CASE REPORT

Malignant Neck Mass in Disguise - Atypical Presentation of Extraskeletal Ewing's Sarcoma

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ABSTRACT

Ewing's sarcoma is the second most malignant bone tumour and commonly occurs in paediatric patients. Extraskeletal Ewing's sarcoma can arise from the head and neck as the primary site of origin of the tumour despite being rare. This soft tissue tumour morphologically mimics Ewing's sarcoma of bone. We report a case of extraskeletal Ewing's sarcoma of the neck region in a 53-year-old lady who presented to the emergency department with a rapidly growing mass over three weeks associated with pain over the posterolateral neck region. It is challenging to reach the diagnosis at the first encounter as this lesion is found at an uncommon location and presented with a sebaceous cyst-like physical appearance.
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INTRODUCTION

Dr James Ewing introduced Ewing sarcoma (ES) of bone in 1921. It is the second most malignant bone tumour and commonly occurs in children (1). Extraskeletal Ewing's sarcoma (EES) is an uncommon solitary solid soft tissue neoplasm involving the pelvis, upper limb, pelvis, abdominal organs, and mediastinum (1). 20-30% of Ewing sarcoma cases occurred extraskeletal, ranging from population age less than five years old and more than 35 years old. (1) Despite being rare, they are usually treated with the same general protocol as sarcoma tumours.

Magnetic resonance imaging (MRI) and fluorodeoxyglucose positron emission tomography (FDG-PET) scan are used to diagnose Ewing's sarcoma and detect evidence of metastasis, respectively. Generally, surgery, chemotherapy and radiotherapy are the available treatment options for treating this neoplasm (1). We are reporting a case of extraskeletal Ewing Sarcoma as a neck mass in the right posterolateral cervical region.

CASE REPORT

A 53-year-old woman with hypertension was referred to our Surgical department complaining of a posterior neck swelling for nine months. The swelling was pea-sized and static in size for the first seven months. It was not associated with pain, discomfort, or any neurological deficits. However, the swelling flared, increased in size in 3 weeks and became painful. Otherwise, she denied a history of trauma. She had no constitutional symptoms, no family history of malignancy, and no previous intraoral infection, surgery, or tuberculosis contact. On examination, she was generally well-nourished with a neck swelling on the right posterolateral aspect measured 7x7cm (Figure 1). It was irregular, firm in consistency, mobile, and tethered to overlying skin with no attachment to the muscle beneath. The central aspect of the swelling was erythematous, warm, and mild tender with no discharge or punctum. There was no other abnormality in the head and neck region, abnormal bony prominence, and no evidence of lung, liver, or distant metastasis. Blood investigations were normal. Ultrasound neck revealed a heterogeneous hypoechoic lesion within the subcutaneous layer with minimal intralesional vascularity (Figure 2). Our initial impression was right posterolateral neck infected sebaceous cyst, and we started her on antibiotics and analgesics. However, due to non-resolving swelling

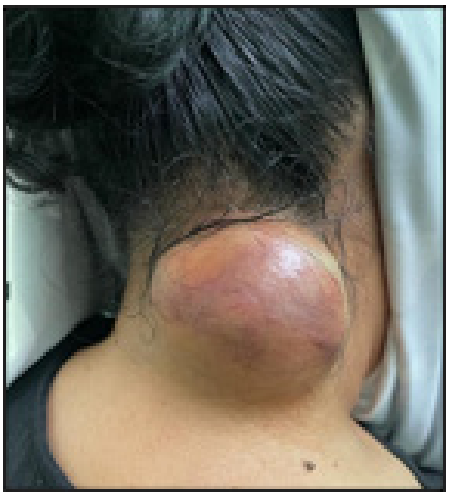

Figure 1: Patient's neck examination showing a 7 x 7 cm mass in the right posterolateral neck

and pain, she presented back to us for further treatment. She underwent an excision biopsy, and intraoperative findings were infected lymph nodes 6x5cm at the neck's nape with minimal pus with friable necrotic lymph node tissue. The excised mass was sent for histopathological examination.

The specimen consisted of a round mass with a multilobulated surface measuring 60x45x45mm. It was encapsulated with capsule thickness measuring 2-3mm. The outer surface appeared irregular, soft to firm in consistency. Serial cut sections showed solid, heterogeneous areas of mainly haemorrhagic tissue with tan-whitish tissue (Figure 3). Focal areas of necrosis were also seen.

Microscopically, sections of the mass showed a malignant tumour, which was arranged in a lobulated pattern composed of large nests and sheets of monotonous cells separated by fibro collagenous septa (Figure 4A). Necrosis and haemorrhage were frequently seen with perivascular preservation of tumour cells around the vessels. These cells were round, small to

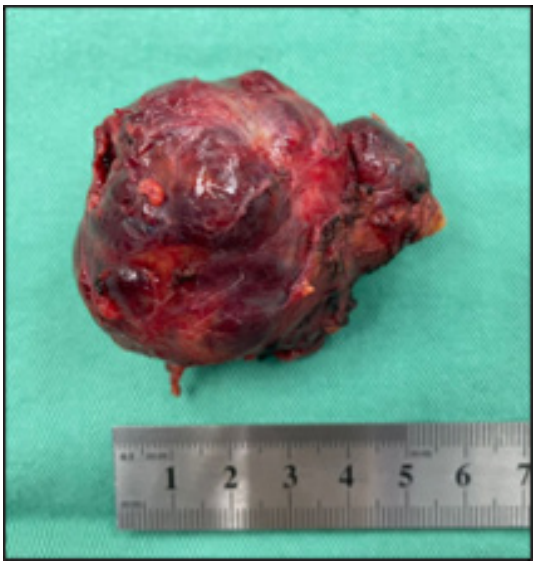

Figure 3: The lesion is composed of a round mass with multi-lobulated outer surface

medium in size, displaying finely stippled chromatin, inconspicuous nucleoli, and eosinophilic to clear cytoplasm. Intracytoplasmic glycogen was highlighted as positive for PAS and negative for PASD stain. Some of these cells had large vesicular nuclei with prominent nucleoli in specific foci and brisk mitosis with atypical type. The surrounding fibro collagenous septa were thickened with some lympho-plasma cell infiltration. These malignant cells were positive for CK AE1/AE3 (focal), Vimentin, BCL2, and FLI1 stain. Negative for CD45, desmin, SMA, S100 and CD34. Overall morphological and immunohistochemical features were compatible with Ewing's sarcoma.

The patient was subsequently referred to the orthopaedic and oncology team for further management. Contrast-enhanced Computed Tomography Thorax and Magnetic Resonance Imaging of the neck were conducted, showing neither evidence of local recurrence nor distant metastasis.

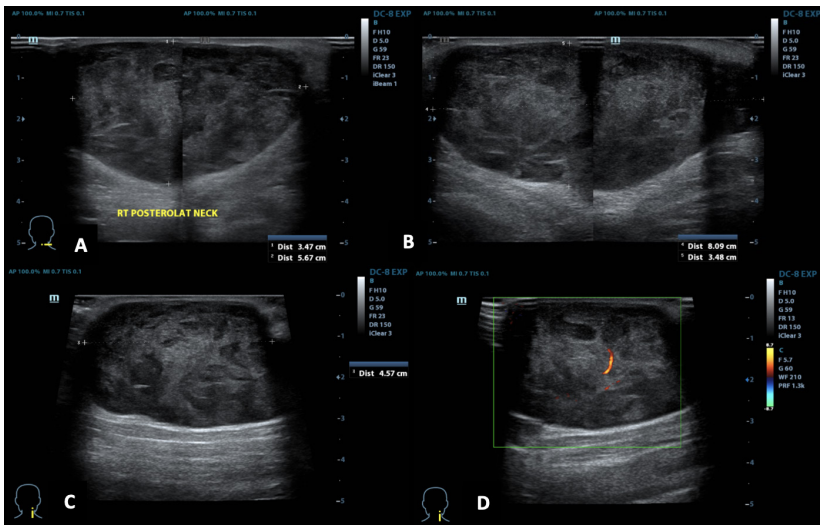

Figure 2: A-D: Ultrasound neck revealed a well-defined heterogeneous hypoechoic lesion seen within the subcutaneous layer of right posterolateral aspect of neck, measuring 3.5x8x4.6cm with minimal moving debris seen within. Minimal intralesional vascularity seen on Doppler, no calcification or intramuscular extension of the lesion. Presence of subcentimetre cervical lymph nodes with preserved fatty hilum, largest measuring 0.4cm in short axis

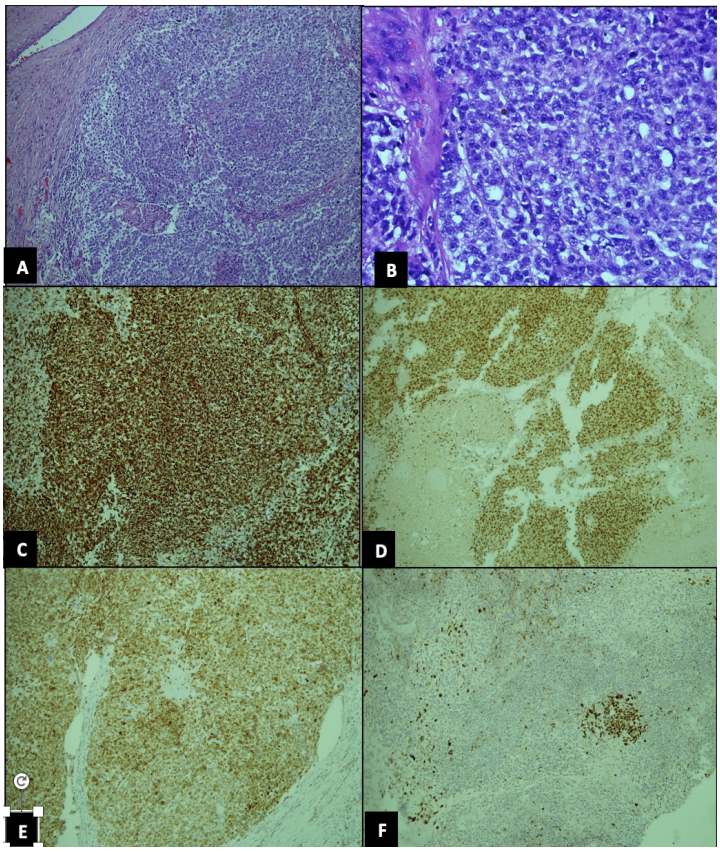

Figure 3: The lesion is composed of a round mass with multilobulated outer surface

DISCUSSION

Extraskeletal Ewing's sarcoma (EES) is an uncommon malignant soft tissue tumour. According to the E99 trial, of all the EES patients, only 3% presented with primary tumours arising from the head and neck region. This shows that the head and neck region is an unusual origin site for EES. Furthermore, its prevalence showed a bimodal pattern which peaked in those less than 5-year-old and more than 35-year-old (1). The peak incidence favours male preponderance with a male to female ratio (1.2:1), similar to the ratio of EWS presenting at any other anatomical site (2). Whilst, in our case study, this patient is a 53 years old lady, which is not within the expected range of age and gender predominance for EES.

EES mainly presented with a painful fast-growing mass over the trunk and extremities. However, in our case, the patient initially presented with a painless mass over the right posterolateral neck, which is static in size for seven months, misleading the clinicians toward a more benign pathology such as an infected sebaceous cyst. The ultrasonography assessment further supported the diagnosis, which showed a well-defined heterogeneous hypoechoic lesion within the subcutaneous layer. Thus, the initial treatment focused on debridement and drainage while achieving local infection control with antibiotics. Nevertheless, a typical ultrasonographic EES exhibits heterogenicity with intratumor flow signals in a Doppler study (1). Retrospectively, further evaluation of the preoperative ultrasonography imaging revealed minimal intralesional vascularity and concordance with features of EES.

Studies revealed that 75% of the patients with primary EES typically presented with initially rapid enlargement of painless mass, which subsequently becomes painful as it grows (3). This is in tandem with our patient, whom she presented twice as the pain worsened. Hence, emergent surgical intervention was planned to alleviate the pain and remove the offending lesion, directly rendering the patient into her premorbid state.

Intraoperatively, the lesion did not resemble a sebaceous cyst. The mass was irregular, solid, friable, and not encapsulated. In accordance with the oncological principle, the marginal excision of normal tissue was preemptively done while avoiding breaching the lesion. Therefore, the specimen was ample for histopathological assessment. At this point, a clinical diagnosis of infected lymph nodes was made, and it had not occurred to us that this lesion could be EES.

Histologically, EES tumour cells usually appear as small blue round cells with scanty cytoplasm, thus making it difficult to distinguish from other small round cell tumours. Nevertheless, it is also histologically indistinguishable from the Ewing Sarcoma of the bone (3). Few initial differential diagnoses can be made based on its morphology, such as neuroblastoma, rhabdomyosarcoma, lymphoblastic lymphoma, desmoplastic small round cell tumour, and round-

cell liposarcoma. As in our case, it was demonstrated as a typical histomorphology of round cell tumours with diffuse positivity for vimentin, BCL2, FL1 and focal positivity for CKAE1/AE3 stain. After several considerations and outweighing all the clinical, radiological and morphology findings, our case is concluded as Ewing's sarcoma (ES). CD99 stain was not done due to unavailability.

For the past 30 years, the standard immunohistochemical marker for Ewing's sarcoma is glycoprotein surface antigen p30/32 (MIC2) CD99, which exhibits high sensitivity but low specificity toward Ewing's sarcoma (3). In current practice, CD99 is still an important diagnostic marker for diagnosing ES. However, FLI1 is also expressed in ES as it reflects the underlying gene fusion (EWSR1-FLI1), which shows diffuse nuclear positivity, as seen in our case. Hence, fluorescence in situ hybridization (FISH) for the detection of EWSR1 was suggested. FLI1 expression has been demonstrated to be relatively sensitive and highly specific for ES. (4) Though its expression is not restricted to ES, we have excluded some of the tumours that can express FLI1 with similar round cell morphology, such as lymphoblastic lymphoma (5). In our case, CD45 is negative hence making lymphoblastic lymphoma exclusive. Nevertheless, molecular diagnosis is desirable in making a diagnosis. Lately, a few other proposed auxiliary diagnostic tests, such as BCL11B and GLG1 stain, when molecular testing is not feasible (5).

EES is typically a type of tumour which is sensitive to multimodality treatment. The early detection and adequate excision margins of the mass, followed by chemotherapy and radiotherapy, might significantly help the survival rates (3). The overall survival rate for patients with EES in the head and neck region was about 70% for localized disease and 30% for those with metastasis disease (3). From the study of management and outcome of EWS of head and neck by Grevener et al., 3-year event-free survival was 74%, while the overall survival rate was 87% in those with localized disease (2). Patients presented with metastasis at the beginning of the diagnosis carried significantly worse outcomes (2). Poor prognostic factors of EES are elderly, involvement in the pelvis, lymphocytosis, high LDH, anaemia and metastatic disease at the time of diagnosis (1). Fortunately, our patient's blood investigations are all normal, with unsuggestive symptoms of metastasis of the disease.

For the treatment of EES, only a few studies reported the optimal options and prognostic factors for EES. The latest treatment recommendations suggested by the National Comprehensive Cancer Network (NCCN) advocated that local treatment, namely surgery with or without radiotherapy and chemotherapy, is the treatment of choice. From the NCCN and European Society for Medical Oncology, all members of the Ewing family can be treated with a similar algorithm. The overall survival rate for five years in a patient with complete surgical resection is better than those tumours with inadequate excision margin or unresectable. In that case, radiotherapy can be offered (1). For our patient, since the surgical resection margin was adequate and there was no evidence of distant metastasis, she was planned for close surveillance under orthopaedic and offered chemotherapy by the oncology team. Radiotherapy was not required as the wide tumour margin was satisfactorily resected.

CONCLUSION

In evaluating and diagnosing the posterior neck swelling, we should always consider the EES of the head and neck for the possible differential diagnosis. Detailed history taking is crucial as the nature of the tumour will show its malignant characteristic. Despite being uncommon and clinically challenging to diagnose, we still can offer the best treatment and care for the disease. Complete oncological excision of the lesion remains the most important treatment strategy for EES besides incorporating other modalities. Subsequent investigations for metastatic surveillance must be done to detect early recurrence of the disease, aiming toward complete surgical re-excision.

REFERENCES

1. Abboud A, Masrouha K, Saliba M, Haidar R, Saab R, Khoury N, et al. Extraskeletal Ewing sarcoma: Diagnosis, management and prognosis. Oncology letters. 2021;21(5):1-6. doi: 10.3892/ol.2021.12615
2. Grevener K, Haveman LM, Ranft A, van den Berg H, Jung S, Ladenstein R, et al. Management and outcome of Ewing sarcoma of the head and neck. Pediatric blood & cancer. 2016;63(4):604-10. doi: 10.1002/pbc.25830
3. Erdogan BA, Sekercan O, Bora F, Altin G, Paksoy M, Koca SB. A Rare Neck Mass: Extraskeletal Ewing's Sarcoma. International Journal of Head and Neck Surgery, 2012;3(3):165-167. doi: 10.5005/jp-journals-10001-1120
4. Folpe AL, Hill CE, Parham DM, O'Shea PA, Weiss SW. Immunohistochemical detection of FLI-1 protein expression: a study of 132 round cell tumors with emphasis on CD99-positive mimics of Ewing's sarcoma/primitive neuroectodermal tumor. The American journal of surgical pathology. 2000;24(12):1657-62. doi: 10.1097/00000478-200012000-00010.
5. Orth MF, Hıılting TL, Dallmayer M, Wehweck FS, Paul T, Musa J, et al. High specificity of BCL11B and GLG1 for EWSR1-FLI1 and EWSR1-ERG positive Ewing sarcoma. Cancers. 2020;12(3):644. doi: 10.3390/cancers12030644