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Case Report

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Ewing's Sarcoma of the Craniovertebral Junction - A Rare Cause of Reversible Quadriplegia. A Case Report with a 10-year Review of Literature

Sibhi Ganapathy*, Adesh Jagadeesh, Rajesh Raykar and Shailesh AV Rao

Department of Neurosurgery, St. John's Medical College Hospital, Bangalore

ABSTRACT

Ewing's sarcoma is a rare cause of spinal compressive, myelopathy. Its presence in the craniovertebral junction is even rarer. The presence of both with reversable myelopathy after surgery makes this a truly rare and fortunate instance of prompt neurosurgical decompression coupled with judicious use of adjuvant therapy to affect the best possible results for the patient. We present our experience in this case mentioned later along with a 10-year review of literature regarding the incidence, distribution and presentation of cervical spinal Ewing's sarcoma to further demonstrate the rare nature of this remarkable case report.

***Corresponding author**

Dr Sibhi Ganapathy MBBS, MS, Mch, DNB, MNAMS, FAGE, FASI, FRCS, Assistant Professor, Department of Neurosurgery and Spine Surgery, St. John's Medical College Hospital, John Nagar, Sarjapura road, Bangalore. Tel: 091-9686617831; Email: sibhig09@gmail.com

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Introduction

Ewing's sarcomas, and indeed the whole gamut of small-round-cell malignancies, are great imitators. They are known to exist in the skull base mimicking schwannomas, chordomas, germinomas, pituitary adenomas, and even Epidermoids and occasionally extend to the vertebral bodies and the cranio-vertebral Junction (CVJ) leading to instability and neurological compression. In the CVJ they mimic vertebral tumors, discitis, infective abscesses, and even myeloma.

Predictably, such an entity is diagnosed last, and diagnosed late, leading to bad consequences for the patient. We present the case of a CVJ mass with bony destruction in a 16-year-old boy with progressive quadriparesis. A radiological diagnosis was made of Ewing's sarcoma Vs. Abscess and the patient was surgically explored. The lesion was biopsied, the cord was decompressed, and the spine was stabilized. After surgery the patient experienced a rapid recovery from the quadriparesis and was walking within a week. A histopathological analysis of the sample sent confirmed the diagnosis of Ewing's sarcoma and the patient was started on chemotherapy.

We present a 10-year review of literature to highlight the rarity of the case as well as a review on management protocols for CVJ Tumors and elaborate on the need for fusion, along with neural decompression and biopsy.

Case Report

A 16-year-old male patient presented to the emergency with pain over the nape of the neck for 3 months, progressive weakness of all 4 limbs for 5 days with urinary retention for 4 days. The patient was apparently normal until 3 months ago when he developed neck pain which was insidious in onset, gradually progressive in nature, and which worsened on bending. He also noticed progressive weakness of both upper and lower limbs for 2 weeks which started as a decrease in fine motor disturbances of the hands, but which progressed to gross spasticity and weakness of all 4 limbs. For the last 4 days, the patient complained of urgency frequency and inability to control urination coupled with constipation.

On examination the patient showed impaired lower cranial nerve function along with trigeminal nerve impairment in the form of decrease in pain and temperature sensation over the face as per the onion peel distribution. Limb power was grossly reduced with both upper limbs having just 1/5 power with distal muscles affected more (hands and wrists), and the lower limbs having 3/5 power (again with ankle and knee affected more than hip) all deep tendon reflexes were 3 with sustained ankle and patellar clonus present and positive Hoffman's sign in the upper limb. Significant spasticity of a grade 3 (modified Ashworth's grading system) was seen in all 4 limbs. Plantars were extensor bilaterally.

With spastic quadriparesis coupled with lower cranial nerve and trigeminal nerve involvement made a clinical localization to the craniovertebral junction possible. Possible bony instability was also considered in view of the neck pain on movement.

An MRI of the craniovertebral junction and cervical spine showed a large extra-osseus pre and paravertebral soft tissue mass with an epidural component involving the C2 vertebrae showing diffusion restriction, heterogenous enhancement and mass effect. This large anterior and lateral epidural soft tissue component was seen causing severe compression, enlargement and altered signal intensity of cord at the level of C2-C3. A CT scan of the CVJ showed altered marrow signal changes involving the anterior and posterior elements of C2 vertebra with evidence of significant

bony destruction, diffuse sclerosis and periosteal reaction of the C2 with surrounding inflammatory changes.

The picture was suggestive of a large abscess with secondary compressive myelopathy of the CVJ. The absence of toxicity in the patient was the only discordant note here. The child was bright and alert without fever or signs of sepsis. Inflammatory markers like procalcitonin were also not elevated as well. Yet in view of the radiology findings and the obvious compression of the cervical cord with instability owing to the eroded C2, surgery was planned.

The patient was subjected to a posterior approach of the craniovertebral junction. The intact lateral masses of the C1, C2 and C3 were fused with lateral mass screws and rods to stabilise the spine. The laminae of C1, C2 and C3 were removed to decompress the cord. Instead of pus, dark brown, gelatinous, & vascular tumor tissue was seen in the interlaminar space extending into the canal and below emanating from the body of C2. A wide decompression of the cord, and its vasculature coupled with a biopsy was done. After the surgery the patient improved dramatically. His upper limb power improved to 4/5 after 2 days and his lower limb power to 5/5 after a week of surgery. Swallowing and voice improved with therapy, and after 2 weeks of rehabilitation, he was able to walk unaided, along with performing other normal functions such as eating and speaking. Urinary control reverted to normal after 1 month.

The Histopathological analysis of the samples collected showed, sheets of highly malignant round cells with interlacing blood vessels. The neoplastic cells were positive for CD99 (3+, >90%), Synaptophysin (2+, 80-90%) and negative for CK, LCA, S100, and Desmin with a Ki67 proliferative index of 50-60%. The INI-1 was retained. Thus, the immunoprofile showing a malignant small round cell neoplasm with features consistent with Ewing's sarcoma.

Once the sutures were removed and rehabilitation was well underway, the patient was referred for chemotherapy. The patient received a combination of Vincristine, Doxorubicin, Cyclophosphamide and PEGfilgastrim. He tolerated the regimen well and entered remission after 2 weeks of therapy. He is currently on oncosurveillance, disease and symptom free.

Discussion

Malignant round cell tumors of the spine are rare and often present as space occupying lesions compressing the cord. Although the clinical presentation of the disease is similar, the radiological presence of an abscess like epidural collection is different and not commonly seen. Ewing sarcoma (ES) and peripheral primitive neuroectodermal tumor (PNET) comprise the same spectrum of neoplastic diseases known as the Ewing sarcoma family of tumors (EFT), which also includes malignant small cell tumor of the chest wall (Askin tumor) and atypical ES. Primary spinal Ewing sarcoma (ES)/peripheral primitive neuroectodermal tumors (pPNETs) are regarded as undifferentiated malignant small round cell tumors, which mostly occur in long bones, flat bones, ribs, and soft tissue. ES/pPNETs account for 6–8% of primary malignant bone tumors, and rarely affect intraspinal/vertebral deep mesenchymal/meningeal tissue [1-3].

Due to a lack of clinic symptoms and specific biomarkers at the early stages of primary spinal ES/pPNETs, most patients are not diagnosed until advanced stages, which concomitantly worsens outcomes. Furthermore, because the tumor has an aggressive clinical course—with a high tendency for both local recurrence and distant metastasis—a timely and accurate preoperative diagnosis of primary spinal ES/pPNETs could provide useful information for surgical planning [3,4]. Therefore, comprehensive studies on the clinical characteristics of primary spinal ES/pPNETs are warranted. The list of Primary Ewing's sarcoma of the cervical spine and CVJ over the last 10 years are listed in table 1. This perhaps more than anything else, explains the difficult nature of research of this particular disease, owing to such few case reports and studies in literature.

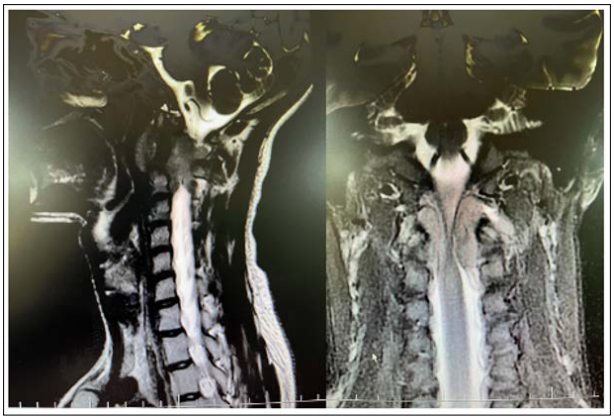

Figure 1: Which shows MRI T2 sequences of the craniovertebral junction in sagittal and coronal planes (A and B respectively) demonstrates the extreme compression of the upper cervical cord secondary to a mass lesion canal posteriorly and medially

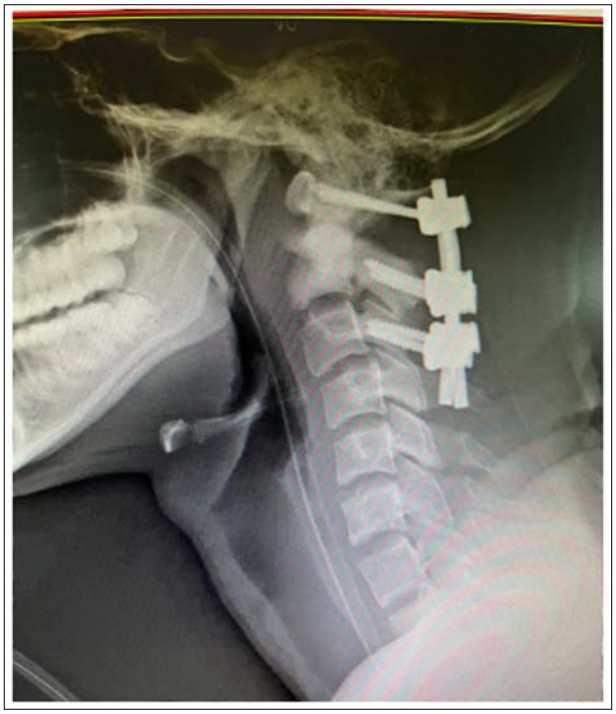

Figure 2: Shows the post op X-ray of the craniovertebral junction after C1, C2 and C3 stabilization with lateral mass screw and rod construct, C1 to C3 Laminectomy and tumor decompression with Biopsy. The implants appear to be in perfect alignment

Diagnosis: Ewings Sarcoma

Table1: table showing the publications of Ewing's Sarcoma in the cervical spine and cranio-vertebral junction over the last 10 years from 2012 to 2022

Sr.no.	Publication	Year	Age	Presenting symptoms	Signs on examination	Surgery employed	Outcome
1	Cabral GA, et al. Peripheral primitive neuroectodermal tumor of the cervical spine. Surg Neurol Int. 2012;3:91.	2012	22	Neck pain since 5 months	Paraesthesia of right arm	Biopsy, Microsurgical removal of the lesion and removal of the right posterior arch of the atlas	Improved
2	Chhabra S, et al. Primary Ewing's sarcoma of cervical vertebra: An uncommon presentation. Asian J Neurosurg 2014;9:99-101.	2014	24	Left temporo-occipital painful swelling since 1 year	B/l upper limb weakness and radiculopathy	Biopsy and partial resection	Improved
3	Gong HS, et al. Cervical Primary Ewing's Sarcoma in Intradural and Extramedullary Location and Skip Metastasis to Cauda Equina. Turk Neurosurg. 2015;25(6):943-7.	2014	39	Left upper limb pain since 1 year	Left upper limb dysesthesia	Biopsy, left hemilaminectomy of C4-6	Recurrence of lesion in cauda equina
4	Marshall T. et al. A Unique Case of Primary Ewing's Sarcoma of the Cervical Spine in a 53-Year-Old Male: A Case Report and Review of the Literature	2015	53	Neck pain since 2 months	Left upper extremity radiculopathy and weakness	C6-C7 laminotomy, decompression of the left C7 nerve root and biopsy	Improved
5	Paraskeva K, et al. Primary Ewing sarcoma of the axis-C2: A case report and the review of the literature. Neurol Neurochir Pol. 2018 Aug;52(4):534-542.	2018	3.5	Progressive neck pain	Intermittent torticollis	Biopsy	Improved
6	Shazia Rahat Chaudhry, et al. , Early recognition and diagnosis of Ewing sarcoma of the cervical spine, Radiology Case Reports, Volume 14, Issue 2, 2019, Pages 160-163,	2019	20	Neck pain since 2 months	B/L Upper limb weakness	Biopsy	Improved
7	Warade AC, et al. A Rare Case of Intradural Extramedullary Ewing's Sarcoma in the Cervical Region. Neurol India 2019;67:1543-4	2019	33	Neck pain since 1 month	Right upper limb paraesthesia	Biopsy and complete resection	Improved
8	Mahlon D. Johnson, et al. Ewing's sarcoma presenting as a cervical intradural extramedullary tumor in a 42 year old: Report of a case, Interdisciplinary Neurosurgery, Volume 20, 2020, 100634, ISSN 2214-7519,	2020	42	Neck pain since 3 months	B/L upper limb radiculopathy	Decompression with a suboccipital craniectomy and C1–C5 laminectomy.	Died

9	Ganapathy S, Subramaniam V, Baliga V. Spinal Ewing's Sarcoma Presenting as an Epidural Collection: A Rare Presentation of a Rare Entity. Asian J Neurosurg. 2020;15(2):445-448. Published 2020 May 29.	2020	33	Neck pain	Upper limb weakness	Posterior laminectomy was done from C3 to C7 decompression	Improved
10	Khatavi A, et al. Primary Ewing's sarcoma of the C2 vertebra with progressive quadriparesis: Report of a rare case and review of the literature. Surg Neurol Int. 2020 Oct 15;11:340.	2020	14	Neck pain since 3 weeks exacerbated by trauma	Left upper limb radiculopathy and spasticity in all four limbs	Biopsy, posterior decompression and occipito-cervical stabilization	Improved
11	Tiwari S, et al. Primary Spinal Epidural Extraosseous Ewing's Sarcoma with Brachial Plexus Infiltration. Asian J Neurosurg. 2020 Oct 19;15(4):1068-1071.	2020	25	Neck pain and stiffness	B/L upper and lower limb weakness	laminectomy with gross tumor resection	Improved

The case reported by Shoubash et al was a primary treatment case [2]. The patient underwent first-stage laminectomy, post-operative radiotherapy and chemotherapy, and second-stage vertebral resection. In our case, the CVJ compression was the primary manifestation. Despite a late diagnosis, the results of post-operative follow-up showed that patients benefited from this positive surgical choice.

Belkoff et al believe that local injection of bone cement can kill tumor cells in the vertebral body via local high temperature, cytotoxicity, and blood supply destruction, but in the current case vertebral injection of bone cement in the first stage failed to effectively inhibit the growth of the primary Ewing's sarcoma. In contrast, increased local pressure in the vertebral body led to passive expansion of the primary tumor and bone cement leakage at the posterior margin of the vertebral body. Such a result reminds us of the importance of choosing bone cement injection during vertebroplasty [3-6]. For patients with vertebral tumors, special attention should be taken during vertebroplasty for bone cement leakage caused by excessive bone cement injection and increased local pressure.

This case further reminds us of the importance of the differential diagnosis of Ewing's sarcoma and compression fractures. For compression fractures of the spine, we must consider the cause with thorough local soft tissue examination before surgery and pay attention to eliminate the possibility of a tumor. In this case, the tumor marker (SF) level was elevated, which is suggestive of Ewing's sarcoma. The patient had abnormal liver function, with no abnormal liver areas on total abdominal CT or hepatitis virus infection, as suggested by hepatitis screening. Statistical analysis of more cases is needed to explore the relationship between liver function abnormalities and the occurrence of Ewing's sarcoma. Histologically, the PNET cells exhibit a primitive, poorly differentiated morphology with varying degrees of pleomorphism and occasional evidence of neuroectodermal differentiation. The final diagnosis requires immunohistochemical analysis and cytogenetic studies to identify (11;22) (q24; q12) translocation. EWS / ETS fusions as the presumed initiating oncogenic event required for proliferation and tumorigenesis [7-11].

Conclusion

Despite their rapid progression, early diagnosis of spinal Ewing's sarcoma can help in deficit limitation and improved quality of life for patients. A high index of suspicion and timely and accurate radiology coupled with aggressive surgery accomplishing the triple aims of stabilisation, decompression and deduction (Biopsy) can ensure optimal results.

References

1. Cabral GA, Nunes CF, Melo JO Jr, Guimarães RD, Gonçalves MB, et al. (2012) Peripheral primitive neuroectodermal tumor of the cervical spine. Surg Neurol Int 3: 91.
2. Chhabra S, Singh S, Sethi D, Mahapatra QS (2014) Primary Ewing's sarcoma of cervical vertebra: An uncommon presentation. Asian J Neurosurg 9: 99-101.
3. Gong HS, Huang QS, Liu GJ, Chen FH, Zhao HB (2015) Cervical Primary Ewing's Sarcoma in Intradural and Extramedullary Location and Skip Metastasis to Cauda Equina. Turk Neurosurg 25: 943-947.
4. Holland MT, Flouty OE, Close LN, Reddy CG, Howard MA (2015) A Unique Case of Primary Ewing's Sarcoma of the Cervical Spine in a 53-Year-Old Male: A Case Report and Review of the Literature. Case Reports in Medicine 2015.
5. Paraskeva K, Giakoumettis D, Nikas I, Georgoulis G, Sfakianos G, et al. (2018) Primary Ewing sarcoma of the axis-C2: A case report and the review of the literature. Neurol Neurochir Pol 52: 534-542.
6. Chaudhry RS, Tsetse C, Chennan SE (2019) Early recognition and diagnosis of Ewing sarcoma of the cervical spine. Radiology Case Reports 14: 160-163.
7. Warade AC, Jha AK, Pattankar S, Madiwale C, Rekhi B, et al. (2019) A Rare Case of Intradural Extramedullary Ewing's Sarcoma in the Cervical Region. Neurol India 67: 1543-1544.
8. Johnson MD, Korones DN, Hazrati L-N, Walter K, Hussain A (2020) Ewing's sarcoma presenting as a cervical intradural extramedullary tumor in a 42 year old: Report of a case. Interdisciplinary Neurosurgery 20: 100634.
9. Ganapathy S, Subramaniam V, Baliga V (2020) Spinal Ewing's Sarcoma Presenting as an Epidural Collection: A Rare Presentation of a Rare Entity. Asian J Neurosurg 15: 445-448.

10. Khatavi A, Dhillon CS, Chhasatia N, Pophale C, Nanakkal S, et al. (2020) Primary Ewing's sarcoma of the C2 vertebra with progressive quadriparesis: Report of a rare case and review of the literature. Surg Neurol Int 11: 340.

11. Tiwari S, Yadav T, Pamnani J, Shukla K, Rao M, et al. (2020) Primary Spinal Epidural Extraosseous Ewing's Sarcoma with Brachial Plexus Infiltration. Asian J Neurosurg 15: 1068-1071.