Clear Cell Renal Cell Carcinoma With a Poorly-Differentiated Component: A Novel Variant Causing Potential Diagnostic Difficulty

Kanika Taneja  
*Henry Ford Health System*

Liang Cheng

Khaleel Al-Obaidy

Chia-Sui Kao

Justine Barletta

Follow this and additional works at: [https://scholarlycommons.henryford.com/merf2019caserpt](https://scholarlycommons.henryford.com/merf2019caserpt)

**Recommended Citation**

Taneja, Kanika; Cheng, Liang; Al-Obaidy, Khaleel; Kao, Chia-Sui; Barletta, Justine; Howitt, Brooke E.; Wasco, Matthew J.; Palanisamy, Nallasivam; Gupta, Nilesh S.; Rogers, Craig G.; Carskadon, Shannon; Chen, Ying-Bei; Antic, Tatjana; Tretiakova, Maria; and Williamson, Sean R., "Clear Cell Renal Cell Carcinoma With a Poorly-Differentiated Component: A Novel Variant Causing Potential Diagnostic Difficulty" (2019). *Case Reports*. 64.  
[https://scholarlycommons.henryford.com/merf2019caserpt/64](https://scholarlycommons.henryford.com/merf2019caserpt/64)
Authors
Kanika Taneja, Liang Cheng, Khaleel Al-Obaidy, Chia-Sui Kao, Justine Barletta, Brooke E. Howitt, Matthew J. Wasco, Nallasivam Palanisamy, Nilesh S. Gupta, Craig G. Rogers, Shannon Carskadon, Ying-Bei Chen, Tatjana Antic, Maria Tretiakova, and Sean R. Williamson

This poster is available at Henry Ford Health System Scholarly Commons: https://scholarlycommons.henryford.com/merf2019caserpt/64
Clear Cell Renal Cell Carcinoma With a Poorly-Differentiated Component: A Novel Variant Causing Potential Diagnostic Difficulty

Kaani Taneja1, Liang Cheng2, Khaled Al-Osubi3, Chia-Sui (Sunny) Kay4, Justinn A. Barletta2, Brooke E Howitt2, Matthew J. Wexner2, Nallapram Palanisamy4, Nilesh S. Gupta5, Craig G. Rogers6, Shannon Carusone1, Ying-Bei Chen1, Tatjana Antic7, Maria Terliakovskaya7, Sean R. Williamson1

1Henry Ford Health System, 2Indiana University School of Medicine, 3Stanford University School of Medicine, 4Brigham and Women’s Hospital, Harvard Medical School, 5St. Joseph Mercy Hospital, 6Memorial Sloan Kettering Cancer Center, 7University of Chicago, 8University of Washington

Background

- Several variant histologic patterns of clear cell renal cell carcinoma (RCC) are well known, particularly sarcomatoid and rhabdoid features.
- However, we have encountered rare cases in which a high-grade adenocarcinoma not otherwise specified (NOS) pattern or urthelial carcinoma-like component would be difficult to appreciate as clear cell RCC.

Design

- We retrieved 26 tumors with histologically typical clear cell RCC juxtaposed to a high-grade non-clear cell component.
- A high-grade non-clear cell component was defined as non-sarcomatoid, non-rhabdoid areas that would be difficult to assign as renal cell in origin if viewed in isolation.
- Tumors were studied with immunohistochemistry and fluorescence in situ hybridization (FISH) or sequencing.

Results

- Median percentage of poorly differentiated component was 50% (IQR20-70).
- All tumors showed abrupt transition from clear cell carcinoma to poorly-differentiated areas, with micropapillary (7/26; 27%), urothelial-like (10/26; 39%), and adenocarcinoma NOS features (9/26; 35%).
- Carboxic anhydrase IX (CA-IX) was uniformly positive in the well-differentiated component (20/20), but the poorly-differentiated component showed a median positivity of 82.5% (IQR 65-100).
- The poorly differentiated component was positive for CK7 (5/19; 26%), CK20 (3/12; 25%), AMACR (7/12; 58%), PAX8 (12/15; 80%), and showed intact FH (6/6; 100%). CD20 was uniformly negative.
- Chromosome 3p loss or VHL mutation was present in 8/13 (62%), tested with either FH (n = 9) or sequencing (n = 4).
- All tested cases were negative for TFE3 (0/11) and TFE2 (0/9) rearrangements using FISH.
- With follow-up, 5/21 (24%) patients were alive with metastatic disease and 5/21 (24%) had died of disease on follow up. One metastasis with biopsy material was composed only of the poorly-differentiated component and was near-negative for CA-IX.

Conclusion

- Clear cell RCC with a poorly differentiated component resembling adenocarcinoma or urthelial carcinoma is a novel source of morphologic heterogeneity that has not been previously well characterized.
- Potential pitfalls include decreased or absent CA-IX staining the high-grade component and aberrant positivity for cytokeratin 7 or 20.
- With the increasing use of renal mass biopsy and biopsies of metastatic sites for targeted therapy, pathologists should be aware of this entity and consider the possibility of clear cell RCC even for morphologically unusual tumors.