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Case study

Primary epithelioid sarcoma of the kidney and adrenal gland: report of 2 cases with immunohistochemical and molecular cytogenetic studies

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Summary Epithelioid sarcoma (ES) is a malignant mesenchymal neoplasm with some morphologic or immunophenotypic evidence of epithelial differentiation. The "classic" subtype occurs in younger patients, often in distal extremities as compared with the "proximal" type. Tumors of the proximal type primarily arising in solid organs are rare with only few case reports in the literature. We report 2 cases of primary ES in the kidney of a 27-year-old woman and the adrenal gland of a 73-year-old man. Clinical examination and imaging, including computed tomography and positron-emission tomography, did not reveal tumor elsewhere in both cases. Histologic features were those of ES, proximal type with epithelioid/rhabdoid phenotype. Immunohistochemical study in both cases showed strong, diffuse expression of epithelial markers, CD34, and CD31. Nuclear expression of SMARCB1 protein was lost, but fluorescence in situ hybridization analysis was negative for *SMARCB1* deletion. We believe that these are the first reports of primary kidney and adrenal gland ES.

1. Introduction

Epithelioid sarcoma (ES) is a distinctive, malignant mesenchymal neoplasm that demonstrates some degree of epithelial differentiation. Since defined by Enzinger [1] in 1970, the description has expanded to include 2 distinct clinicopathological subtypes: "classic" and "proximal." The former, and more common, affects young adults and adolescents in distal extremities, most often in deep dermal or subcutaneous locations. Morphologically, the tumor forms well-circumscribed nodules and is composed of relatively bland to mildly atypical epithelioid cells with fairly abundant eosinophilic cytoplasm. Some cases exhibit central necrosis, forming a "granuloma-like" pattern. The second subtype, first described by Guillou et al [2] in 1997, tends to affect older adults in the proximal soft tissues, such as the limb girdle, trunk, and pelvis. The cytomorphology of the tumor cells in this subtype is generally higher grade, with vesicular nuclei and prominent nucleoli. Often, at least some malignant cells demonstrate rhabdoid phenotype.

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Table Immunohistochemical antibodies

Antigen	University of Chicago (clone, dilution, source)	NorthShore University Health System (clone, dilution, source)
Wide-spectrum cytokeratins	AE1/AE3, 1:2000; Millipore, Billerica, MA	AE1/AE3/PCK26, prediluted; Ventana
EMA	E29, 1/400; Dako, Carpinteria, CA	MC-5, prediluted; Biocare
CD31	JC70A, 1:500; Dako	JC/70A, prediluted; Ventana
CD34	QBEnd/10, 1:50; Dako	QBEnd/10, prediluted; Biocare
ERG	9FY, 1:100; Biocare, Concord, CA	9FY, 1:100; Biocare
INI-1 protein	25/BAF47, 1:50; BD Biosciences, San Jose, CA	25/BAF47, 1:50; BD Biosciences
PAX-8	Polyclonal, 1:600; Protein Tech Group, Rosemont, IL	BC12, 1:100; Biocare
S100 protein	Polyclonal, 1:2000; Dako	Polyclonal, 1:100; Biocare
Melan-A	A103, 1:100; Dako	Polyclonal, 1:100; Biocare
Inhibin	R1, 1:50; ABD Serotec, Kidlington, UK	R1, Cell Marque, 1:100; Ventana

Despite the clinical and morphologic differences between the 2 subtypes, both show strong expression of multiple epithelial markers by immunohistochemistry, particularly low-molecular-weight cytokeratins and epithelial membrane antigen (EMA) [3]. About 50% of cases also demonstrate CD34 expression. A characteristic immunohistochemical finding is the loss of nuclear SMARCB1 expression and molecular genetic studies show a high frequency of *SMARCB1* (*INI1*) deletion at the 22q11 locus in both subtypes [4], although a subset can show retention of *SMARCB1* with loss of protein expression, alluding to various possible epigenetic mechanisms of SMARCB1 loss.

ES is primarily a soft tissue neoplasm. Although solid organ involvement can occur by metastatic hematogenous spread, primary ES of solid organs is extremely unusual. Herein, we describe 2 cases of primary proximal type ES in the kidney and the adrenal gland. To our knowledge, this is the first description of ES arising from these organs, and thus expands the differential diagnosis of solid organ epithelioid tumors with keratin expression. Awareness of its occurrence and the usefulness of CD34 and SMARCB1 immunostaining would help avoid potential misdiagnosis of this entity in these uncommon locations.

2. Materials and methods

All slides of both cases were retrieved from the archives of the 2 institutions. The hematoxylin and eosin slides and immunohistochemical stains for both cases were reviewed. The immunohistochemical methods used to evaluate the 2 cases are detailed in the Table.

Fluorescence in situ hybridization (FISH) analysis was performed on a representative 4-μm thick unstained, formalin-fixed, paraffin-embedded tissue section of the tumor sample. For detection of deletion of the *SMARCB1* (22q11.23) locus, the following FISH probes were used: Vysis CEP4 probe (Abbott Molecular, Des Plaines, IL) and *SMARCB1* and *BCL2L13* (22q11.21) spanning probes using cocktails of BAC clones ([RP11-124F9] and [RP11-91O6 and RP11-143D17], respectively) selected on the basis of their location per the UCSC Human Genome Browser (http://genome.ucsc.edu/cgi-bin/hg,hg19) and obtained from BAC/PAC Resources Center (Children's Hospital Oakland Research Institute, Oakland, CA).

With respect to the custom spanning probes, each BAC clone was directly labeled by nick translation with either Spectrum Green– or Spectrum Orange–dUTP as per the manufacturer's protocol (Abbott Molecular). The abnormal range for scoring a specimen as positive for loss of the *SMARCB1* (*INI1*; 22q11.23) locus is 25% to 100% of the cells evaluated. Images were prepared using the Cytovision Image Analysis System (Applied Imaging, Santa Clara, CA). For this study, 200 interphase nuclei with strong and well-delineated signals were examined.

3. Case reports

3.1. Case 1

A 27-year-old white woman presented with a 30-day history of left flank pain associated with nausea, vomiting, dehydration, and constipation. A computed tomographic scan showed a 3.3-cm mass in the upper pole of the left kidney, without additional radiographically detected disease elsewhere. A fine needle aspiration showed tumor cells with rhabdoid morphology, and a subsequent radical nephrectomy was performed. After the diagnosis of ES of the kidney, the patient underwent 5 cycles of adjuvant chemotherapy with doxorubicin and ifosfamide over a 3-month period, followed by radiation therapy. The patient subsequently developed metastatic disease to the lung, mediastinal lymph nodes, pelvic lymph nodes, and right ovary, all of which were resected. Additional lesions were demonstrated radiographically in the liver and sacrum. The patient died 31 months after initial diagnosis.

3.2. Case 2

A 72-year-old white man presented with abdominal pain and nausea and admitted for "food poisoning." Subsequent computed tomographic scan and magnetic resonance imaging