Annals of Diagnostic Pathology 19 (2015) 221–225

Contents lists available at ScienceDirect

Annals of Diagnostic Pathology

Sclerosing epithelioid fibrosarcoma of the kidney: clinicopathologic and molecular study of a rare neoplasm at a novel location☆

Carsten-Henning Ohlmann, MD [a,1], Ines B. Brecht, MD [b,1], Kerstin Junker, MD [a], Jill A. van der Zee, MD, PhD [a], Adriana Nistor, MD [c], Rainer M. Bohle, MD [c], Michael Stöckle, MD [a], Markus Metzler, MD [b], Arndt Hartmann, MD [d], Abbas Agaimy, MD [d,*]

[a] Department of Urology & Pediatric Urology, Saarland University, Homburg/Saar, Germany
[b] University Children's Hospital, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany
[c] Institute of Pathology, Saarland University, Homburg/Saar, Germany
[d] Institute of Pathology, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany

ARTICLE INFO

Keywords:
sclerosing epithelioid fibrosarcoma
kidney
renal
MUC4
EWSR1

ABSTRACT

Sclerosing epithelioid fibrosarcoma (SEF) is a rare fibrosarcoma variant with specific histomorphology and consistent translocation (EWSR1-CREB3L1/2). To date, 110 cases have been reported; only 15 originated within the abdomen. With only 2 cases reported parallel to our study and one case briefly mentioned in a previous series, primary renal SEF is exceptionally rare but might be underrecognized. We herein describe 2 cases affecting a 23-year-old woman and a 43-year-old man. Tumor size was 22 and 4.2 cm, respectively. Patient 1 developed skeletal and multiple pulmonary metastases. She died of disease 82 months later, despite aggressive multimodality therapy. Patient 2 has no evidence of recurrence or metastasis (8 months after surgery). Histologic examination showed similar appearance with monotonous bland medium-sized epithelioid cells with rounded slightly vesicular nuclei and clear cytoplasm imparting a carcinoma-like appearance set within a highly sclerotic hyaline fibrous stroma. The tumor cells were arranged in nests, single cell cords, trabeculae, or solid sheets with frequent entrapment of renal tubules and glomeruli. Immunohistochemistry showed strong expression of vimentin, bcl2, CD99, and MUC4, whereas cytokeratin and other markers were negative. Fluorescence in situ hybridization showed a translocation involving the EWSR1 gene locus in case 2. Molecular analysis in case 1 was not successful due to poor signal quality. To our knowledge, this is the second report documenting primary renal SEF. Awareness of this entity would help avoid misinterpretation as clear cell carcinoma, sclerosing perivascular epithelioid cell tumor, Xp.11 translocation carcinoma, and other more frequent neoplasms at this site.

1. Introduction

Sclerosing epithelioid fibrosarcoma (SEF) is a rare variant of soft tissue fibrosarcoma that features rounded carcinoma-like epithelioid cells arranged into compact nests, cords, and single cell patterns within a highly sclerotic stroma [1]. SEF was first described in 1995 by Meis-Kindblom et al. based on a set of characteristic reproducible histopathologic criteria as defined above [2]. Although awareness of the highly distinctive histologic appearance of SEF facilitates recognition of this very rare sarcoma subtype on hematoxylin and eosin–stained slides, presence of frequent sclerosis and epithelioid cell appearance in neoplasms of different histogenetic derivation (carcinoma, lymphoma, sarcoma, etc) might result in overdiagnosis of SEF, if strict diagnostic criteria are not applied. On the contrary, SEF can be easily mistaken for metastatic carcinoma due to its frankly epithelioid appearance in most cases [2], particularly when encountered at unusual or unexpected sites. Furthermore, SEF showing ossification and prominent osteoid-like sclerosis might lead to misinterpretation as osteosarcoma, particularly those occurring primarily in bone [3]. To date, no more than 110 cases of pure SEF have been reported [4]. A majority of tumors affect adults and originate mainly in the deep soft tissue of the extremities [1,2,4]. SEF occurring at intraabdominal sites (retroperitoneum, pelvis, and abdominal viscera) are rare with no more than 15 well-documented cases (reviewed in [5]). Primary SEF of the kidney is exceptionally rare. A single case of renal SEF has been recently included in a series analyzing molecular features of SEF from different sites, but there were no detailed description of the histologic findings in that case [6]. However, an article describing 2 cases of primary renal SEF was just published during writing this manuscript [7]. We herein document 2 further cases of SEF presenting as primary kidney neoplasm and discuss their histologic differential diagnoses and molecular pathogenesis.

☆ Conflict of interest: None to declare.

* Corresponding author at: Pathologisches Institut, Universitätsklinikum Erlangen, Krankenhausstrasse 8-10, 91054 Erlangen, Germany. Tel.: +49 9131 85 22288; fax: +49 9131 85 24745.
E-mail address: abbas.agaimy@uk-erlangen.de (A. Agaimy).

[1] Equal contribution.

http://dx.doi.org/10.1016/j.anndiagpath.2015.04.005
1092-9134/

2. Material and methods

The 2 cases were identified from our surgical pathology files. Tumor specimens were fixed in buffered formalin overnight and embedded routinely for histologic examination. Immunohistochemical stains were performed on freshly cut 3-μm paraffin sections using a fully automated slide preparation system "Benchmark XT System" (Ventana Medical Systems Inc, Tucson, AZ) according to the manufacturer's instructions and the following antibodies: epithelial membrane antigen (clone E29, 1:200; Dako), pancytokeratin (clone KL-1, 1:200; Immunotech), vimentin (V9, 1:100; Dako), α–smooth muscle actin (clone 1A4, 1:200; Dako), desmin (clone D33, 1:250; Dako), protein S-100 (polyclonal, 1:2500; Dako), HMB45 (clone HMB45, 1:50; Enzo Life Sciences GmbH), CD34 (clone BI-3C5, 1:200; Zytomed), ERG (EPR3864, prediluted; Ventana), MUC4 (clone 8G7, 1:500, Santa Cruz), CK7 (OV-TL, 1:1000; Biogenex), CK20 (KS20.8, 1:50; Dako), p63 (4A4, 1:100; Zytomed), GATA3 (clone L50-823, 1:100; Biocare), PAX8 (polyclonal rabbit anti-PAX8, 1:50; Cell Marque), bcl-2 (clone 124, 1:100; Dako), CD99 (clone 12E7, 1:100; Dako), and Ki-67 (clone MiB1, 1:100; Dako).

Fluorescence in situ hybridization (FISH) was performed using a ZytoLight SPEC Dual Color Break Apart Probe mapped to the EWSR1 gene locus and another probe mapped to the FUS gene locus retrieved from Zytovision GmbH (Bremerhaven, Germany). The staining was performed on fresh cut 3-μm-thick slides cut from paraffin blocks using the protocol described previously [8]. Fifty interphase nuclei were evaluated for presence of translocation involving the EWSR1 gene locus. Clear-cut break-apart signals in more than 20% of assessed nuclei was considered evidence of translocation at the EWSR1 gene or the FUS gene locus.

3. Case description

3.1. Case 1

A 24-year-old woman was diagnosed with a huge retroperitoneal mass with clinical suspicion of Wilms tumor of the right kidney. She underwent radical nephrectomy. A diagnosis of adult nephroblastoma was favored by the local pathologist. A second opinion favored "anaplastic tumor of the kidney," and a third opinion within a pediatric pathology panel favored to call the tumor "highly malignant mesenchymal neoplasm, unclassified." Surgery was followed by chemotherapy (etoposide, carboplatin, doxorubicin, and cyclophosphamide) and radiation to the tumor bed (36 Gy). Three years later, imaging showed bilateral pulmonary metastases and vertebral metastasis at level of Th11/12. This was followed by high-dose chemotherapy, radiation therapy, and autologous stem cell therapy. Shortly thereafter, a metastasis was detected in the distal left femur. Multiple lung metastases were then resected as well as a metastasis from the eight right rib. After 1 month, progression of lung metastases necessitated maintenance chemotherapy according to the German Soft Tissue Sarcoma Study (CWS) protocol. After application of diverse therapeutic trials with surgery and radiochemotherapy, the patient died of her disease 82 months from initial diagnosis. A diagnosis of SEF was first suggested when a spinal metastasis was reviewed by one of the authors (AA).

3.2. Case 2

A 43-year-old man presented with an incidental finding of a renal mass on sonography. Abdominal computed tomography (scan) showed a mass occupying the middle field of the right kidney with extension into the upper pole and encasement of the adrenal gland (Fig. 1). A right-sided nephrectomy was performed. Intraoperatively, the tumor infiltrated the middle field of the kidney and reached the upper pole with involvement of the adrenal gland, so that partial nephrectomy was not feasible. Synchronous metastases have not been detected. The patient is currently alive with no evidence of disease (8 months after surgery).

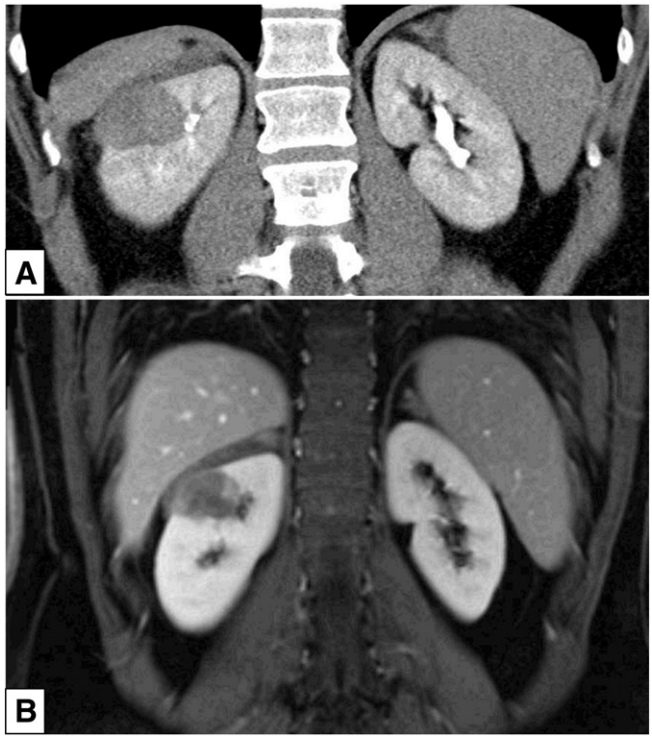

Fig. 1. Case 2. Abdominal computed tomographic scan (A) and magnetic resonance tomogram (B) showed a mass with soft tissue density localized mainly into the right kidney and bulging through the renal capsule into perirenal fat.

4. Results

4.1. Gross findings

The nephrectomy specimen in case 1 contained a 22 × 11 × 10 cm large tumor centered in the upper kidney pole and infiltrating the renal capsule as well as the renal pelvis. The cut surface was described as whorled, multinodular, and variegated with very hard areas as well as focal necrotic soft friable areas. The adrenal gland was not infiltrated by the tumor. In case 2, the upper kidney pole contained a 4.2 × 3.9 × 3.7 cm measuring poorly marginated tumor with whitish firm cut surface and infiltration through the kidney capsule into the perirenal fat.

4.2. Histologic findings

Both tumors showed highly similar histologic and immunohistochemical features and will be thus described together. They displayed closely packed nests and communicating thin cords and trabeculae of medium-sized polygonal epithelioid cells with distinctive clear cytoplasm and well-delineated cell borders (Fig. 2A and B). Some cells showed peripheral cytoplasmic retraction with a rim of eosinophilic condensed cytoplasm adjacent to the nucleus imparting a plasmacytoid (rhabdoid) cell appearance, but high-grade nuclear features were absent as well as true rhabdoid inclusions. The stroma was variably hyaline or sclerotic with fine reticular appearance in areas and extensive osteoid-like appearance in other areas including also in the lung metastases of case 1 (Fig. 2C-E). The periphery of the tumor was well delineated in some areas (Fig. 3A) and diffuse infiltrating in others (Fig. 3B). The cell arrangement in some areas took the form of compact cell nests (Fig. 3C). On occasion, the stromal sclerosis predominated over cellular component with a few tumor cells being compressed by dense hyaline stroma (Fig. 3D). Focal areas with clear cell carcinoma-like