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Case Report

A Deceptive Dermal Blue-Ball at the Cervico-Occipital Region: A Superficial Ewing Sarcoma Mimicking Spiradenoma

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Abstract

Superficial Ewing sarcoma of the skin and dermis is extremely rare and may closely simulate benign adnexal tumors or neuroendocrine carcinomas, leading to major diagnostic pitfalls. We report the case of a 19-year-old woman presenting with a painful, rapidly enlarging 1.5 cm nodule at the cervico-occipital region. Histologically, the lesion exhibited a compact multilobulated architecture within the dermis, with a striking "blue ball in dermis" appearance suggestive of spiradenoma. Immunohistochemistry was misleading, showing focal dot-like AE1/AE3 staining, heterogeneous low-to-moderate synaptophysin and chromogranin expression, CD56 positivity, and CK20 dot-like staining, raising the possibility of Merkel cell carcinoma. Strong diffuse CD99 positivity and nuclear NKX2.2 expression supported a Ewing sarcoma family tumor. Molecular analysis confirmed an EWSR1 rearrangement. This case highlights the diagnostic challenges of superficial small round blue cell tumors and emphasizes the need for integrated histologic, immunohistochemical, and molecular assessment.

Keywords: Chromosomal Translocation, EWSR1 Gene, FLI1 Gene, Chimeric Oncoprotein, GGAA Microsatellites.

INTRODUCTION

Ewing sarcoma is a highly aggressive small round blue cell tumor typically arising in bone or deep soft tissue of children and young adults. Primary superficial forms confined to the skin or dermis are exceptional. Their unusual location, combined with compact architecture and lobulated patterns, can closely mimic benign adnexal neoplasms such as spiradenoma, as well as neuroendocrine tumors including Merkel cell carcinoma. Misdiagnosis may result in major therapeutic consequences. In this report, we present a rare superficial Ewing sarcoma occurring in the cervico-occipital region of a young woman, illustrating multiple diagnostic traps related to both morphology and immunohistochemistry.

CASE REPORT

Clinical Presentation

A 19-year-old woman presented with a solitary painful nodule of the posterior neck, located at the cervico-occipital region. The lesion appeared two months earlier and enlarged progressively to approximately 1.5 cm. It was firm, mobile, non-ulcerated, and clinically suspected to be a benign adnexal lesion. The mass was excised completely.

PATHOLOGIC FINDINGS

Histology

Low-power examination revealed a well-circumscribed nodular proliferation entirely confined to the dermis, without extension into the subcutis (Figure 1). At medium magnification, the tumor exhibited a multilobulated architecture with a compact cellular arrangement, producing the classic "blue ball in dermis" aspect (Figure 2), highly suggestive of spiradenoma. High-power examination (Figure 3) showed sheets of small round cells with scant cytoplasm, hyperchromatic nuclei, and focal areas demonstrating a biphasic pattern with clearer cells interspersed with slightly eosinophilic cells, reinforcing the spiradenoma-like impression.

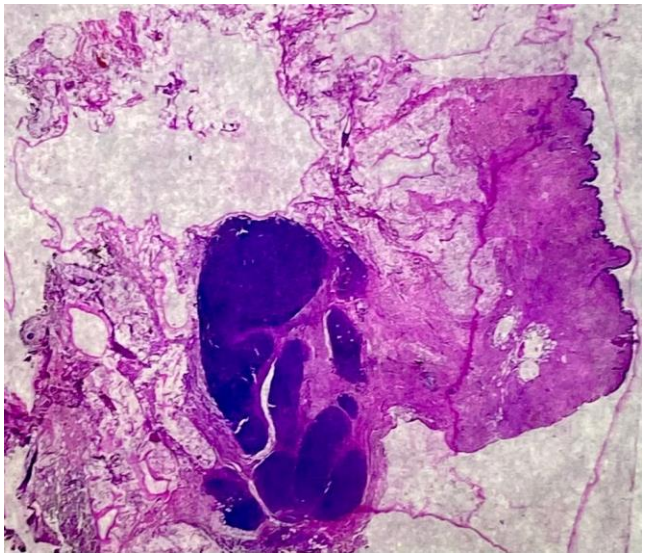

Figure 1: Low-magnification scanned HE image showing a well-circumscribed dermal nodule

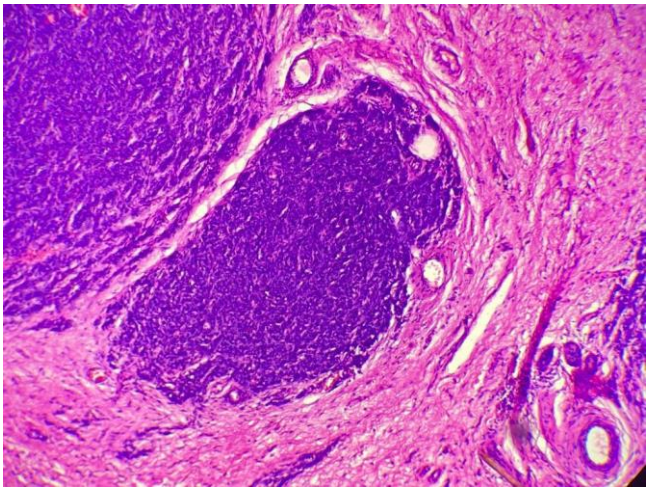

Figure 2: HE ×25 showing the multilobulated architecture and the characteristic "blue ball in dermis" appearance

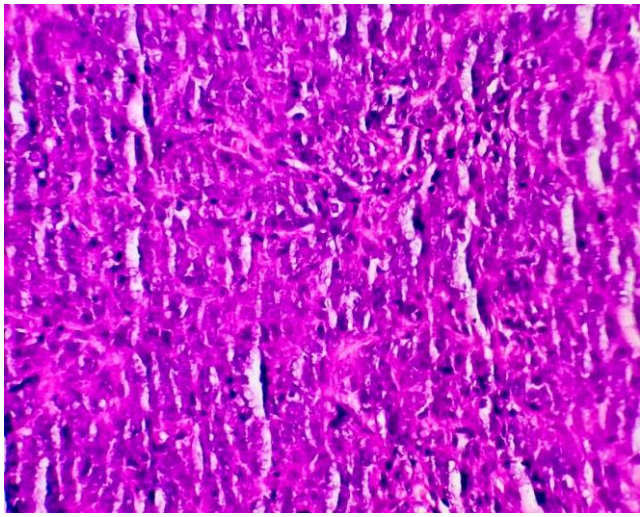

Figure 3: HE ×40 highlighting a focal double population with clearer and eosinophilic cells

Immunohistochemistry

Immunostaining demonstrated:

- CD99: strong, diffuse membranous expression (Figure 4).
- Synaptophysin: heterogeneous, weak-to-moderate positivity (Figure 5).
- Chromogranin: heterogeneous weak positivity (Figure 6).

- Pancytokeratin AE1/AE3: dot-like focal staining (Figure 7).
- CD56: positive.
- NKX2.2: strong, diffuse nuclear positivity (Figures 8–9).
- CK20: dot-like staining in scattered cells (Figure 10).
- TTF1: negative.

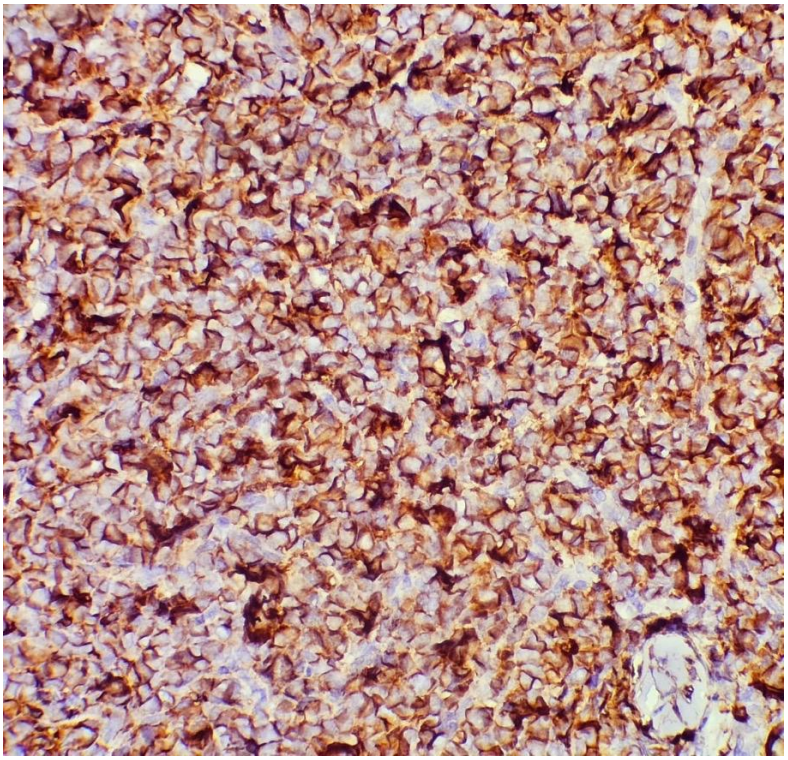

Figure 4: CD99 immunostaining with strong, diffuse membranous expression

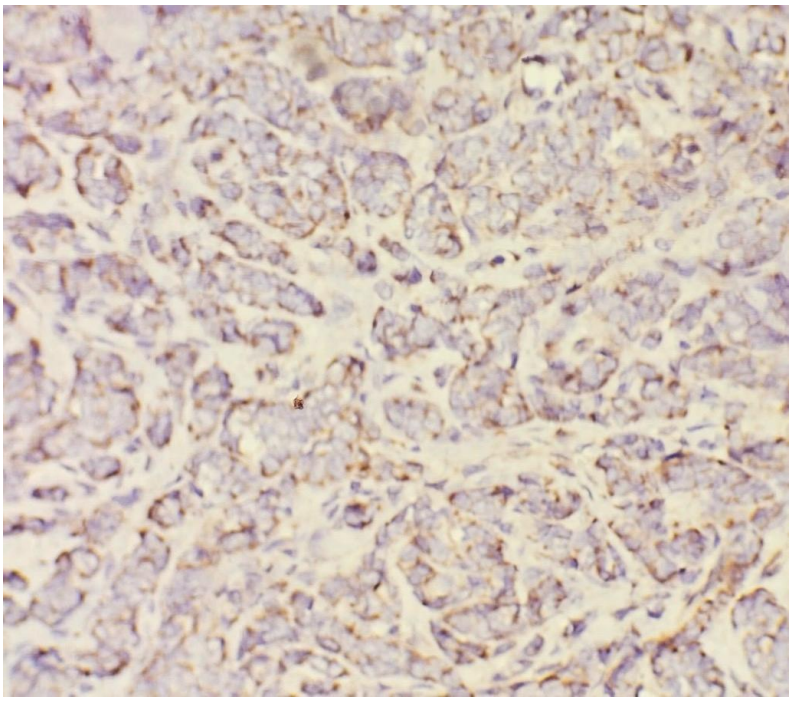

Figure 5: Synaptophysin immunostaining showing heterogeneous weak-to-moderate positivity

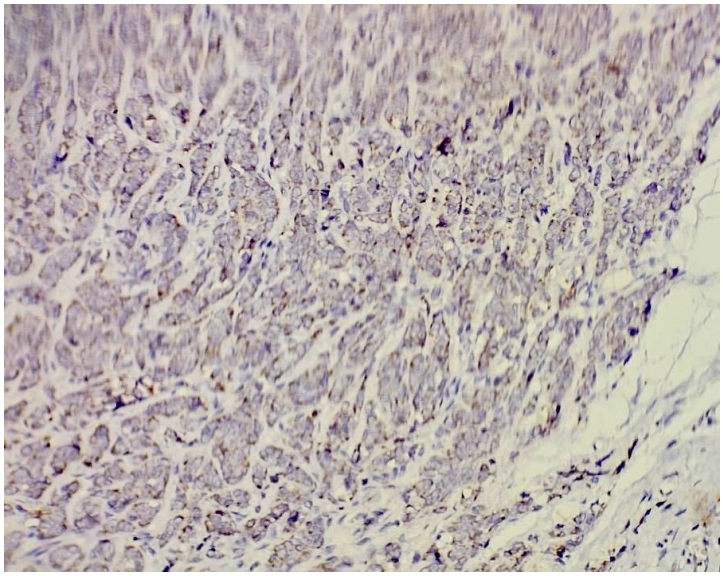

Figure 6: Chromogranin immunostaining showing heterogeneous weak positivity

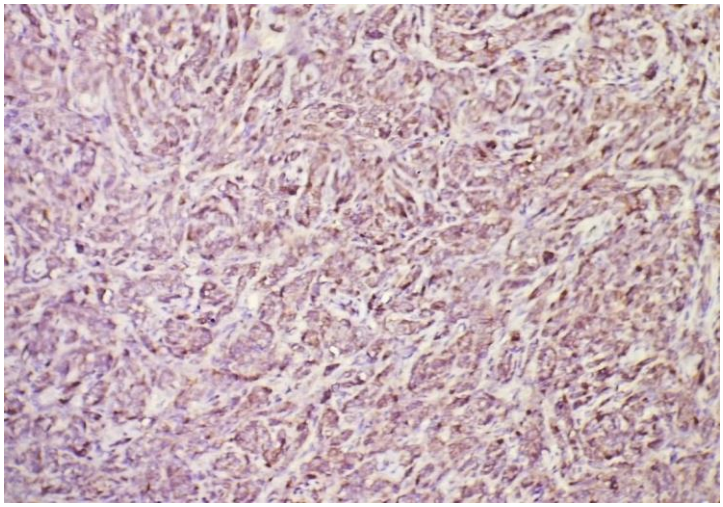

Figure 7: Pancytokeratin AE1/AE3 immunostaining showing focal dot-like positivity

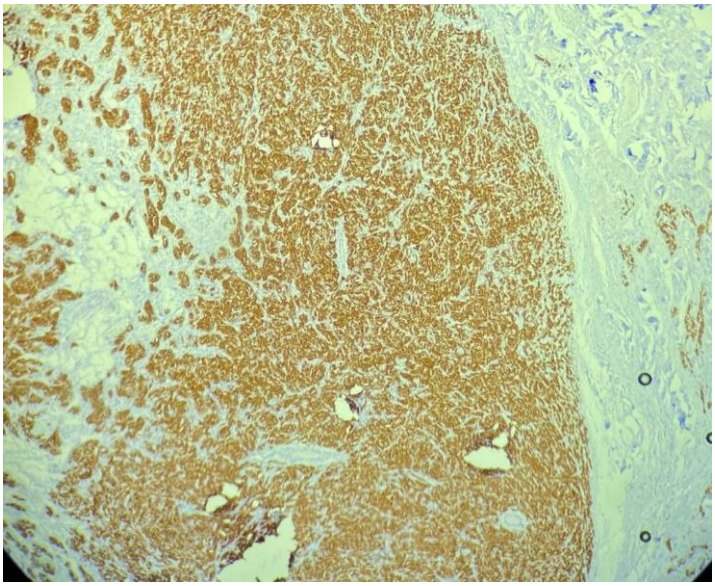

Figure 8: NKX2.2 immunostain showing strong diffuse nuclear expression

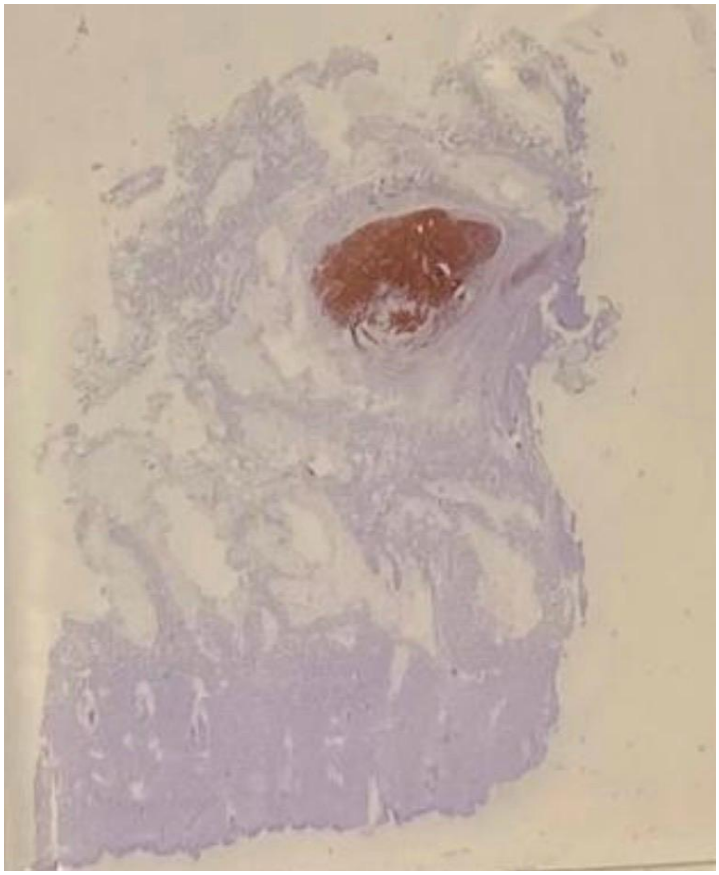

Figure 9: Additional scanned NKX2.2 panel confirming diffuse nuclear staining

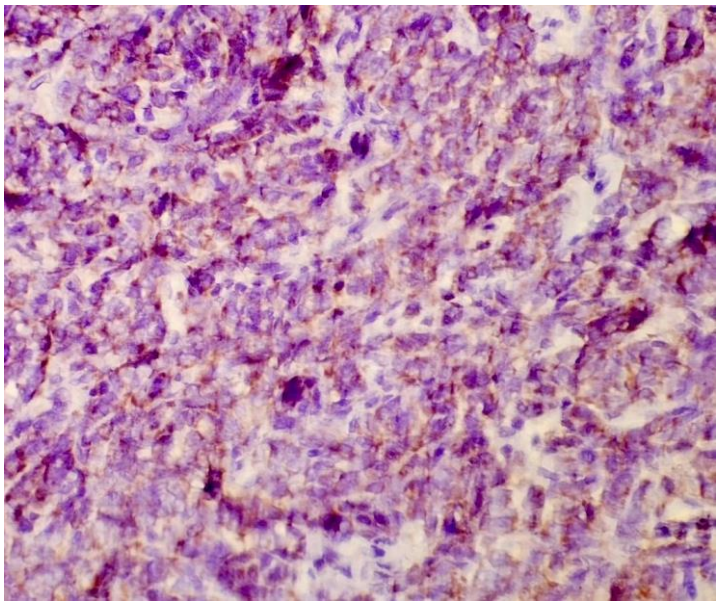

Figure 10: CK20 immunostaining showing dot-like staining in scattered tumor cells

The CK20 dot-like pattern and neuroendocrine marker expression initially suggested Merkel cell carcinoma, while the focal cytokeratin expression supported an adnexal tumor. However, the strong diffuse CD99 and NKX2.2 staining favored a tumor of the Ewing sarcoma family.

Molecular Testing

Molecular analysis confirmed the presence of an EWSR1 gene rearrangement, establishing the final diagnosis of superficial Ewing sarcoma.

DISCUSSION

Superficial Ewing sarcomas confined to the skin or dermis are exceedingly uncommon and may

create substantial diagnostic confusion. In this case, the tumor's location within the dermis and its multilobulated, sharply circumscribed appearance led to the classic "blue ball in dermis" pattern, a feature most commonly associated with spiradenoma. The biphasic appearance with clear and eosinophilic cells further contributed to the adnexal mimicry. Immunohistochemistry added to the complexity: focal dot-like AE1/AE3 and CK20 staining together with heterogeneous neuroendocrine marker expression could easily support a diagnosis of Merkel cell carcinoma. This pitfall is well recognized, as superficial Ewing sarcomas may display limited cytokeratin or neuroendocrine staining. However, Merkel cell carcinoma typically shows strong diffuse CK20 dot-like positivity and lacks expression of NKX2.2. The strong membranous expression of CD99 and diffuse nuclear NKX2.2 were critical clues indicating a tumor of the Ewing family. Because the morphology and immunophenotype may be misleading, molecular confirmation of an EWSR1 rearrangement remains the diagnostic gold standard. Awareness of this entity is essential to prevent misclassification, as a mistaken diagnosis of spiradenoma could lead to undertreatment, whereas diagnosing Merkel cell carcinoma could result in overtreatment and inappropriate management pathways.

CONCLUSION

This case highlights the deceptive presentation of superficial Ewing sarcoma, which may closely mimic spiradenoma or neuroendocrine carcinoma on both histology and immunohistochemistry. Pathologists should consider Ewing sarcoma in the differential diagnosis of dermal small round blue cell tumors, especially in young patients. CD99 and NKX2.2 are key markers, but molecular confirmation remains essential for establishing the correct diagnosis and guiding appropriate therapy.

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