Succinate dehydrogenase deficient renal cell carcinoma: A case report

Raj A. Kumar\textsuperscript{a,}\textsuperscript{*}, Hiroko Miyagi\textsuperscript{b}, Vimal Mittal\textsuperscript{c}, Paul Crispen\textsuperscript{b}, Udaya Kumar\textsuperscript{c}

\textsuperscript{a} Catherine & Joseph Aresty Department of Urology, Keck Medicine of USC, University of Southern California, Los Angeles, CA, USA
\textsuperscript{b} Department of Urology, University of Florida College of Medicine, University of Florida, Gainesville, FL, USA
\textsuperscript{c} Citrus Memorial Hospital, Inverness, FL, USA

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\textbf{ABSTRACT}

Succinate dehydrogenase (SDH) deficient renal cell carcinoma (RCC) are uncommon renal tumors that typically present in relatively younger patients. SDH mutations are known to cause cancer, but often presents with hereditary paragangliomas, pheochromocytomas, and gastrointestinal stromal tumors. This report details a case of SDH deficient RCC in a patient with no known contributing family history. Patient presented with recurrent urinary tract infections and groin pain. Computerized tomography (CT) revealed a 4 cm mass in the right kidney. Partial nephrectomy was performed, and the patient had an uneventful recovery. Immunohistochemical staining revealed the tumor was SDH negative.

\section*{1. Introduction}

Succinate dehydrogenase (SDH) deficient renal cell carcinoma (RCC) was only recently accepted as a provisional entry in the 2013 International Society of Urological Pathology Vancouver Classification. Of the four subunits of succinate dehydrogenase (SdhA, SdhB, SdhC, and SdhD), SdhB mutation is known to lead to tumorigenesis. However, this is more commonly associated with hereditary paragangliomas, pheochromocytomas, and gastrointestinal stromal tumors. Here we present a case of SdhB deficient renal cell carcinoma (RCC).

\section*{2. Case presentation}

37-year-old female presented with recurrent urinary tract infections and groin pain. The patient’s primary care physician ordered an ultrasound scan to evaluate her recurrent urinary tract infections. The ultrasound scan showed a solid renal mass or a complicated cyst in the lower lateral aspect of her right kidney. A computerized tomography (CT) scan was ordered to evaluate the mass further. CT revealed an exophytic 4 \times 3.5 \times 2 cm mass on the inferior aspect of the right kidney (Fig. 1). The patient was referred to urology. In view of likely malignant nature of the mass the patient was advised to undergo partial nephrectomy. Patient underwent robotic-assisted partial nephrectomy, which was uneventful. Histological analysis of the excised renal mass showed a well-circumscribed tumor with pushing borders (Fig. 2). Neoplastic cells were uniform containing low-grade nuclei and cytoplasmic vacuoles with pale eosinophilic material. Cells were arranged in a nested and tubular pattern. Tumor was interspersed with cysts containing pale eosinophilic material (Fig. 3).

Immunohistochemical staining was performed for PAX-8 and SdhB. Tumor cells were positive for PAX-8, supportive of renal origin. However, neoplastic cells did not stain positive for SdhB. Adjacent benign tissue served as an internal positive control, staining positive for SdhB.

The patient had an uneventful recovery from her surgery. Patient was referred to and seen by oncology for genetic counseling. Unfortunately, the patient was lost to follow up after 6 months.

\section*{3. Discussion}

Very few cases of SDH-deficient RCC have been documented. One study estimated that between 0.05\% and 0.2\% of all RCCs are SDH deficient.\textsuperscript{1} Sdh deficient renal cell carcinomas are rare with a mean age of 38–40 years. Tumors are typically described similar to the above case: well-circumscribed with cytoplasmic vacuoles containing eosinophilic, fluid-like material. Analysis often shows cystic change, and cells are typically arranged in nests or tubules.\textsuperscript{2} However, one retrospective study found that only four out of eight SDH-deficient RCCs presented with characteristic cytoplasmic vacuoles and inclusions.

The precise mechanism through which SdhB mutation induces tumorigenesis is unknown. Interestingly, while SdhB, SdhC, and SdhD mutations are all associated with RCC development, there have only been two documented cases of SdhA mutation resulting in RCC.\textsuperscript{3} While

\textsuperscript{*} Corresponding author. Research Assistant Urology Institute, University of Southern California, USA.
E-mail address: rkumar28@uic.edu (R.A. Kumar).

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SDH-deficient RCC with sarcomatoid differentiation can present as aggressive, familial tumors, prognosis is typically favorable if excised completely. Though the management of SDH-deficient RCC is similar to other masses of differing etiology, genetic screening may be considered in first- and second-degree relatives. This should include assessment for associated concurrent tumors. A series of 27 patients revealed that 15%
of patients developed concurrent GISTs and 15% developed concurrent paragangliomas. 19% had first-degree relatives with RCC, and 1 patient had a second-degree relative with RCC. Additionally, 5 patients had first degree relatives and 2 had second-degree relatives with pheochromocytomas or paragangliomas.

4. Conclusion

SDH-deficient RCC is a rare, aggressive tumor that presents in relatively young patients. When identified, patients and immediate family should be surveilled for other SDH deficient tumors including pheochromocytomas, paragangliomas, GISTs, and RCCs. With increased awareness, patients can be diagnosed appropriately and treated in a timely manner.

References

1. Gill AJ, Hes O, Paphthomas T, et al. Succinate dehydrogenase (SDH)-deficient renal carcinoma: a morphologically distinct entity: a clinicopathologic series of 36 tumors from 27 patients. *Am J Surg Pathol*. 2014;38(12):1588–1602.
2. Gill AJ, Fachtar NS, Chou A, et al. Renal tumors associated with germline SDHB mutation show distinctive morphology. *Am J Surg Pathol*. 2011;35(10):1578–1585.
3. Li Y, Reuter VE, Matoso A, Netto GJ, Epstein JI, Argani P. Re-evaluation of 33 ‘unclassified’ eosinophilic renal cell carcinomas in young patients. *Histopathology*. 2018;72(4):588–600.
4. Yakirevich E, Ali SM, Mega A, et al. A novel SDHA-deficient renal cell carcinoma revealed by comprehensive genomic profiling. *Am J Surg Pathol.* 2015;39(6):858–863.
5. Ricketts CJ, Shuch B, Vocke CD, et al. Succinate dehydrogenase kidney cancer: an aggressive example of the Warburg effect in cancer. *J Urol.* 2012;188(6):2063–2071.