive neuroectodermal cells, many now reason it to be arising from a mesenchymal stem cell (MSC). Expression of the EWS-FLI1 fusion gene in MSC changes the cell morphology to resemble Ewing's Sarcoma and induces expression of neuroectodermal markers [26].

Cranial ES classically grows as an extradural mass lesion rarely breaching the duramater and hence can attain a huge size before detection [4, 20]. It often presents as a tender, expansile mass causing symptoms of increased intracranial pressure especially when involving the cranial bones, and can easily be confused with signs of inflammation, as we initially did in our case. Temporal cranial ES involving skull base present with symptoms like cranial nerve involvement and those arising in cranial vault present with swelling or headache. Overall, headache and other features of raised intracranial pressure are most commonly presented complaints followed by localized scalp swelling, hemiparesis, diplopia and seizures [14]. Site specific signs and symptoms like, facial palsy when involving the petrous part of temporal bone and proptosis with deterioration of vision when affecting the orbit have also been reported [3, 11, 17–21, 24].

Typically, plain radiographs of the cranium show characteristic laminated periosteal changes in the form of onion-peel appearance with mottling, cortical erosion and bone expansion, however this diagnostic feature may be absent on many occasions [3, 14]. CT scans reveal an isodense or mildly hyperdense mass which enhances

uniformly on contrast enhancement [7]. Radioisotope scans are required to rule out distant lesions. Histopathology shows monomorphic round cells with scanty cytoplasm, prominent nuclei, bony spicules and mitotic figures arranged in sheets. It is differentiated from embryonic rhabdomyosarcoma by demonstration of periodic-acid-Schiff staining with diastase control in its intracellular glycogen [7, 14].

Broadly, the treatment of ES aims at eradication of the primary tumor and metastatic disease, if present. Initially, it used to be treated with surgery or radiotherapy alone with a 5-year survival rate of approximately 15 %. With the advent of chemotherapy in the last three decades, the long-term survival rates have increased to 50–60 %. Originally used as adjuvant therapy, chemotherapy is indispensable in the current scenario as first-line treatment because of its local and systemic efficacy [1, 7, 27]. Treatment modality followed in lesion involving the skull bones varies from those of the long bones because of an urgent need for intervention necessitated due to elevated intracranial pressure and impending neurological deficits resulting from close proximity of the lesion to the vital structures.

A large number of studies have consistently shown poor prognostic relationship of ES with larger size of lesion, female sex, presence of metastasis, pelvic location, high serum LDH, greater than 17 years of age, leukocyte count >7000/dl and lymphocyte count >2000/dl [1, 13, 27]. Radiochemotherapy followed by autologous bone marrow transplantation is a newer therapy option with promising preliminary results, especially for these high-risk patients [27].

In most of the earlier reported cases, due to the accelerated intracranial pressure and impending neurological deficit, an urgent surgical intervention in the form of surgical resection of the primary lesion was performed. As achieving complete clearance of the margins was doubtful, in consideration to the young age of the patients as well as the tumor size and its localization, surgical resection was followed up by radiotherapy or chemotherapy. A more aggressive surgical resection in these cases may have led to a limited quality of life, as a result of mutilation and loss of function of the vital structures. In cases of absence of any surgical emergency, i.e. no signs of raised intracranial tension, the patients could be started on radiotherapy or chemotherapy followed by surgery. We propose placement of a ventriculoperitoneal shunt to tackle the raised intracranial tension and buy time to allow the chemotherapeutic agents to act. This modality of treatment will prevent the morbidity associated with the extensive surgical resection, meanwhile maintaining the benefits of chemotherapy.

In our case, the little girl was completely treated using multi-drug chemotherapy. As has already been proven in previous multiple trials, multi-drug regimens are more effective than single drug therapy [13, 14, 28]. In 1974,

Table 1 Brief overview of cases of Primary Ewing's Sarcoma of temporal bone in last 50 years

S. No.	References	Age at presentation and gender	Symptoms	Main part involved	Treatment	Follow up
1	Fitzer et al. [3]	9 years/F	Otorrhoea, hearing loss, otalgia, facial nerve palsy	Petrous	Facial nerve decompression through middle fossa approach, procedure abandoned fb RT, CT	Not mentioned
2	Hara et al. [5]	5 years/F	Swelling	Temporal	Surgery (twice), RT, CT	3 years
3	Steinbok et al. [2]	3 years/M	Headache, emesis, left temporal swelling	Petrous	Subtotal removal, CT, RT	Not mentioned
4	Carroll et al. [6]	4 years/M	Swelling	Temporal	Surgery, RT, CT	3 years
5	Davidson [7]	11 years/M	Left temporal swelling	Petrous, squamous	CT, RT	4 years-death
6	Watanabe et al. [8]	19 years/M	Swelling, headache	Temporal	Surgery, CT, RT	12 months
7	Krishnan et al. [9]	12 years/M	Headache, swelling	Petrous	Surgery, CT, RT	Not mentioned
9	Majumdar et al. [10]	6 years/F	Swelling, headache	Temporo-parietal	Biopsy, RT, CT	2 years
10	Kuzeyli et al. [11]	10 years/F	Right temporal swelling, diplopia, Rt eye proptosis	Temporal (with Orbit)	Surgery, CT, RT	Died in 6 months (lung metastasis)
11	Nakane et al. [12]	32 years/F	Headache, swelling	Petrous	Surgery, CT, RT	2 years
12	Bhatoo et al. [13]	27 years/M	Headache	Temporal	Surgery, CT, RT	14 months
13	Desai et al. [14]	1.6 years/M	Headache, increased ICT	Petrous	Surgery, CT, RT	27 months
14	Desai et al. [14]	10 years/M	Headache, swelling	Temporal	Surgery, CT, RT	26 months
15	Seckin et al. [15]	15 years/F	Swelling, pain, vomiting	Mastoid	Surgery, CT, RT	Not mentioned
16	Boundin et al. [16]	13 years/M	Swelling	Temporal	Surgery, CT	2 years
17	Boundin et al. [16]	14 years/M	Headache	Temporo-parietal	Surgery, CT	2 years
18	Encabo et al. [17]	20 years/M	Left facial palsy	Mastoid	Surgery, CT, RT	12 months
19	Pfeiffer et al. [4]	5 months/M	Facial palsy, increased ICT	Petrous	CT, RT	Not mentioned, alive
20	Bawa et al. [18]	9 years/M	Swelling, right facial palsy	Petrous, mastoid, squamous	Not described	12 months
21	Balasubra-maniam et al. [19]	17 years/M	Headache, decreased hearing, cranial palsies	Petrous, mastoid	Surgery, CT, RT	12 months
22	Kadar et al. [20]	16 years/M	Right facial palsy, ipsilateral headache, Ipsilateral tinnitus	Petrous	Surgery, CT, RT	9 months
23	Singh et al. [21]	13 years/F	Headache, swelling, proptosis	B/L temporal	Surgery, CT, RT	6 months
24	Choudhary et al. [22]	11 years/F	Headache, temporal swelling, vomiting	Temporo-parietal	Surgery, CT, RT	Not mentioned
25	Salunke et al. [23]	3 years/M	Increased intracranial tension, ataxia	Temporo-squamous, petrous	Surgery, CT, RT	Recurrence at 8 months died
26	Salunke et al. [23]	12 years/M	Increased intracranial tension	Temporo-squamous, petrous	Surgery, CT, RT	Recurrence at 12 months, died
27	Salunke et al. [23]	16 years/F	Seizures, raised intracranial tension	Temporo-parietal	Surgery, CT, RT	24 months, alive
28	Cugati et al. [24]	16 years/M	Rt frontotemporal headache, decreased vision, facial paresis	Petrous (with middle cranial fossa)	Surgery, CT, RT	Not mentioned
29	(2014)	8 months/F	Temporal swelling, facial palsy, increased intracranial tension	Temporal	CT	4 years, alive

RT radiotherapy, CT chemotherapy

Rosen et al. [28] from Memorial Sloan-Kettering Cancer Centre used vincristine, actinomycin D, cyclophosphamide and doxorubicin (VACD) for ES and marked the beginning of multimodality therapy era. Incorporation of etoposide and ifosfamide has decisively been found to be associated with increased survival of these patients because of their synergistic antitumor effect and the efficacies of both these agents improve further with fractionated administration. Since ES shows very good response to radiotherapy and chemotherapy, a relatively less emphasis on radical surgical approaches should be sought [2, 8, 13, 14, 27] as is supported by our case report.

Conclusion

Despite Ewing's Sarcoma of the temporal bone being a rare entity, the clinical suspicion should be high in cases where the patient develops signs of raised intracranial tension along with facial nerve palsy and local signs of inflammation. These tumors typically respond quickly and dramatically to chemotherapy. Local control with surgery or radiotherapy should ideally be delayed until after this initial response to chemotherapy because of its intimate relationship with critical neurovascular structures. A ventriculoperitoneal shunt can be placed to tide over the emergency caused by accelerated intracranial tension. Given the rarity of Ewing's Sarcoma involving the skull bones especially the temporal bone, our experience adds to the global understanding of presentation, management and outcome of such patients.

Compliance with Ethical Standards

Conflict of interest None.

References

- Galindo CR, Liu T, Krasin MJ, Wu J, Billups CA, Daw NC, Spunt SL, Rao BN, Santana VM, Navid F (2007) Analysis of prognostic factors in ewing sarcoma family of tumors-review of St. Jude Children's Research Hospital Studies. *Cancer* 110:375–384
- Steinbok P, Flodmark O, Norman MG, Chan KW, Fryer CJ (1986) Primary Ewing's sarcoma of the base of the skull. *Neurosurgery* 19:104–107
- Fitzer PM, Steffey WR (1976) Brain and bone scans in primary Ewing's sarcoma of the petrous bone. *J Neurosurg* 44:608–612
- Pfeiffer J, Boedeker CC, Ridder JJ (2006) Primary Ewing sarcoma of the petrous temporal bone: an exceptional case of facial palsy and deafness in a nursingling. *Head Neck* 28:955–959
- Hara N, Kaneko H, Inoue K, Watanabe M (1980) Primary Ewing's sarcoma of the temporal bone (in Japanese). *No Shinkei Geka* 8:557–562
- Carroll R, Micketie L (1987) Ewing's sarcoma of the temporal bone: CT appearance. *J Comput Assist Tomogr* 11:362–363
- Davidson MJC (1991) Ewing's sarcoma of the temporal bone—a case report. *Oral Surg Oral Med Oral Pathol* 72(5):534–536
- Watanabe H, Tsubokawa T, Katayama Y, Koyama S, Nakamura S (1992) Primary Ewing's sarcoma of the temporal bone. *Surg Neurol* 37:54–58
- Krishnan VV, Saraswathy A, Misra BK, Rout D (1993) Primary Ewing's sarcoma of the base of skull: a case report. *Indian J Pathol Microbiol* 36:477–479
- Majumdar J, Basu S, Dutta S, Rowchowdhary J (1994) Ewing's sarcoma of temporoparietal Region: a rare presentation. *J Indian Med Assoc* 92:202–204
- Kuzeyli K, Akturk F, Reis A, Cakir E, Baykal S, Pekince A, Usul H, Soylev E (1997) Primary Ewing's sarcoma of the temporal bone with intracranial, extracranial and intraorbital extension. *Case Report. Neurosurg Rev* 20:132–134
- Nakane T, Hashizume Y, Tachibana E, Mizutani N, Handa T, Mutsuga N, Yoshida J (1994) Primary Ewing's sarcoma of the skull base with intracerebral extension: a case report. *Neurol Med Chir (Tokyo)* 34:628–630
- Bhatote HS, Deshpande GU (1998) Primary cranial Ewing's sarcoma. *Br J Neurosurg* 12(2):165–169
- Desai KI, Nadkarni TD, Goel A, Muzumdar DP, Naresh KN, Nair CN (2000) Primary Ewing's sarcoma of the cranium. *Neurosurgery* 46:62–69
- Seckin H, Varan A, Demirhan B, Altinok D, Kars HR (2001) Primary Ewing's sarcoma of the cranium: case report. *Turk Neurosurg* 11:130–133
- Boumdin H, Quessar A, Chakir N, Hassani MR, Jiddane M (2001) Primary Ewing's sarcoma of cranial vault: report of two cases. *J Neuroradiol* 28(3):200–204
- Encabo RS, Britez A, Gil R, Luengo EP, Yurrita BS (2005) Primitive neuroectodermal tumor/extracranial Ewing sarcoma of the temporal bone. *Acta Otorrhinolaryngol Esp* 56:38–40
- Bawa SS, Hegde KK (2006) Primary Ewing's sarcoma of the temporal bone—a case report. *Ind J Radiol Image* 16(4):623–625
- Balasubramaniam S, Nadkarni T, Menon R, Goel A, Rajashekar P (2008) Primary Ewing's sarcoma of the petroclival bone. *J Clin Neurosci* 15:714–716
- Kadar AA, Hearst MJ, Collins MH, Mangano FT, Samy RN (2010) Ewing's sarcoma of the petrous temporal bone: case report and literature review. *Skull Base* 20(3):213–217
- Singh DK, Gupta V, Acharya S, Chopra S, Bagaria H (2011) Multicentric primary cranial Ewing's sarcoma. *Pan Arab J Neurosurg* 15(2):93–95
- Choudhury KB, Sharma S, Kothari R, Majumder A (2011) Primary extraosseous intracranial Ewing's sarcoma: case report and literature review. *Indian J Med Paediatr Oncol* 32(2):118–121
- Salunke PS, Gupta MV, Kumar N, Henke LE, Cai C, Chen WS, Pfeifer JD (2011) Primary Ewing's sarcoma of cranial bones: analysis of ten patients. *Acta Neurochir* 153:1477–1485
- Cugati G, Singh M, Pande A, Symss NP, Chakravarthy VM, Ramamurthi R (2013) Isolated skull base primary Ewing's sarcoma: an extremely rare location. *J Cancer Res Ther* 9(4):741–742
- Allam A, Hussein GE, Khafaga Y, Kandil A, Gray A, Ezzat A, Schultz H (1999) Ewing's sarcoma of the head and neck: a retrospective analysis of 24 cases. *Sarcoma* 3:11–15
- Lin PP, Wang Y, Lozano G (2011) Mesenchymal stem cells and the origin of Ewing's sarcoma. *Sarcoma* 2011:8. doi: [10.1155/2011/276463](https://doi.org/10.1155/2011/276463)
- Carlotti CG, Drake J, Hladky JP, Teshima I, Becker LE, Rutka JT (1999) Primary Ewing's sarcoma of the skull in children—utility of molecular diagnostics, surgery and adjuvant therapies. *Pediatr Neurosurg* 31:307–315
- Rosen G, Wollner N, Tan C, Wu SJ, Hajdu SI, Cham W et al (1974) Proceedings: disease-free survival in children with Ewing's sarcoma treated with radiation therapy and adjuvant four drug sequential chemotherapy. *Cancer* 33:384–393