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Adolescent male with bilateral succinate dehydrogenase-deficient renal cell carcinoma in a horseshoe kidney managed successfully with staged bilateral robotic-assisted partial nephrectomies: A case report

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ABSTRACT

Succinate dehydrogenase (SDH) deficient renal cell carcinoma (RCC) is a rare subset of familial RCC with only 59 cases reported. SDH deficiency is associated with hereditary paraganglioma/pheochromocytoma syndrome. Most of the cases are solitary tumors with only two reported cases of bilateral tumor. The identification of SDH deficient RCC is often the sentinel event of patient's syndromic diagnosis. We present a case of an adolescent male with bilateral tumors in a horseshoe kidney who was treated with staged robotic-assisted partial nephrectomies without complication. Both tumors were SDH negative on immunohistochemical staining.

1. Introduction

The incidence of renal cell carcinoma (RCC) is estimated to be approximately 2–3% of all adult malignant neoplasms.[1,2] Of these, the majority are sporadic with only 4–6% secondary to familial disease and predominantly autosomal inheritance pattern.[1,2] A strong suspicion for familial RCC should be suspected when the affected individual is < 40 years old and presenting with bilateral or multicentric disease. RCC in children and young adults tends to be symptomatic, high grade, and unfavorable pathology.[1] The following is a case of an adolescent male with a horseshoe kidney found to have bilateral succinate dehydrogenase (SDH) deficient RCC.

2. Case presentation

A 19-year-old male with no past medical history presented to the emergency department with a chief complain of 10-day history right lower quadrant abdominal pain, nausea, and vomiting. His initial labs were unremarkable. The emergency department physician ordered a computerized tomography (CT) scan of the abdomen and pelvis with contrast due to concern for appendicitis. The CT was negative for any gastrointestinal pathology but revealed a horseshoe shaped kidney with bilateral predominantly exophytic renal masses. The right mass was located anteroinferior measuring 3.1 × 4.0 × 3.0 cm and the left mass posteroinferior measuring 3.6 × 3.0 × 3.2 cm (Fig. 1). The patient was referred to urology for further evaluation and management.

At initial urologic consultation, there was no family history of previous urological malignancy. The patient underwent an MRI of the abdomen with contrast, which demonstrated similarly sized masses bilaterally seen on CT, and a heterogenous appearance that was concerning for RCC. No adenopathy was identified, and the inferior vena cava and renal veins were patent. Through shared decision making, the patient and his family decided to undergo staged robotic surgical excision of both tumors.

Two months after the initial diagnosis, the patient underwent an uncomplicated robotic-assisted partial right nephrectomy. Total operative time was 140 minutes with 170 mL of blood loss. Hospital stay was three days and there were no postoperative complications. Six weeks later the patient underwent a second uncomplicated robotic-assisted partial left nephrectomy. Total operative time was 160 minutes with 600 mL of blood loss. Hospital stay was only one day, and again without any postoperative complications.

Abbreviations: SDH, succinate dehydrogenase; RCC, renal cell carcinoma; CT, computerized tomography; WHO, World Health Organization; SDHB, succinate dehydrogenase B; IHC, immunohistochemistry; PGL/PCC, hereditary paraganglioma/pheochromocytoma.

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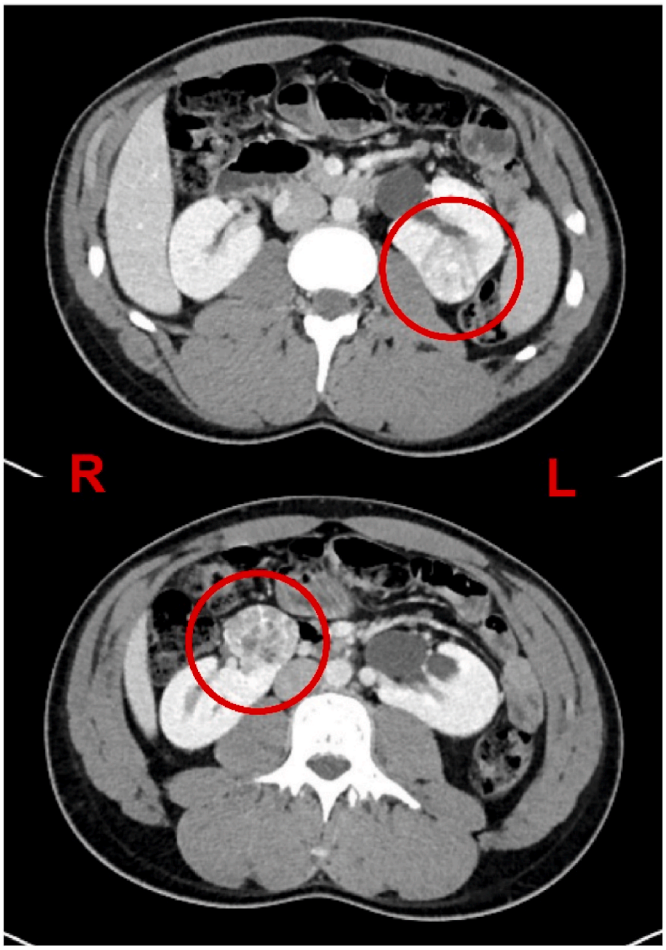

Fig. 1. Emergency Department Computed Tomography. Axial scan obtained during the patient's index emergency department visit. Due to the patient's horseshoe kidney, the left renal mass is located posteroinfero and the right renal mass is located anteroinferior.

The pathology report for the first resection of the right renal mass was remarkable for a 3.5 cm succinate dehydrogenase deficient renal cell carcinoma, World Health Organization (WHO) grade 2 without necrosis, sarcomatoid or rhabdoid features. All margins were negative for invasive carcinoma. Pathological surgical staging was T1aN0M0. The second pathology report was remarkable for a 3.4 cm succinate dehydrogenase deficient renal cell carcinoma, WHO grade 2. Grossly, the left tumor was like the right tumor, however the left tumor contained larger amounts of solid components. Both tumors were a soft pink-tan in color and well circumscribed. Pathological surgical staging was same as the right tumor. Microscopically, the tumors were predominantly oncocytic cells with clear cytoplasm and cytoplasmic vacuoles scattered throughout (Fig. 2). Histologically, both tumors were negative for succinate dehydrogenase B (SDHB), carbonic anhydrase IX (CAIX), cytokeratin 7 (CK7), c-KIT (CD117) on immunohistochemistry (IHC). Both tumors had positive IHC for fumarate hydratase (FH), CD10, E-cadherin, and Vimentin. The patient subsequently underwent genetic testing that was positive for SDHB germline mutation.

3. Discussion

Succinate dehydrogenase (SDH)-deficient RCC is rare and associated with hereditary paraganglioma/pheochromocytoma (PGL/PCC) syndrome. PGL/PCC syndrome is primarily characterized by paragangliomas, pheochromocytomas, papillary thyroid cancer, and gastrointestinal stromal tumors.[2] Tumorigenesis is believed to be second

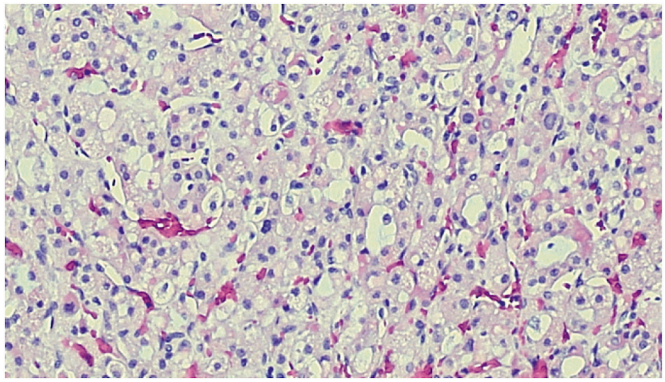

Fig. 2. Pathology Slide from Right Tumor. Final pathology slide of the first resected tumor demonstrating the hallmark features of succinate dehydrogenase deficient renal cell carcinoma with cytoplasmic vacuoles containing eosinophilic and flocculent materials.

hit loss of function mutation in an individual with a germline mutation in succinate dehydrase allele.[3,4] Any of the subunits for the Krebs cycle enzyme succinate dehydrogenase (SDHA, SDHB, SDHC, SDHD, and SHDAF2) can be affected, but almost all cases report the SDHB subunit to be mutated. Patient's with SDHB mutation carry a 10–15% lifetime risk developing RCC.[2] A recent retrospective analysis performed by T.L. Fuchs et al. reported 59 cases including 62 tumors worldwide of SDH-deficient renal cell carcinoma.[4] The minority of the reported cases have a relevant family history of PGL/PCC syndrome.[2,4] Overall survival after diagnosis is not known at this time due to limited reported outcomes. Of the described cases, only two patients had bilateral tumors, neither of those two patients had a horseshoe kidney making the above case presentation exceedingly rare.

In the presented case, the fusion anomaly presented unique challenges. However, the relatively anterior aspect of the right tumor, the lateral aspect of the left tumor, and the well circumscribed appearance of the tumors on imaging were favorable for nephron sparing surgery (Fig. 3). Careful preprocedural analysis of the imaging to identify vessels was important as approximately only 36% of horseshoe kidneys have classic vascular configuration.[5] Difficulty in mobilization was also encountered with the left resection due to the midline fusion decreasing the ability to rotate the kidney for best posterior exposure. With the advantages of utilizing the robotic approach for his surgeries, these difficulties were able to be mitigated.

Typical pathological findings for SDH-deficient RCC include well demarcated tumors with pushing borders. The hallmark histopathological features of SDH-deficient RCC include cytoplasmic vacuoles containing eosinophilic and flocculent materials.[3,4] IHC of the reported tumors is always negative for SDHB and required for diagnosis. High grade pathological features include coagulative necrosis, rhabdoid, or sarcomatoid differentiation and indicate a worse overall prognosis.[1,4] In a cohort of 62 reported SDH-deficient RCC, the relative presence of

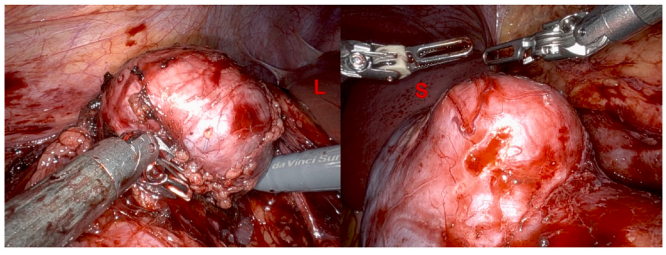

Fig. 3. Intraoperative Views. Intra-operative view of the tumors, noting the abnormal orientation of the horseshoe kidney. The view is looking medial to lateral using a 30° downward angled scope, Liver (L), and spleen (S). Tumors are right and left, respectively.

high-grade features was approximately 20%.[4] Radical nephrectomy is recommended when the tumor exhibits clinical high-grade features, however a partial nephrectomy is as an acceptable mode of management for a tumor with low-risk features.[1]

4. Conclusion

The adolescent male in the above case does not fit the expected demographic of a patient with succinate dehydrogenase deficient renal cell carcinoma. Additionally, the presentation was uniquely challenging given the horseshoe kidney anomaly and tumor locations. This case exemplifies the broad spectrum of patients that are susceptible to this disease and adds further information to the limited number of cases published.

Patient consent

Due to the nature of this case report, UMH-West IRB policies, this project was deemed exempt from IRB review. Authors have received and archived patient consent for publication prior to surgery.

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CRediT roles

Christopher Pulford: conceptualization, formal analysis, roles/writing – original draft.

Kevin Keating: writing – review and editing.

Richard Eames: writing – review and editing.

Charla Holdren: writing – review and editing.

David Peifer: supervision, writing – review and editing.

Thomas Maatman: supervision, conceptualization, data curation, writing – review and editing.

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