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CASE REPORT

Case Report: Multifocal biphasic squamoid alveolar renal cell carcinoma [version 1; peer review: 2 approved, 1 approved with reservations]

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Abstract

A multifocal biphasic squamoid alveolar renal cell carcinoma in a 68-year-old man is reported. Four different peripheral tumor nodules were identified on gross examination. A fifth central tumor corresponded to a conventional clear cell renal cell carcinoma. Biphasic squamoid alveolar renal cell carcinoma is a rare tumor that has been very recently characterized as a distinct histotype within the spectrum of papillary renal cell carcinoma. Immunostaining with cyclin D1 seems to be specific of this tumor subtype. This is the first reported case with multifocal presentation.

Keywords

Kidney , biphasic squamoid alveolar renal cell carcinoma , papillary renal cell carcinoma , immunohistochemistry

Open Peer Review

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- Guido Martignoni, AOUI Verona, Verona, Italy Anna Calió, University of Verona, Verona, Italy - Jose Luis Rodriguez-Peralto, Complutense University of Madrid, Madrid, Spain - Claudio Doglioni, Vita-Salute San Raffaele University, Milan, Italy Any reports and responses or comments on the article can be found at the end of the article.			

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Competing interests: No competing interests were disclosed.

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Introduction

The so-called biphasic squamoid alveolar renal cell carcinoma (BSARCC) was described for the first time in 2012 by Petersson *et al.*¹ and has been very recently revisited and fully characterized by Hes *et al.*². Histological, immunohistochemical, comparative genomic hybridization and fluorescence *in situ* hybridization analyses have revealed that BSARCC is a renal neoplasm closely related to papillary renal cell carcinoma (PRCC)².

The present paper describes a new BSARCC with multifocal presentation that was associated with a conventional clear cell renal cell carcinoma (CCRCC). To note, multifocality has not been reported in BSARCC so far.

Case report

A 68-year-old man presented with transient hematuria. CT scan revealed multiple tumors on his right kidney, four of them being located at the periphery (Figure 1). Radical nephrectomy was performed. The post-surgery period did not show any clinical complications. The patient was asymptomatic and free of disease at the last contact, 6 months after diagnosis.

On gross examination up to five tumors and several small intrarenal micronodules were discovered (Figure 1). Four tumors

were subcapsular and showed a whitish homogeneous cut surface, measuring between 1 and 3 cm in diameter. The fifth tumor was centrally located, presented mixed solid and cystic areas with a yellowish cut surface and measured 4.5 cm in diameter.

Histologically, the yellowish central tumor was a conventional organ-confined CCRCC grade 1 (ISUP 2013)³. On low-power view, all the whitish peripheral tumors and the micronodules displayed a similar histology consisting in areas reminiscent to glomerular-like structures (Figure 2 and Figure 3) alternating with others typical of type 1 PRCC. On high magnification, these structures were composed of a single row of small cells with scant cytoplasm displaying an alveolar disposition. The alveoli were filled with cell groups with large cytoplasm and squamoid appearance. True squamous cell differentiation, however, was not observed. Mitosis and necrosis were not seen.

By immunohistochemistry, the tumor was positive with CK7, vimentin, PAX-8, racemase, RCC marker, AE1/AE3, 34βE12, carbonic anhydrase IX, CD10, and cyclin D1. Immunostaining pattern was distinct depending on the cell type. For instance, cyclin D1 and 34βE12 immunostained selectively the squamoid cells whilst RCC marker and carbonic anhydrase IX did it only in small alveoli-forming cells. The rest of the antibodies immunostained both cell types. The tumor was negative with p63 and CK20.

Figure 1. CT scans show multiple tumors in the right kidney (A and B). Gross examination displays a yellowish central tumor with solid-cystic areas corresponding to a clear cell renal cell carcinoma (C) and four peripheral whitish tumors and several intrarenal micronodules corresponding to biphasic squamoid alveolar renal cell carcinomas (C and D).

Figure 2. Panoramic view of one of the biphasic squamoid alveolar renal cell carcinomas displaying a conventional type 1 papillary renal cell carcinoma component (A). Alveolar structures filled with large cells are typical of biphasic squamoid alveolar renal cell carcinoma (B).

Figure 3. Microscopic detail of the alveolar structures containing small groups and single large squamoid cells positive for cyclin D1.

Discussion

BSARCC is a recently recognized variant of renal carcinoma^{1,2}. Its pathological diagnosis can be suggested on hematoxylin-eosin slides and is based on the recognition of two different cell types arranged in a distinct architecture. Small groups of large cells with abundant cytoplasm and squamoid appearance are surrounded by small cells with scant cytoplasm forming alveolar-like structures. This distinct growth pattern can be more or less evident in different tumor areas and, same as happens in the case here presented, can be combined with areas of conventional PRCC². The combination of BSARCC and PRCC histologies in almost half of the previously published cases favors the inclusion of this tumor within the broad spectrum of PRCC². No association of BSARCC with CCRCC, as in the case here presented, has been reported so far.

Morphological diagnostic features of BSARCC can be supported by immunohistochemistry and, if necessary, by genetics. All BSARCC reported to date are positive with cytokeratin 7, epithelial membrane antigen, vimentin and, interestingly, cyclin D1. Cyclin D1

immunostaining is specific of this tumor and helps in its recognition in daily practice. Interestingly, Cyclin D1 immunostaining is restricted to the centrally located squamoid cells. Molecular-genetic data show gains of chromosomes 7 and 17, thus linking BSARCC to PRCC.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images and/or other details that could potentially reveal the patient's identity.

Competing interests

No competing interests were disclosed.

Grant information

The author declared that no grants were involved in supporting this work.

References

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[PubMed Abstract](#) | [Publisher Full Text](#)
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Claudio Doglioni

Anatomy and Histopathology Department, IRCCS (Scientific Institute of Hospitalization and Care), San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy

The Author describes an unusual multifocal presentation of Biphasic squamoid alveolar renal carcinoma associated with a conventional Clear Cell Carcinoma. BSARCC is a recently described rare entity with a peculiar squamoid differentiation characterized by cyclin D1 immunoreactivity; Cyclin D1 per se is not limited to this type of renal tumor, but its pattern of reactivity seems specific for BSARCC. I suggest, considering some, although limited, similarity to squamoid morules in other epithelial tumors (colon, endometrium) to perform also immunostaining for beta-catenin.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 28 April 2016

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Jose Luis Rodriguez-Peralto

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The authors report for the first time a multifocal variant of the recently described squamoid alveolar renal cell carcinoma, a distinct microscopic tumor in the spectrum of papillary renal cell

carcinoma.. This is the first reported case on this location. The paper is original, elegant and well written, and the quality of figures nicely reflect the morphologic, and immunohistochemical aspects of this infrequent neoplasm. The references are acceptable and recent. Thus, I consider this paper acceptable in the current version, but some changes may improve the content of the manuscript:

- Since Cyclin D1 has also been reported in other variant of renal cell carcinoma, I recommend to the author to delete in the discussion the sentence Cyclin D1 immunohistochemistry is specific of this tumor. Moreover, I also included a sentence emphasizing that although Cyclin D1 is characteristic of BSARCC, it may be rarely observed in other variants of RCC.
- I considered that there are many immunohistochemical pictures of Cyclin D1, I would change figure C by a new H&E of the conventional clear cell renal cell carcinoma

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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Guido Martignoni

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Anna Calió

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The study describes a multifocal biphasic squamoid alveolar renal cell carcinoma in association of clear cell renal cell carcinoma. The Author claims that staining for cyclin D1 is specific for this entity; however, labelling for cyclin D1 has been reported in clear cell renal cell carcinoma, papillary renal cell carcinoma, chromophobe renal cell carcinoma and oncocytoma (1, 2) and more recently in clear cell papillary renal cell carcinoma (3) and SDH-deficient renal cell carcinoma (4). Since the immunoreactivity might depend of the clone used, the Author should supply information regarding the antibody to cyclin D1. It would be also interesting to know whether cyclin D1 is positive in the clear cell renal cell carcinoma. Finally, pictures of clear cell renal carcinoma and more detailed pictures demonstrating the squamoid features of biphasic squamoid alveolar renal cell carcinoma should be added.

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level

of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

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