Urology Case Reports 35 (2021) 101553

Contents lists available at ScienceDirect

Urology Case Reports

journal homepage: http://www.elsevier.com/locate/eucr

Oncology

Repeat partial nephrectomy for recurrence of Von Hippel-Lindau-related renal cell carcinoma in an autotransplanted kidney

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ARTICLE INFO

Keywords:
Carcinoma
Renal cell
Autotransplantation
Partial nephrectomy
Recurrence
Von hippel-lindau disease

ABSTRACT

Von Hippel-Lindau disease predisposes to develop renal cell carcinoma (RCC). Treatment is frequently challenging due to presence of bilateral tumors and high risk of recurrence. We present the case of a VHL-patient with bilateral recurrence of clear-cell RCC after bilateral partial nephrectomy and autotransplantation on one side. Recurrence on the transplanted kidney was treated with repeat partial nephrectomy with good oncological and functional outcomes. This approach is feasible in centres with wide experience in partial nephrectomy and renal transplantation when minimally invasive tumor ablation is not indicated.

Introduction

Von Hippel-Lindau (VHL) disease is an autosomal dominantly inherited syndrome which predisposes to the development of different tumors, including renal cell carcinoma (RCC) and pheochromocytomas. Renal tumors occur in 25–45% of VHL-patients, tend to be low grade and stage and usually have clear-cell histology.[1]

Since renal lesions are often multifocal or bilateral, and risk of recurrence is high, treatment represents a challenge. Nephron-sparing surgery (NSS) has become the standard of care, although percutaneous ablative therapies are currently widely used.

We present the case of a VHL-patient with bilateral RCC managed with bilateral NSS and autotransplantation. During follow-up a bilateral synchronous recurrence occurred, which was dealt with repeated partial nephrectomy (PN) in the autotransplanted kidney and contralateral percutaneous RFA.

Case presentation

A 75-year-old woman was diagnosed with VHL-syndrome in 2014 when bilateral renal masses and a left adrenal nodule were incidentally found (Fig. 1A). Baseline serum creatinine (Crs) was 0.83 mg/dl and eGFR 69 ml/min. The patient underwent bilateral open PN and left adrenalectomy. Due to the surgical complexity, left kidney PN was performed on the bench and the kidney was reimplanted in the right iliac fossa. After removal, the left kidney was put on ice and perfused with Belzer solution. Resection of the lesion that involved collecting system and segmental vessels was performed with macroscopically negative margins. Integrity of the collecting system was tested with injection of methylene blue through the ureter; integrity of the vascular structures was tested with infusion of saline through renal artery and vein. The renal cortex was sutured with 3/0 monofilament (Fig. 1B). Meanwhile, a second equipe performed an on site clampless right PN. Through a Gibson incision, the left kidney was allocated in the right iliac fossa and renal vessels were anastomosed to right external iliac vessels. Cold ischemia time was 25 minutes. Finally, a Lich-Gregoire ureteral anastomosis on a 6-Fr ureteral stent was performed.

Pathology showed pT1b, Fuhrman grade 2, clear-cell RCC (ccRCC) for the left renal lesion; pT1b, Fuhrman grade 1, ccRCC for the right renal lesion, both with negative surgical margins. The adrenal nodule turned out to be pheocromocytoma.

Four years later, a CT scan revealed a bilateral disease recurrence. Two recurrent lesions of 20 mm and 22 mm were found in the bed of previous surgical resections. The location of the recurrence in the transplanted kidney (Fig. 2A) did not allow a percutaneous ablation. Therefore, a repeat open PN was performed. Conversely, the right lesion was amenable to percutaneous RFA. The margins of the right renal lesion were identified with the use of intraoperative ultrasonography

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https://doi.org/10.1016/j.eucr.2020.101553
Received 7 December 2020; Accepted 24 December 2020
Available online 28 December 2020

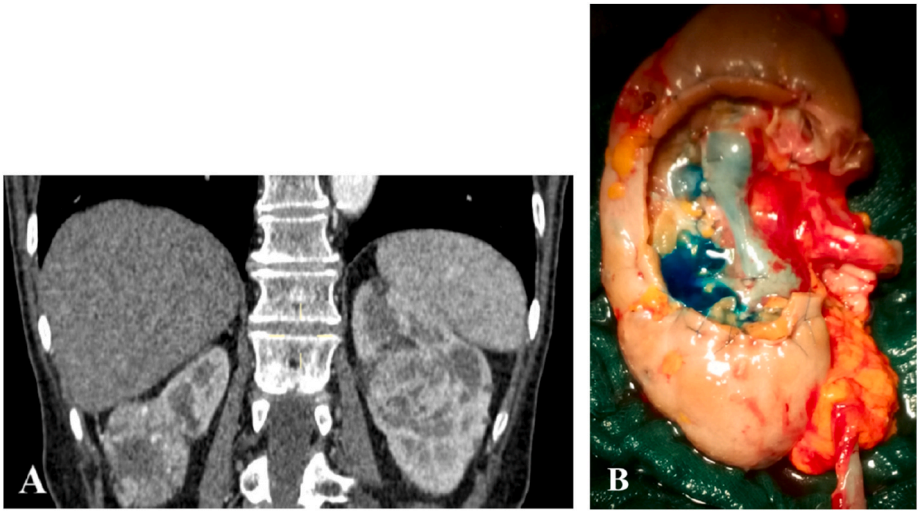

Fig. 1. CT scan showing VHL-associated bilateral renal masses (A); left kidney after partial nephrectomy on the bench with methylene blue showing the integrity of the intrarenal collecting system (B).

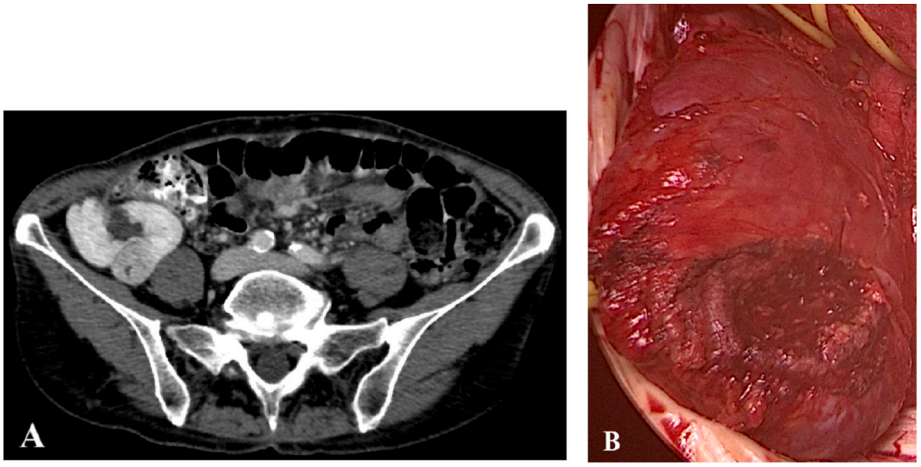

Fig. 2. CT scan showing a 22 mm local recurrence in the autotransplanted kidney (A); open enucleation of the recurrence in the autotransplanted kidney (B).

and enucleation was performed (Fig. 2B). Pathology showed clear-cell RCC, Fuhrman grade 3, with negative margins.

The post-operative course was uneventful. At last follow-up 18 months after repeat PN, the patient was free of disease with acceptable renal function (Crs 1.47 mg/dl, eGFR 35 ml/min).

Discussion

VHL disease is a neoplastic genetic syndrome. Since renal tumors tend to be multifocal or bilateral and residual renal tissue is at risk for recurrence, management is often challenging. The aim of treatment is to control cancer while preserving healthy parenchyma. However, conflicting evidence exists about the safest management of bilateral tumors. Novick and Streem analysed the outcomes of NSS in 9 VHL-associated bilateral RCC: 78% of patients experienced local recurrence and researchers concluded that outcomes of NSS were less satisfactory, with bilateral nephrectomy more likely to be curative.[2]

Due to the high recurrence rate and to the challenges of repeat surgery, ablative treatments are used as alternatives to surgery. According to literature, overall success rate for RFA ranges from 85% to 100% in treatment of hereditary RCCs.[3]

A threshold of 3 cm is generally used as a safe cut-off to indicate surgery over active surveillance. In a cohort of VHL-patients, no patients with $\leq$3 cm tumor developed metastatic disease or end-stage renal disease (ESRD); conversely, 20 of 73 patients with >3 cm tumor developed metastasis and 5 ESRD.[4] The 3 cm size as trigger for surgery can provide good cancer control while minimizing active intervention and renal damage.

The need to treat bilateral and recurrent tumors puts VHL-patients at risk for the development of ESRD, requiring eventually dialysis or renal transplantation. Moreover, immunosuppressive therapy could predispose patients to further tumor recurrence. In a review of renal transplantations in VHL-patients, no statistically significant differences in graft and patient survival or renal function were seen compared to non-VHL-patients; the risk of recurrence was limited.[5]

We described the case of a surgically treated bilateral renal lesion with a subsequent bilateral recurrence, that was managed with repeat nephron-sparing treatment to preserve both renal units.

Due to the large size and surgical complexity, PN was necessary at first diagnosis to remove the left renal lesion on the bench, with subsequent autotransplantation in the right iliac fossa. When recurrence was detected a repeat PN was performed. Non-surgical ablative therapy is the first choice in this clinical setting (as perfomed for the other recurrent nodule), but was not feasible in this case due to the location of the recurrence (Fig. 2A). Post-surgical decline of renal function to CKD stage III occurred, but the patient avoided the need of dialysis.

Progression to ESRD would have been likely if radical nephrectomy was performed.

This is to our knowledge the first reported case to show the feasibility of repeat PN in a case of recurrence of VHL-associated RCC in an autotrasplanted kidney. Surgery should be performed in selected patients with imperative indications in centres with extensive experience with partial nephrectomy and renal transplant since the benefits potentially outperform the risk of surgical complications, such as haemorrhage and urinary leakage.

Conclusion

Based on our experience, treatment of bilateral renal lesions in patients with VHL-associated RCC with a high risk of recurrence should be carried out in experienced centres with high surgical volume. Oncologic and functional outcomes should be balanced. Repeat NSS is feasible in selected cases even for recurrences in autotransplanted kidneys when minimally invasive percutaneous tumor ablation is not indicated.

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