Diagnostically Challenging Epithelioid Soft Tissue Tumors

Aaron W. James, MD, Sarah M. Dry, MD*

KEYWORDS

• Epithelioid sarcoma • Alveolar soft part sarcoma • Clear-cell sarcoma
• Ossifying fibromyxoid tumor • Malignant extrarenal rhabdoid tumor

ABSTRACT

In this article, we focus on the histologic features, differential diagnosis, and potential pitfalls in the diagnosis of epithelioid sarcoma, alveolar soft part sarcoma, clear-cell sarcoma, ossifying fibromyxoid tumor, and malignant extrarenal rhabdoid tumor. Numerous other soft tissue tumors also may have epithelioid variants or epithelioid features. Examples include epithelioid angiosarcoma, epithelioid malignant peripheral nerve sheath tumor, epithelioid gastrointestinal stromal tumor, and perivascular epithelioid cell tumor, among others.

OVERVIEW

In this article, we focus on the histologic features, differential diagnosis, and potential pitfalls in the diagnosis of epithelioid sarcoma (ES), alveolar soft part sarcoma (ASPS), clear-cell sarcoma (CCS), ossifying fibromyxoid tumor (OFMT), and malignant extrarenal rhabdoid tumor (MERT). Numerous soft tissue tumors may have epithelioid variants or epithelioid features. Examples include epithelioid angiosarcoma, epithelioid malignant peripheral nerve sheath tumor (MPNST), epithelioid gastrointestinal stromal tumor, and perivascular epithelioid cell tumor (PEComa), among others. Other articles in this special issue discuss many of these sarcomas.

EPITHELIOID SARCOMA

ES is a distinctive neoplasm of uncertain lineage of differentiation, which may be mistaken for either a benign granulomatous process or a carcinoma. First described as a distinct entity by Enzinger in 1970,[1] current understanding is of 2 types of ES, including the originally described conventional (classic-type or distal-type) ES, and the later described proximal-type ES. As we review, the 2 differ in their typical anatomic locations, histopathologic features, and prognosis. Both types are characterized by epithelioid cytomorphology, tumor necrosis, epithelial marker expression, and inactivation of the hSNF5/SMARCB1/INI1 gene. Classic-type ES typically involves young adults in the second to fourth decades of life,[2] with a male:female ratio of approximately 2:1.[2,3] It is uncommon in children and the elderly.[4] Proximal-type ES involves slightly older individuals (typically a decade older).[5,6]

GROSS FEATURES

The characteristic appearance of ES is a small indurated, ill-defined dermal and subcutaneous nodule or nodules. The flexor surface of the fingers, hand, wrist, and forearms are most commonly involved,[2] followed by other locations of the proximal and distal extremities.[1,2,7] ES rarely involves the trunk or head and neck areas. Large coalescent and variably necrotic mass lesions may also be seen to involve the tendons and aponeuroses. Tumor size varies from a few millimeters to 5 cm, whereas deep-seated lesions have been reported up to 15 cm in dimension.[1,2,8] Ulceration is a common feature, and clinical suspicion may be of an indurated ulcer or draining abscess. Proximal-type ESs are generally deep-seated tumors that involves the pelvis, perineum, and genital tract.[5,6] On cut section, ES is most often

Department of Pathology & Laboratory Medicine, David Geffen School of Medicine, University of California, Los Angeles, 10833 Le Conte Avenue, Los Angeles, CA 90077, USA
* Corresponding author. Department of Pathology & Laboratory Medicine, David Geffen School of Medicine, University of California, Los Angeles, 10833 Le Conte Avenue, CHS A3-251, Los Angeles, CA 90077.
E-mail address: sdry@mednet.ucla.edu

Surgical Pathology 8 (2015) 309–329
http://dx.doi.org/10.1016/j.path.2015.05.002
1875-9181/15/$ – see front matter Published by Elsevier Inc.

gray-white and may have yellow or brown areas owing to either necrosis or hemorrhage.

MICROSCOPIC FEATURES

Classic-type (distal-type) ES has a distinctive nodular arrangement of epithelioid to spindled tumor cells, with frequent central necrosis (**Fig. 1**A). The nodular pattern may vary somewhat from distinct tumor nodules in some cases to an irregular and conglomerate multinodular mass in others. Perineural and perivascular invasion are frequent findings. Ulceration is also frequent and may create diagnostic confusion

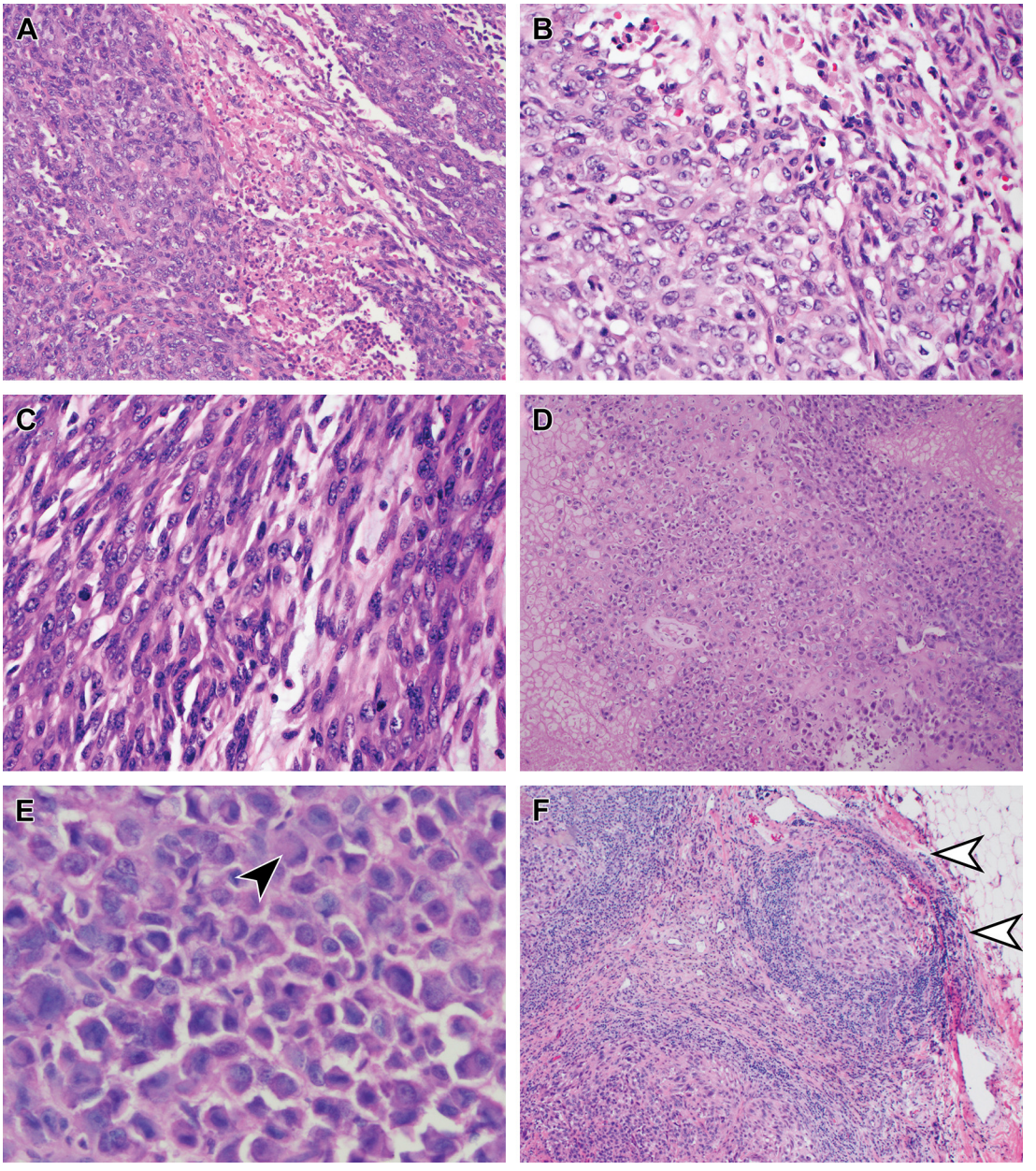

Fig. 1. Histologic appearance of ES. (*A*) Typical appearance of ES with nodules of epithelioid to focally spindled cells with central necrosis (×200). (*B*) Epithelioid tumor cells show enlarged round to ovoid nuclei. Tumor cell apoptosis and necrosis is readily identified (×400). (*C*) Focal spindling of tumor cells may be seen (×400). (*D*) Appearance of proximal-type ES typically includes larger lesions with a more confluent growth pattern composed of enlarged tumor cells (×200). (*E*) Cytologically, proximal-type ES demonstrates enlarged nuclei, prominent pseudoinclusions, and focal rhabdoid features (*arrowhead*) (×500). (*F*) Effacement of a lymph node with metastastic ES, *arrowhead* shows residual lymphoid tissue (×200).