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CASE REPORT

A cervical nerve root ewing sarcoma resembling a schwannoma

Amro F. Al-Habib[1], Khulood K. AlRaddadi[1], Hisham Alkhalidi[2]

[1]*Division of Neurosurgery, Department of Surgery, College of Medicine, King Saud University, Riyadh, Saudi Arabia*
[2]*Department of Pathology, College of Medicine, King Saud University, Riyadh, Saudi Arabia*

ABSTRACT

A 31-year-old lady treated four years prior to the recent presentation from thyroid papillary cancer with surgery and radioactive iodine. She presented with neck stiffness and left C7 radiculopathy and numbness for 6 months. Physical examination revealed left elbow extension weakness, muscle wasting, decreased sensation to pain, and absent left triceps jerk. Cervical MRI showed a 1×2 cm well-defined T2-hyperintense mass with heterogeneous enhancement suggestive of a nerve sheath tumor-like schwannoma and a mildly expanded left C6-C7 neural foramen. Surgical intervention included facetectomy and gross total removal of the tumor. Histopathology showed features of Primitive Neuroectodermal Tumor (PNET)/ Ewing's sarcoma. Accordingly, the patient was treated with chemotherapy. Post-operative MRI cervical spine did not show any residual tumor. The patient is independent at one year following her treatment and is back to work.

Key words: Ewing Sarcoma, cervical nerve root, schwannoma, PNET.

INTRODUCTION

Ewing's sarcoma (ES) is a malignant primitive neuroectodermal tumor (PNET) thought to arise from neural crest cells.[1] It is the second most common malignant bone tumor after osteosarcoma, with a peak incidence in the second decade of life.[2-4] Overall, it is rare, making up about 10% to 15% of all primary bone tumors and 6% of all malignant bone tumors.[5] Between 1973 and 2004, the incidence of ES in the United States of America (USA) was 2-93 per 1,000,000 individuals.[1] Almost 85% of those cases present primarily with skeletal ES, while the rest have extraskeletal disease in the region of the head and neck, buttocks, lower extremities, chest wall, and retroperitoneal space.[4-7] ES is reported to affect the pelvic bone and femur, but rarely the cervical spine.[1,3,8] The incidence of primary vertebral Ewing's sarcoma is 3.5%.[1,3,8]

The occurrence of primary ES in the spine is unusual. The current case presents a unique case of an extraskeletal ES arising within a cervical nerve root and resembling a schwannoma. It adds to the understanding of ES location and significance of carefully following the final pathology report of the resected lesion.

Correspondence:
Amro F. Al-Habib, MD, FRCSC, MPH
Assistant Professor and Head, Division of Neurosurgery
Department of Surgery, College of Medicine,
King Saud University—59220, Riyadh 11525, Saudi Arabia
Tel: +96 611 4672505
E-mail: amro.alhabib@gmail.com

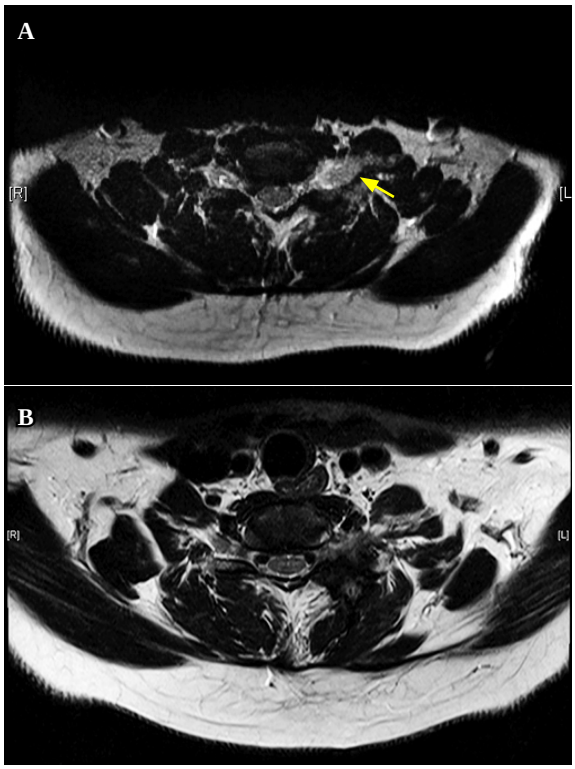

Figure 2, (A) Pre-op Contrast-enhanced T2-weighted sagittal MRI shows a 1 x 2 cm well-defined T2 hyperintense mass lesion with heterogeneous enhancement in mildly expanded left C6-C7 neural foramen. The features are suggestive of a nerve sheath tumor, mostly schwannoma. No associated bony destruction or intraspinal extension is seen. (B) Post-operative T2-weighted MRI (10 months after surgery and chemotherapy) demonstrated an interval appreciable reduction in the size of the tumor with no visible tumor.

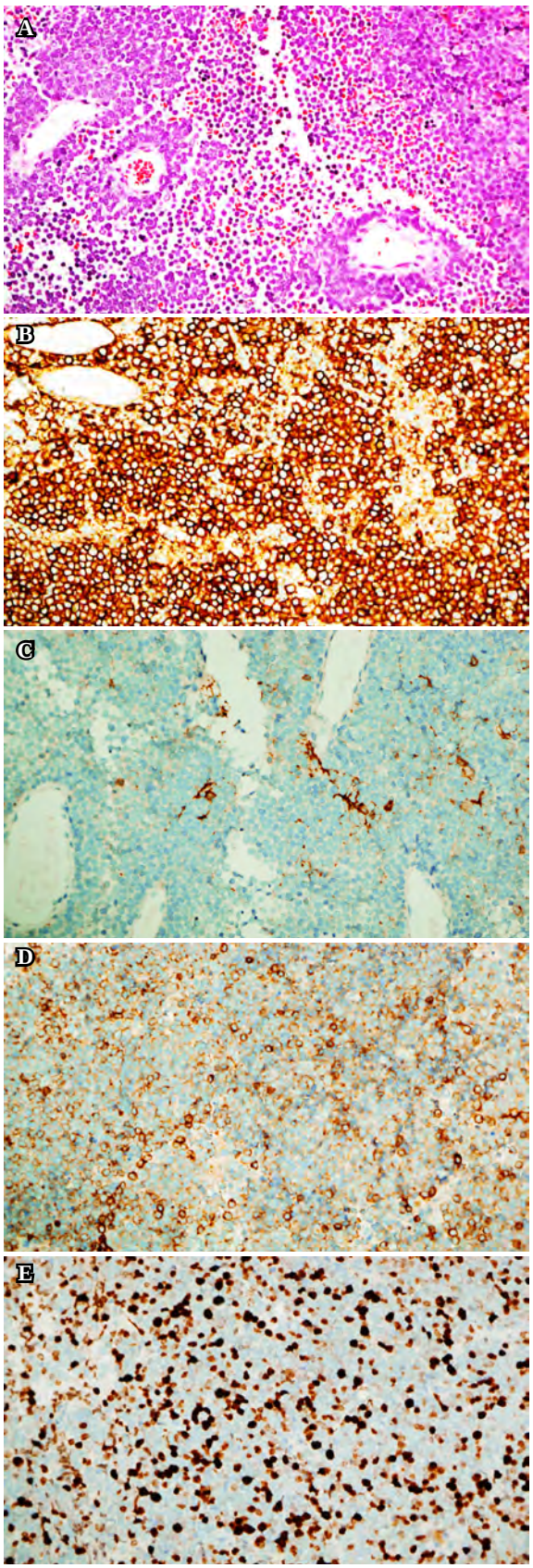

Figure 2, (a) The tumor exhibits small round/ oval cells with scanty cytoplasm, with a concentration of the tumor cells around blood vessels. (b) The tumor cells have a strong membranous reaction to CD99. (c and d) Patchy reactivity to CD 56 and synaptophysin is evident. (e) Ki-67 proliferative index is high (about 40%).

CASE REPORT

A 31-year-old Indian woman presented with progressive left upper limb C7 radiculopathy for the 6 months. The patient had total thyroidectomy 4 years prior to the current presentation followed by high dose of radioactive iodine (^{131}I) for thyroid papillary cancer. Her current pain was reaching to the left middle finger. It was electric and burning in nature and was more severe at night. She also experienced neck stiffness and left upper limb numbness. She had no other significant symptom. Physical examination revealed left upper limb muscle wasting, decreased sensation to pain, weakness of left elbow extension, and absent left triceps jerk. Cervical magnetic resonance imaging (MRI) showed a 1×2 cm well-defined T2-hyperintense mass lesion with heterogeneous enhancement in a mildly expanded left C6-C7 neural foramen. Imaging features were suggestive of a nerve sheath tumor-like schwannoma (Fig. 1A).

Operation technique and post-operative course

Under general anesthesia, the patient was positioned prone. A left paramedian incision was done directed by intra-operative fluroscopy corresponding to C6-C7 level. Sequential muscle dilators were introduced and the left C6-C7 facet joint was identified. Left C6-C7 facetectomy was performed and the nerve was identified. The nerve sheath was opened and the tumor was found to be soft, grey, and separable from the surrounding nerve roots. It was removed in piecemeal achieving a gross total tumor removal. The patient experienced an uneventful post-operative recovery with marked improvement in the radiculopathy and power. Post-operative cervical spine MRI did not show any tumor residual (Fig. 1B). Systemic imaging did not show any tumor elsewhere.

Histopathology and Immunohistochemistry

Histopathology showed an undifferentiated densely cellular tumor that consisted of small round to oval cells with scanty cytoplasm (Fig. 2). The stroma was minimal and the tumor cells exhibited predilection to cluster around the blood vessels. The tumor cells were strongly and diffusely positive for CD99 and focally for CD56, S100 and synaptophysin. They were negative for LMWCK, CD3, CD20 and CD45. Ki-67 proliferative index was high (about 40%) (Fig. 2). The overall findings were compatible with Primitive Neuroectodermal Tumor (PNET)/ Ewing's Sarcoma.

Chemotherapy-radiotherapy treatments and follow-up

The patient received adjuvant therapy including combined chemotherapy regimen of Etoposide (VP-16, a topoisomerase inhibitor) and Ifosfamide (nitrogen mustards alkylating agents) with Mesna (sodium 2-mercaptoethanesulfonate).

On follow-up at one year, the patient had no active complaints. She was independent and back to work as a health care worker.

DISCUSSION

The current case demonstrated a rare occurrence of spinal ES resembling a nerve sheath tumor. ES is a member of the Ewing's Sarcoma Family Tumors (ESFTs), which includes osseous Ewing's sarcoma, extraskeletal Ewing sarcoma (EES), Peripheral Primitive Neuroectodermal Tumors (pPNET), and Askin's tumor.[2,4,8] Most ES tumors occur in the long bones, pelvis, or ribs, but rarely may have an extraskeletal origin, hence the name extraskeletal Ewing sarcoma (EES); which has similar histology to skeletal ES and commonly affects the epidural spaces and paravertebral regions.[5,9] The differential diagnosis of small round cell tumors includes neuroblastoma, primitive neuroectodermal tumors of bone (PNET), malignant lymphoma, rhabdomyosarcoma, and ES.[3,5,6]

MRI is the method of choice for assessing the full extent of ES tumor and their relationships to neurovascular structures.[5,7,10] MRI characteristics of Primary Spinal Extradural Ewing's Sarcoma (PSEES) are not specific and indistinguishable from other tumors.[7] It is low to intermediate signal on T1, heterogeneous but prominent enhancement on T1 with contrast and heterogeneously high signal on T2 with hair on end low signal striations.11 On the other hand, radiographs usually show a lytic lesion or less commonly sclerotic changes.[3] However, these findings appear late on X-ray when neurological signs have become obvious.[3,5] Based on imaging, similar to the current case, ES tumors are often misdiagnosed as neurogenic tumors (schwannoma, neurofibromatosis) or giant cell tumors.[1] ES/PNET may be considered when a focal circumscribed spinal lesion is found in a young individual.[4] Rarely, ES may appear as a spinal dumbbell tumor with an incidence 17.5% of ES in the spine present as dumbbell shape tumors.[1]

The relation of the current tumor to the patient's previous radioactive treatment is uncertain. Radioactive iodine (^{131}I) has been used to diagnose and to treat hyperthyroidism and thyroid carcinoma patients.[12] However, ionizing radiation is itself a known carcinogen and there is a risk of developing sarcomas in the irradiated bone or soft tissues.[1,3] The risk to develop secondary primary malignancies (SPMs) linked to radioiodine (^{131}I) was not increased in adult patients in which radioiodine (^{131}I) was used for hyperthyroidism due to the relatively low dose of radiation.[13] However, in case of treating thyroid cancer, it carries a significant radiation exposure with a potential risk of radiation-induced sarcoma (RIS) because of a cumulative radioiodine (^{131}I) dose ≥ 37.0 GBq.[12,13] The risk of RIS was about 0.06% at an averaged latency of 15 years (3-64 years) after radiation therapy and influenced by factors such as dose, age at initial exposure, exposure to chemotherapeutic agents, the environment and genetic susceptibility.[14,15] The most common histologic types of RIS were osteosarcoma, chondrosarcoma, malignant fibrous histiocytoma/sarcoma nitric oxide synthase, and fibrosarcoma.[13] To differentiate RIS from the sporadic type, the sarcoma should arise within the irradiated field; which is the situation in the current case, histologically distinct from the index lesion and there must be a latency of several years after the exposure.[15]

The clinical presentation of spinal ESS includes compression of the spinal cord, nerve roots or cauda equina syndrome.[4] The patient could present with axial spine pain with or without radicular pain, limb paresis, or sphincter dysfunction.[4,5] Some patients may experience systemic manifestations like fever, anemia, leukocytosis, and increased erythrocyte sedimentation rate at admission.[5] The age of presentation ranges from 12 to 24 years (median 21 years) with a distinct predilection for males.[1,3,4]

The diagnosis of ES relies on histopathology and immunohistochemistry.3,4 The p30/32MIC-2 gene product, CD99, is a cell-surface glycoprotein expressed in Ewing's sarcomas and primitive neuroectodermal tumors.[3,5,6,8] Strong membrane staining for CD99 is consistently seen in Ewing's sarcoma with monoclonal antibodies 12E7, HBA-71, and O13.[5] Cytogenetic and molecular genetic studies can also be useful adjunctive tools in diagnosing Ewing's sarcoma.[5] The t(11; 22) (q24; q12) chromosomal translocation can be identified in most Ewing's sarcomas and primitive neuroectodermal tumors.[3,5,6] In our case, the diagnosis of Ewing's Sarcoma was confirmed by histopathology and immunohistochemistry.

Ewing sarcoma is an aggressive tumor, which has a high incidence of recurrence and metastasis.[8,9] Delay in diagnosis and treatment may lead to early metastasis, which remains the most important prognostic factor affecting outcome along with extraskeletal involvement at presentation.[4,5,9] About 25% of ES patients will present with metastatic disease and the most common sites for metastases are the lung (50%), bone (25%) and bone marrow (20%).[4]

The definitive treatment of ES consists of wide surgical resection within safe limits, followed by chemo-radiation and local irradiation, which may lead to 40 % improvement in the prognosis.[3,4,7,8,9] Ideally, the treatment should begin with 2-3 cycles of neoadjuvant chemotherapy; aiming to shrink the tumor and achieve marginal resection.[1,5,13] ES tumors have variable sensitivity to radiation and chemotherapy due to biological heterogeneity.[3] The classical chemotherapy regimen followed in ES consists of VACA (vincristine sulfate, dactinomycin, cyclophosphamide, and doxorubicinhydrochloride).[13] Recently, insulin-like growth factor 1 receptor (IGF1R) targeted therapies have resulted in responses in a small number of patients with advanced metastatic Ewing's sarcoma.[1]

CONCLUSION

This case adds to the understanding of ES location and significance of carefully following the final pathology report of the resected lesion.

CONFILICT OF INTERESTS

None.

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