Reappraisal of Morphologic Differences Between Renal Medullary Carcinoma, Collecting Duct Carcinoma, and Fumarate Hydratase–deficient Renal Cell Carcinoma

Ohe, Chisato, MD[*]; Smith, Steven, C., MD, PhD[†]; Sirohi, Deepika, MD[*]; Divatia, Mukul, MD[‡]; de Peralta-Venturina, Mariza, MD[*]; Paner, Gladell, P., MD[§]; Agaimy, Abbas, MD[‖]; Amin, Mitual, B., MD[¶]; Argani, Pedram, MD[#]; Chen, Ying-Bei, MD, PhD[**]; Cheng, Liang, MD[††]; Colecchia, Maurizio, MD[‡‡]; Compérat, Eva, MD, PhD[§§]; Werneck da Cunha, Isabela, MD, PhD[‖‖]; Epstein, Jonathan, I., MD[#]; Gill, Anthony, J., MD, FRCPA[¶¶]; Hes, Ondřej, MD, PhD[##]; Hirsch, Michelle, S., MD, PhD[***]; Jochum, Wolfram, MD[†††]; Kunju, Lakshmi, P., MD[‡‡‡]; Maclean, Fiona, FRCPA[§§§]; Magi-Galluzzi, Cristina, MD, PhD[‖‖‖]; McKenney, Jesse, K., MD[‖‖‖]; Mehra, Rohit, MD[‡‡‡]; Nesi, Gabriella, MD, PhD[¶¶¶]; Osunkoya, Adeboye, O., MD[###]; Picken, Maria, M., MD, PhD[****]; Rao, Priya, MD[††††]; Reuter, Victor, E., MD[**]; de Oliveira Salles, Paulo, Guilherme, MD, PhD[‡‡‡‡]; Schultz, Luciana, MD[§§§§]; Tickoo, Satish, K., MD[**]; Tomlins, Scott, A., MD, PhD[‡‡‡]; Trpkov, Kiril, MD, FRCPC[‖‖‖‖]; Amin, Mahul, B., MD[*,¶¶¶¶]

The American Journal of Surgical Pathology: March 2018 - Volume 42 - Issue 3 - p 279–292
doi: 10.1097/PAS.0000000000001000
Original Articles

Abstract **Author Information** **Authors** **Article Metrics** **Metrics**

Renal medullary carcinomas (RMCs) and collecting duct carcinomas (CDCs) are rare subsets of lethal high-stage, high-grade distal nephron-related adenocarcinomas with a predilection for the renal medullary region. Recent findings have established an emerging group of fumarate hydratase (FH)-deficient tumors related to hereditary leiomyomatosis and renal cell carcinoma (HLRCC-RCCs) syndrome within this morphologic spectrum. Recently developed, reliable ancillary testing has enabled consistent separation between these tumor types. Here, we present the clinicopathologic features and differences in the morphologic patterns between RMC, CDC, and FH-deficient RCC in consequence of these recent developments. This study included a total of 100 cases classified using contemporary criteria and ancillary tests. Thirty-three RMCs (SMARCB1/INI1-deficient, hemoglobinopathy), 38 CDCs (SMARCB1/INI1-retained), and 29 RCCs defined by the FH-deficient phenotype

(FH^{-}/2SC^{+} or FH$^{\pm}$/2SC^{+} with *FH* mutation, regardless of HLRCC syndromic stigmata/history) were selected. The spectrum of morphologic patterns was critically evaluated, and the differences between the morphologic patterns present in the 3 groups were analyzed statistically. Twenty-five percent of cases initially diagnosed as CDC were reclassified as FH-deficient RCC on the basis of our contemporary diagnostic approach. Among the different overlapping morphologic patterns, sieve-like/cribriform and reticular/yolk sac tumor–like patterns favored RMCs, whereas intracystic papillary and tubulocystic patterns favored FH-deficient RCC. The tubulopapillary pattern favored both CDCs and FH-deficient RCCs, and the multinodular infiltrating papillary pattern favored CDCs. Infiltrating glandular and solid sheets/cords/nested patterns were not statistically different among the 3 groups. Viral inclusion–like macronucleoli, considered as a hallmark of HLRCC-RCCs, were observed significantly more frequently in FH-deficient RCCs. Despite the overlapping morphology found among these clinically aggressive infiltrating high-grade adenocarcinomas of the kidney, reproducible differences in morphology emerged between these categories after rigorous characterization. Finally, we recommend that definitive diagnosis of CDC should only be made if RMC and FH-deficient RCC are excluded.

[*]Department of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center, Los Angeles, CA

[†]Departments of Pathology and Urology, VCU School of Medicine, Richmond, VA

[‡]Department of Pathology, Houston Methodist Hospital, Weill Medical College of Cornell University

[††††]MD Anderson Cancer Center, Houston, TX

[§]Department of Pathology, University of Chicago, Chicago

[****]Department of Pathology, Loyola University, Maywood, IL

[¶]William Beaumont Hospital, Royal Oak

[‡‡‡]Department of Pathology and Michigan Center for Translational Pathology, University of Michigan, Ann Arbor, MI

[#]Johns Hopkins Hospital, Baltimore, MD

[**]Memorial Sloan Kettering Cancer Center, New York, NY

[††]Indiana University School of Medicine, Indianapolis, IN

[***]Brigham and Women's Hospital, Boston, MA

[‖‖]Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, OH

[###]Emory University School of Medicine, Atlanta, GA

[¶¶¶¶]Department of Pathology and Laboratory Medicine and Urology, University of Tennessee Health Science Center, Memphis, TN

[‖]Institute of Pathology, Friedrich-Alexander-University, Erlangen, Germany

[‡‡]Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

[¶¶¶]Division of Pathological Anatomy, University of Florence, Florence, Italy

[§§]Department of Pathology, Hôpital Tenon, Assistance Publique-Hôpitaux de Paris, UPMC Paris VI, Paris, France

[||]Department of Pathology, AC Camargo Cancer Center, São Paulo

[‡‡‡‡]Anatomic Pathology, Mario Penna Institute, Hospital Luxemburgo, Belo Horizonte, Brazil

[§§§§]Institute of Anatomic Pathology, Piracicaba, Brazil

[¶¶]Cancer Diagnosis and Pathology Group, Kolling Institute of Medical Research Royal North Shore Hospital and University of Sydney

[§§§]Douglass Hanly Moir Pathology, Sydney, NSW, Australia

[##]Charles University Hospital, Pilsen, Czech Republic

[†††]Institute of Pathology, Kantonsspital St Gallen, St Gallen, Switzerland

[||||]Calgary Laboratory Services, University of Calgary, Calgary, AB, Canada

Presented in part at the annual meeting of the United States and Canadian Academy of Pathology, Seattle, March 2016.

Conflicts of Interest and Source of Funding: S.A.T is supported by the A. Alfred Taubman Medical Research Institute. O.H. acknowledges support of the Charles University Research Fund (project number P36) and by the project CZ.1.05/2.1.00/03.0076 from European Regional Development Fund. C.O. received research fellowship training support from the Uehara Memorial Foundation. The authors have disclosed that they have no significant relationships with, or financial interest in, any commercial companies pertaining to this article.

Correspondence: Mahul B. Amin, MD, Department of Pathology and Laboratory Medicine, University of Tennessee Health Science Center, 930 Madison Avenue, Suite 531, Memphis, TN 38163 (e-mail: mamin5@uthsc.edu).

^ Back to top