Case Report

Proximal-Type Epithelioid Sarcoma with Unusual Morphology: A Diagnostic Challenge with Detailed Immunohistochemical Workup

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Abstract

Background:An uncommon and aggressive soft tissue sarcoma, Epithelioid sarcoma (ES) has a significant risk of recurrence and metastasis. The proximal variant overlaps with other epithelioid malignancies, it can be diagnostically challenging particularly in young patients. Case Presentation:We report a single-patient case of a 14-year-old male with a painful deep-seated calf mass. Trucut biopsy showed deceptively bland epithelioid–rhabdoid cells with lymphocytic admixture. After Immunohistochemistry (IHC), lesion was reported as a polygonal cell neoplasm on biopsy. Wide local excision was performed, morphology showed myxoid matrix making it more difficult to diagnose and extended IHC demonstrated PanCK and EMA positivity with complete loss of INI1, while S100, GFAP, CD34, Desmin, SALL4, and CD138 were negative, confirming proximal-type epithelioid sarcoma. Conclusion:This case emphasizes that proximal-type epithelioid sarcoma may present with deceptively bland histology and unusual myxoid stromal changes. Definitive diagnosis requires extended immunohistochemical panel, particularly assessment of INI1 loss.

Keywords: Epithelioid Sarcoma; proximal type; INI1 loss; unusual morphology

Introduction

Epithelioid sarcoma (ES) is an uncommon, high-grade soft tissue sarcoma with a strong propensity for local recurrence and distant metastasis [1]. ES subdivided into proximal and classic types. Classic (distal) type ES presents usually as a subcutaneous or deep dermal mass in distal extremities of adolescents [2]. Compared to the classic form, the other, more aggressive proximal type has been seen at proximal body sites in younger individuals and is more likely to metastasize and recur early [2]. Proximal subtype tends to have epithelioid and rhabdoid morphology and lacks typical pseudogranulomatous architecture seen in classic type. For a pathologist, proximal type ES presents a diagnostic challenge in distinguishing these

tumors from malignancies with similar morphology and immunohistochemistry (IHC) overlap. Broad range of neoplasms including benign neoplasms can be mistaken for this entity on morphology alone. We report a case of this rare neoplasm with unusual morphology, detailed discussion on histomorphology, cytology, IHC based approach and possible diagnostic challenges.

Case report

A 14 years male presented with complaints of swelling on posterior aspect of left leg below knee for six months which is gradual in onset associated with pain and discomfort. At presentation, the patient had no gait disturbance or functional limitation of the affected limb. On examination reveal 10x8cms hard swelling in the left calf region. Magnetic Resonance Imaging (MRI) and Fine needle aspiration (FNA) done elsewhere showed 7.8x7.7x4.2cms multilobulated lesion located deep to fascia and involving lateral head of gastrocnemius muscle without any intrarticular extension and FNA reported as rhabdomyosarcoma elsewhere. Patient was planned for trucut biopsy and microscopy of biopsy showed polygonal cells closely admixed with many mature lymphocytes. These polygonal cells showing epithelioid, rhabdoid to plasmacytoid morphology with abundant eosinophilic cytoplasm, slightly eccentrically placed uniform nuclei with open chromatin and prominent nucleoli. There is no nuclear pleomorphism, mitosis or necrosis (Figures 1A-B). Immunohistochemistry (IHC)

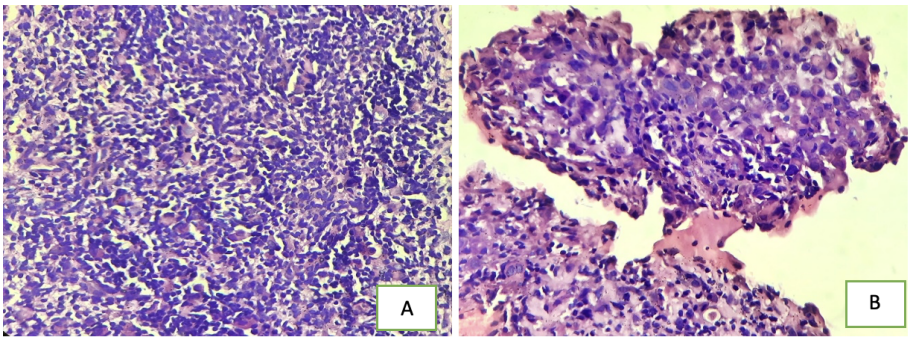

Figure 1: Images from biopsy. A) Tumor cells closely admixed with many lymphocytes (H &E, 100X), B) tumor cells are rhabdoid to plasmacytoid in morphology without any nuclear pleomorphism, mitosis (H &E, 400X).

was performed on formalin-fixed paraffin-embedded sections using ready-to-use (RTU) antibodies. Immunostaining was carried out using a polymer-based horseradish peroxidase (HRP) detection system with 3,3-diaminobenzidine (DAB) as the chromogen, on the Ventana automated platform. IHC done on biopsy showed positivity for PanCK (AE1/AE3 clone, Path n Situ, RTU, antigen retrieval 60 min), CD99 (EP 8 clone, Path n Situ, RTU, antigen retrieval 60 min) and negativity for Desmin (GM007 clone, Path n Situ, RTU, antigen retrieval 60 min), LCA (RB-2B11 clone, Path n Situ, RTU, antigen retrieval 90 min), CD34 (QB-END10 clone, Path n Situ, RTU, antigen retrieval 60 min) and CD68 (KP1 clone, Path n Situ, RTU, antigen retrieval 30 min). On biopsy, correlating morphology with IHC pattern of expression, diagnosis given as polygonal cell neoplasm and the possibilities according to IHC narrowed down to ES, Extra renal rhabdoid tumor (ERT), Myoepithelioma of soft tissue and Ewing sarcoma group of tumors.

Wide local excision was done and grossly, tumor is deep to dermis, multilobulated measuring 7x 6cms, infiltrating in nodular pattern and all margins are beyond 1cm from lesion (Figure 2A). Scrape smears from fresh specimen showed dyshesive epithelioid, plasmacytoid to rhabdoid cells with similar morphology described above admixed with lymphocytes and background showed myxoid matrix material on MGG stain (Figure 2B). Cytological features are highly suspicious for myoepithelioma of soft tissue. Microscopically showed lobulated lesion with areas of myxoid matrix and morphology of the tumor on excision confirmed the morphology seen on biopsy (Figures 2C -D). There is no nuclear pleomorphism, mitosis, necrosis or any vascular invasion after extensive grossing. In view of Pan CK and CD 99 positivity on biopsy (Figure 3A and 3B), extended IHC panel done on excision specimen included S100 (BETA-EP32 clone, Path n Situ, RTU, antigen retrieval 30 min), GFAP (G-A-5 clone, BIO SB, RTU, antigen retrieval 60 min), EMA (E 29 clone, Path n Situ, RTU, antigen retrieval 60 min), SALL4 (EP 299 clone, Path n Situ, RTU, antigen retrieval 80 min), INI1(25 clone, Path n Situ, RTU, antigen retrieval 80 min) and CD138 (EP 201, Path n Situ, RTU, antigen retrieval 60 min). EMA showed diffuse positivity (figure 3C) and loss of expression of INI1 in tumor cells (Figures 3D). Rest all IHC markers are negative. The diagnosis of proximal-type epithelioid sarcoma was considered based on morphology, diffuse epithelial marker expression (PanCK, EMA), complete loss of INI1, negative SALL4 staining and clinical presentation. Although molecular testing for SMARCB1 alteration was not available, the overall findings were most consistent with ES.

Postoperatively, the patient remains fully ambulatory without pain or functional deficit. After surgery, metastatic workup did not reveal any abnormality elsewhere and patient was kept on close follow up as the tumor was localized with wide negative margin status. The patient has been followed for 6 months after surgery and is currently asymptomatic, with no evidence of local recurrence or distant metastasis.

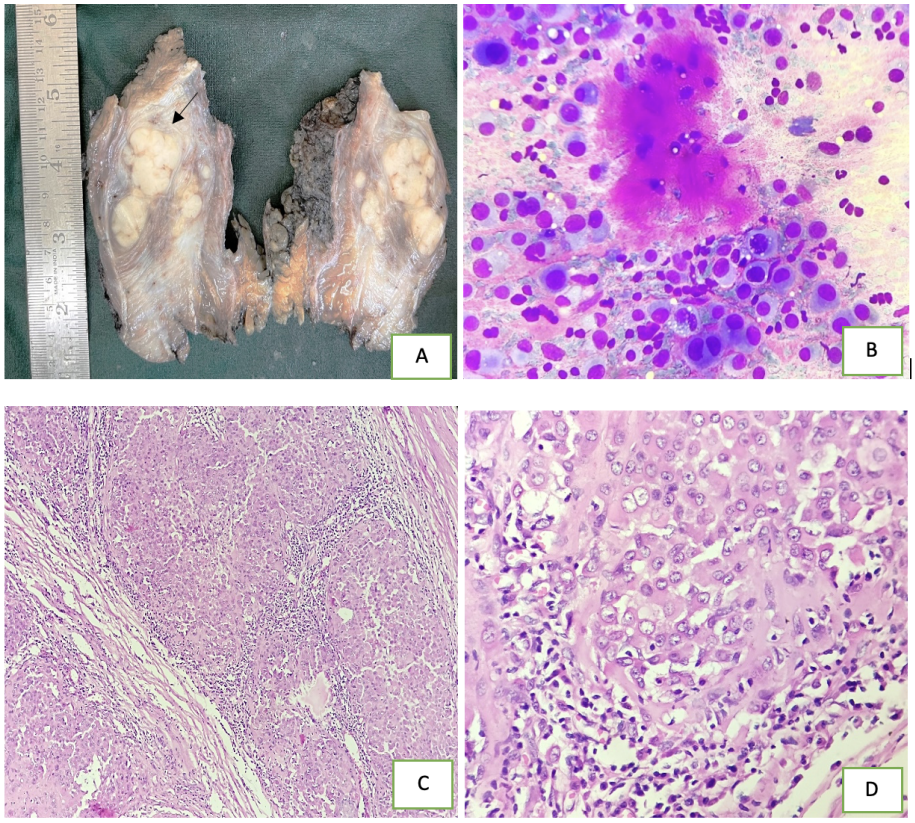

Figure 2: Images from wide local excision. A) Gross image showing infiltrating deep seated multinodular grey white tumor B) scrape cytology showing epithelioid, rhabdoid to plasmacytoid individual cells with adjacent myxoid matrix (MGG, 400X), C) excision showing multilobulated lesion (H &E, 100X), D) lobules surrounded by rim of lymphocytes and the tumor cells are rhabdoid in morphology without any nuclear pleomorphism or mitosis (H &E 400X).

Discussion

Epithelioid sarcoma (ES) is a highly invasive tumor originating from primitive mesenchymal cells with multilineage differentiation [2]. Proximal type epithelioid sarcoma is very rare and hence can be misdiagnosed frequently with entities ranging from non neoplastic, benign to malignant neoplasms with epithelioid morphology. The unusual morphological features seen in this case has scant mention in the literature. Unlike most reported cases that occur in young adults and involve proximal locations, this tumor occurred in a pediatric patient with a distal calf location. In addition, the tumor showed deceptively bland cytomorphology, prominent lymphocytic admixture, and focal myxoid stromal change, features that are infrequently described in proximal-type epithelioid sarcoma. These unusual findings contributed to significant diagnostic difficulty and broaden the histomorphological spectrum of this rare entity.

Though the usual age group for epithelioid sarcoma is childhood, proximal type occurs in young adults. The unusual morphologic features in the present case are lymphocytic infiltrate which is usually seen in classic type, presence of myxoid matrix and lack of nuclear pleomorphism, mitosis, necrosis, vascular invasion seen commonly in ES proximal type. The possibilities considered in the present case are mentioned in the literature in addition to malignant melanoma, metastatic carcinoma and clear cell sarcoma. In the present case, tumor cells are positive for Pan CK, EMA, CD99, negative for CD34, Desmin, CD68, LCA, myoepithelial markers S100, GFAP, P63, SALL4, CD138 and showed loss of INI1 expression in tumor cells. CD99 positivity was diffuse, mild to moderate membranous instead of strong, diffuse crisp membranous positivity seen in classic ewings and synovial sarcoma. Pan CK and EMA positivity favoured ES, ERT, myoepithelial tumor of soft tissue and plasmablastic lymphoma. Further myoepithelial markers S100, GFAP were negative to consider myoepithelial tumor of soft tissue and in view of CD138 negativity plasmablastic lymphoma is less likely. In the present scenario, loss of INI1 expression suggested the possibility of ES proximal type and ERT. However since SALL4 was negative [3], correlating with morphology, IHC findings and overall clinical presentation, the lesion was signed out as ES proximal type.

Similarities in morphology and IHC between ERT and proximal-type ES present a diagnostic conundrum for the pathologist. Though both of the tumors exhibit loss of expression of SMARCB1 (INI1), molecular events that occur in these two entities are different, with deletions occurring in the proximal type of ES and point mutations being more prevalent in ERT [4, 5]. The distinction between these two entities is important because of the prognostic difference as ERT behaves worse than ES proximal type [4].

For ES, early radical surgery is the preferred course of treatment. Recurrence risk is higher with positive surgical margins.

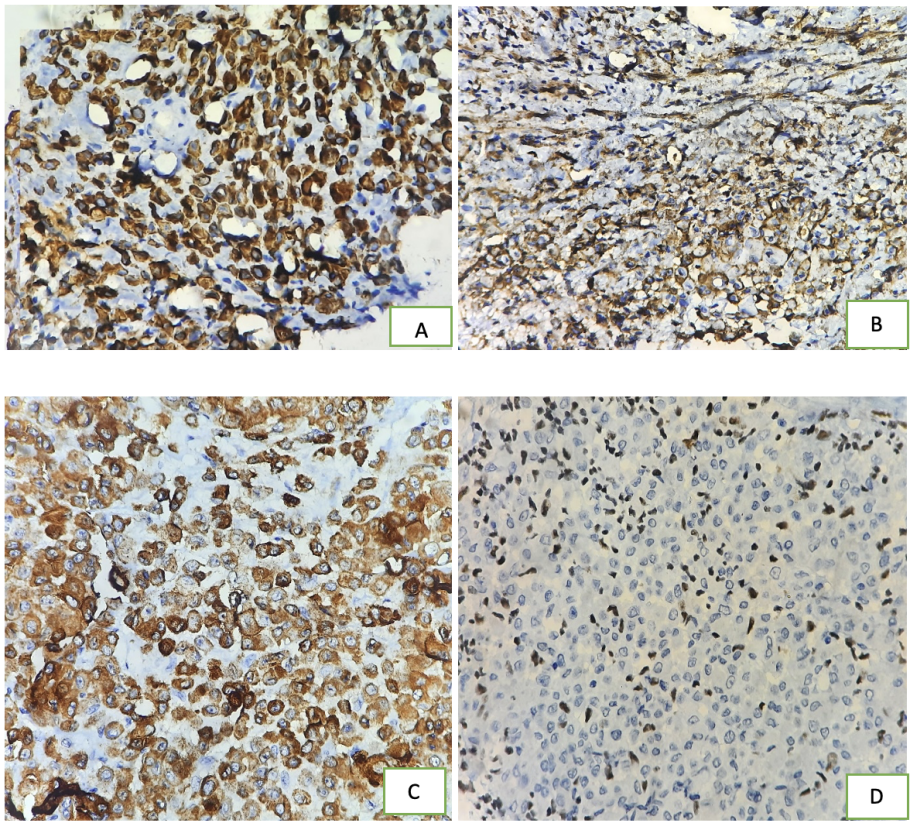

Figure 3: Immunohistochemistry expression within tumor cells. A) Pan-cytokeratin (AE1/AE3) showing diffuse cytoplasmic positivity in tumor cells (DAB, 400X) – biopsy B) CD99 showing mild to moderate membranous positivity in tumor cells (DAB, 400X) – biopsy C) epithelial membrane antigen (EMA) showing diffuse strong membranous positivity (DAB, 400X) - resection specimen D) INI1 showing complete loss of nuclear expression in tumor cells, with retained expression in background lymphocytes serving as internal control (DAB, 400X) - resection specimen.

Perioperative chemotherapy typically utilized for large radioresisitant high-grade tumors with or without incomplete resection and/or metastases. ES is typically thought of as radioresistant [2, 6]. Anthracycline-based therapy is one of the common and palliative chemotherapy for ES [7, 8]. Anthracyclines combined with ifosfamide used to improve the median overall survival of the patient [7, 8].

Proximal, deep location, rhabdoid morphology, large size, older age, necrosis, vascular invasion are associated with poor prognosis [9, 10]. In the present case, tumor was located in distal body site and presence of rhabdoid morphology was the only poor prognostic factor.

Conclusion

To conclude, proximal type epithelioid sarcoma can present with bland histological features which can mimic less aggressive neoplasms and not all tumors are located proximally. In such cases, detailed IHC approach is essential for definitive diagnosis.

Ethics and consent

Written informed consent was obtained from the patient's parents. Ethics committee approval was waived as this was a retrospective single-patient case report.

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Competing Interests

No conflicts of interest to declare

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