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Osteoclast-rich, proximal-type epithelioid sarcoma: clinicopathologic features of 3 unusual cases expanding the histomorphological spectrum

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ABSTRACT

Epithelioid sarcoma (ES) displays a wide clinicopathologic spectrum. On histopathology, osteoclast-like giant cells have been rarely described in these tumors. A 45-year-old gentleman presented with a perineal swelling of 6-month duration. Radiologic imaging disclosed a large, highly vascular tumor mass in his perineal region that was diagnosed elsewhere as pigmented villonodular synovitis. A 58-year-old lady presented with a recurrent tumor in her right inguinolabial region for which she underwent multiple tumor resections in the past. A 33-year-old lady presented with a right inguinal swelling of 1-month duration that was diagnosed elsewhere as a non-Hodgkin lymphoma on fine needle aspiration cytology. Histopathologic examination of tumors in all the 3 cases revealed epithelioid to "rhabdoid-like" cells arranged in a diffuse pattern interspersed with many osteoclast-like giant cells. The first tumor also revealed focal pseudoangiosarcomatous areas and heterotopic bone formation. By immunohistochemistry, tumor cells in all 3 cases were positive for AE1/AE3, epithelial membrane antigen, and CD34 and were completely negative for INI1/SMARCB1. CD68 immunostaining in 2 tumors highlighted osteoclast-like giant cells. Osteoclast-rich, proximal-type ES are unusual tumors, indicative of an expanding spectrum of ESs. Awareness of this histopathologic pattern and diagnostic confirmation with necessary immunohistochemical stains is crucial to avoid misinterpretation, as these tumors are clinically aggressive and are treated with wide local excision and optional adjuvant radiation therapy.

1. Introduction

Epithelioid sarcoma (ES) is a tumor of uncertain lineage and mostly occurs in adolescents and young adults. It is histopathologically defined as a malignant mesenchymal tumor that exhibits epithelioid cytomorphology and predominantly epithelial phenotype. Epithelioid sarcoma is subclassified into conventional and proximal subtypes [1]. Proximal-type ES/"large-cell" variant of ES differs from a conventional ES, as it commonly occurs in the proximal sites of relatively older individuals, is mostly deep-seated, histopathologically displays "rhabdoid-like" cells, and is characterized by a relatively more aggressive clinical behaviour [1-5]. Irrespective of these subtypes, most ESs display complete loss of immunohistochemical expression of INI1/SMARCB1 within the tumor cells [6-9].

Apart from conventional and proximal subtypes, certain other histopathologic variants of ES have also been described, such as fibroma-like, angiomatoid, and myxoid variants [3,10-12]. In addition, certain unusual morphologic features have been identified in an ES, including pseudoglandular formation, calcification, and bone formation [13,14]. Variable histopathologic features can pose a diagnostic challenge, especially when these appear as a predominant component of the tumor. Previously, 12 cases of ES, almost all proximal types, have been reported containing scattered osteoclast-like giant cells [2,4,5,15]. Rarely, an osteoclast-rich ES has been described [14]. Herein, we describe 3 cases of ES, rich in osteoclast-like giant cells, all proximal type. One of these tumors was misdiagnosed as pigmented villonodular synovitis. Histopathologic features, differential diagnoses, and implications in such cases are presented.

2. Materials and methods

In all 3 study cases, resection specimens were studied. Immunohistochemical staining was performed on formalin-fixed, paraffin-embedded tissue sections using the polymer technique (Dako REAL Envision detection system, Glostrup, Denmark) including peroxidase/3-3′-diaminobenzidine tetrahydrochloride (DAB). Various immunohistochemical antibody markers used in the 3 cases have been enlisted in Table 1.

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Table 1
List of various antibody markers used in the present study

Antibody marker	Clonality, clone	Dilution	Antigen retrieval	Manufacturer
EMA	Monoclonal, E29	1:1200	Pepsin (enzymatic)	Dako, Produkionsveg, Glostrup, Denmark
Pan CK	Monoclonal, MNF116, AE1/AE3	1:200	Heat microwave (sodium citrate)	Dako, Biocare CA
CD34	Monoclonal, QBEnd 10	1:100	Heat microwave (sodium citrate)	Dako
INI1/SMARCB1/BAF47	Monoclonal, 3E10	1:600	Heat, pressure cooker (sodium citrate)	Acris, GmbH, Herford, Germany
S100P	Polyclonal	1:600	Pepsin (enzymatic)	Dako
Melanosome	Monoclonal, HMB45	1:250	Pronase (enzymatic)	Dako
CD31	Monoclonal, JC70A	1:40	Heat microwave (sodium citrate)	Dako
Desmin	Monoclonal, D33	1:40	Heat microwave (sodium citrate)	Dako
LCA	Monoclonal, T29/33	1:100	Heat microwave	Dako

Abbreviations: EMA, epithelial membrane antigen; LCA, leukocyte common antigen.

3. Results

Clinicopathologic features of the 3 cases, including immunohistochemical results, have been summarized in Table 2. Individual clinical histories, radiologic findings, and treatment details with follow-up of each case are described as follows:

Case 1 A 45-year-old-gentleman presented with a perineal lump of 6-month duration, accompanied with a discharging sinus of 2-month duration. He did not have any other significant history. He underwent a biopsy of the lump at another hospital that was reported as pigmented villonodular synovitis. Subsequently, he was referred to us for another opinion.
His routine laboratory investigations, including hematological and biochemical tests, were within biological reference range.
Magnetic resonance imaging scan revealed a highly vascular, lobulated soft tissue mass involving the adductor and obturator muscles of his left thigh with erosion of the left inferior pubic rami, abutting the left corpora cavernosa and corpora spongiosa.
After review of the initial biopsy, the patient underwent a local wide excision of the tumor. Subsequently, he underwent adjuvant radiation therapy and has been free of disease for the last 6 months.

Case 2 A 58-year-old lady presented with a recurrent tumor in her right inguinolabial region. Four years and 5 months back, she underwent a wide local excision for a residual tumor at the same site, followed by postoperative radiation therapy. Three years back, she underwent a repeat wide local excision for the tumor recurrence, along with resection of a metastatic nodule over her abdominal wall. She was a known diabetic and hypertensive.
Her recent magnetic resonance imaging scans revealed an ill-defined, irregular residual soft tissue lesion in the skin and subcutaneous fat on the anterior and inferior aspect of the pubic symphysis on either sides of the midline, extending more towards the right side, with focal erosion of bilateral pubic bones and the right superior pubic ramus. The mass was seen extending inferiorly along the right inferior ischiopubic ramus, encasing it and infiltrating into the adjacent right sided adductor muscles, locally eroding the right inferior ischiopubic ramus. The soft tissue mass was isointense to muscle on T1-weighted images and heterogeneously hyperintense on T2-weighted and STIR images and exhibited marked enhancement on postcontrast scans. Positron emission tomogram (PET) computed tomography scan showed a fluorodeoxyglucose (^{18}F) avid soft tissue mass in the pubic symphysis, along with a lytic lesion in the right superior pubic ramus, extending posteriorly along the right inferior pubic ramus, measuring 6.0 × 4.9 cm with an standardized uptake value of 25.13. The lesion was seen extending into the right labia.
She underwent a biopsy, followed by a type III internal hemipelvectomy with microscopically clear resection margins. She is free of disease since the last 4 months.

Case 3 A 33-year-old lady with no comorbidities presented with a right inguinal lump of 1-month duration. Fine needle aspiration cytology of the mass was reported as a non-Hodgkin lymphoma, elsewhere.
On clinical examination, bilateral, inguinal lumps were noted, larger on the right side, measuring 3.5 × 3.0 cm. The lump was firm and nontender. Her routine hematological and biochemical investigations were within biological reference range. She underwent a right inguinal "lymph node" excision biopsy along with right-sided pelvic and obturator node resection (Figs. 1-4).
Postexcision PET scan revealed a low-grade uptake at the biopsy site most likely due to residual disease or postbiopsy changes. There was no significant uptake elsewhere in the body. Subsequently, the patient underwent a scar resection for adequate margins along with pelvic and obturator lymph node

Table 2
Clinicopathologic features of 3 cases of osteoclast-rich, proximal-type ES

Age/sex	Site	Tumor size (cm)	Histopathologic findings	Immunohistochemical results	Treatment	Outcome
45/M	Perineum	9	Nodular tumor infiltrating muscles and bone. Epithelioid to rhabdoid cells in a diffuse/sheet-like arrangement, focal pseudoangiosarcomatous pattern, hemosiderin deposition, tumor necrosis, calcification, bone formation and many osteoclast-like giant cells.	EMA+, AE1/AE3+, CD34+, INI1/SMARCB−, CD31−, S-100P−, HMB45−, Desmin−, LCA−, CD30−, MIB1 ~30%	Local wide excision of tumor + adjuvant RT	FOD (6 mo)
58[a]/F	Inguinolabial	5	Epithelioid to rhabdoid cells in a diffuse/sheet-like arrangement, tumor necrosis and many osteoclast-like giant cells.	EMA+, AE1/AE3+, CD34+, CD68+, INI1/SMARCB−, CD31−, S-100P−, HMB45− Desmin−, Calretinin−	Local wide excision of tumor	FOD (4 mo)
33/F	Inguinal	3.2	Epithelioid to rhabdoid cells in a diffuse/sheet-like arrangement and many osteoclast-like giant cells.	EMA+, AE1/AE3+, CD34+, CD68+, INI1/SMARCB−, CD31−, S-100P−, HMB45−, Desmin−	Local wide excision of tumor, pelvic and obturator lymphadenectomy + adjuvant RT	FOD (7 mo)

Abbreviations: F, female; FOD, free of disease; M, male; RT, radiation therapy.
[a] Presented with tumor recurrence and history of multiple tumor resections, adjuvant radiation therapy, and an abdominal metastatectomy.