

Bilateral Renal Adenocarcinoma Associated with Von Hippel Lindau Disease: A Case Report

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Abstract

Case Report

The von Hippel-Lindau (VHL) is an autosomal dominant disease predisposing to the development of various tumors (hemangioblastomas central nervous system and retina, endolymphatic sac tumors, clear cell cancer or renal cysts, pheochromocytoma, cysts or tumors pancreatic, epididymal cystadenoma). We report here a report case of a man aged 57 who present bilateral renal clear cell carcinoma. This patient underwent a bilateral tumorectomy three-month intervals between the two interventions. The postoperative evolution was favorable with a 24-month decline without local recurrence.

Keywords: Von-Hippel-Lindeau ; Adenocarcinoma ;Kidney.

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INTRODUCTION

Von Hippel-Lindau (VHL) disease is an inherited disease predisposing to the development of richly vascularized benign and malignant tumors that is due to germline mutations in the VHL tumor suppressor gene. Major clinical manifestations include CNS and retinal hemangioblastomas, endolymphatic sac tumors, clear cell cancers and renal cysts, pheochromocytomas, cysts, and pancreatic endocrine tumors [1]. Oncogenetic consultation of one or more affected subjects and then of family members allows the detection and screening of mutations in the VHL gene and the identification of subjects predisposed to this disease. In this article we

present the clinical case of a patient with bilateral RCC in the context of VHL disease.

Observation: This is a 57 year old patient with a family history of a brother who died of a renal tumor and his sister operated for a brain tumor, the patient accuses of isolated chronic bilateral low back pain. The clinical examination showed tenderness in both flanks.

Biologically, the renal function was normal. It was completely normalized after a small deterioration after the clamping of the 2nd operation.

Radiologically, the abdominal CT scan showed two bilateral renal tumors in each kidney with cortical cysts. (Fig. 1A, 1B, 1C),

(1A)



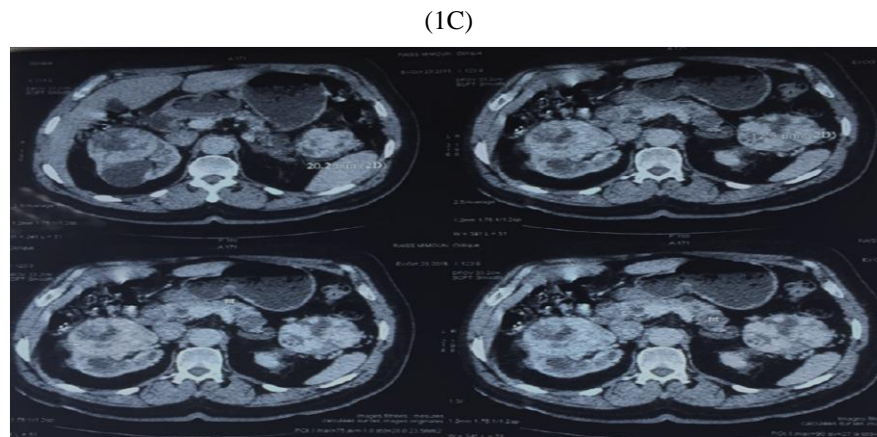
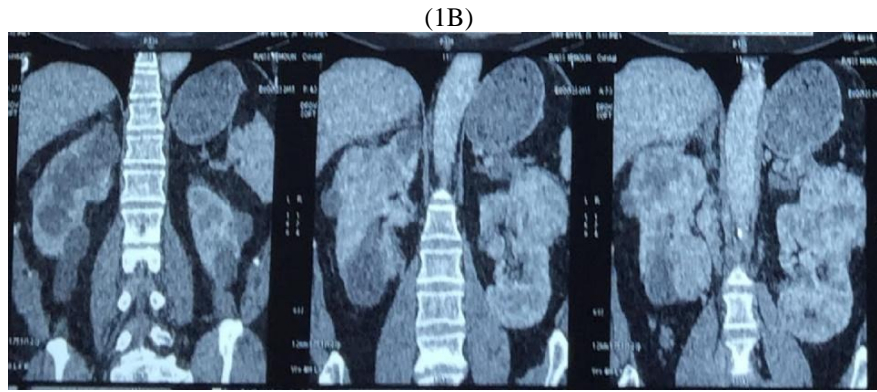


Fig-(1A, 1B, 1C): Sagittal (1A), Frontal (1B), and Axial (1C) Sections of Abdominal CT Scan with Contrast Injection (PDC) Showing a Bilateral, Multi-Lobulated Renal Tumor Process Enhancing Heterogeneously with Cortical Cysts

The diagnosis of VHL disease was evoked, we completed by a brain CT which was normal. Our patient was not tested for the VHL gene. The treatment consisted of a bilateral open tumorectomy with a three-month interval between the two procedures. Histological examination of the surgical material led to a diagnosis of renal clear cell carcinoma. (Fig-2) (Fig-3) The postoperative follow-up was simple with a 12-month follow-up without recurrence.

- A small nodule of 1cm of dirty grayish appearance with presence of areas of hemorrhagic remodeling and a Führmann grade of 1.
- A medium nodule of 7 x 5.5 x 4cm and a large nodule of 8 x 6.5 x 5.5cm, with a polychromatic appearance on section with orange-yellow areas, areas of haemorrhagic changes and a Führmann grade of 2.



Fig-2: Macroscopic appearance of three nodules of the enucleo-resection of the left renal tumor well circumscribed by a thin capsule with a total weight of 260g :

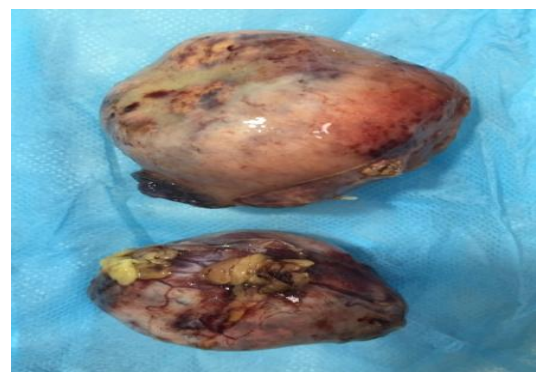


Fig-3: Macroscopic appearance of two tumor masses on the right side, one weighs 63g and measures 7 x 6 x 4cm and the other weighs 120g and measures 8 x 8 x 4.5cm, they are surrounded by a fibrous capsule. On section, almost similar aspect, fleshy, sulphur yellow, and in places greyish, with haemorrhages, with a yellowish focus of necrosis in the center of the small mass and a focus of fibrosis in the large mass.

DISCUSSION

VHL disease is a rare hereditary phacomatosis; its incidence fluctuates from 1/36000 to 1/45500 births. It is an autosomal dominant disease with high penetrance (95% at 60 years of age), for which a single gene is responsible: the VHL gene located on the short arm of chromosome 3 (3p25-p26) [2]. It associates retinal and central nervous system hemangioblastomas (60-80%), renal adenocarcinomas and cysts (30-60%), pancreatic cysts and tumors (30-70%), pheochromocytomas (10-20%), endolymphatic sac tumors (2-11%), epididymal cystadenomas (20-50%) (Fig-4) [3].

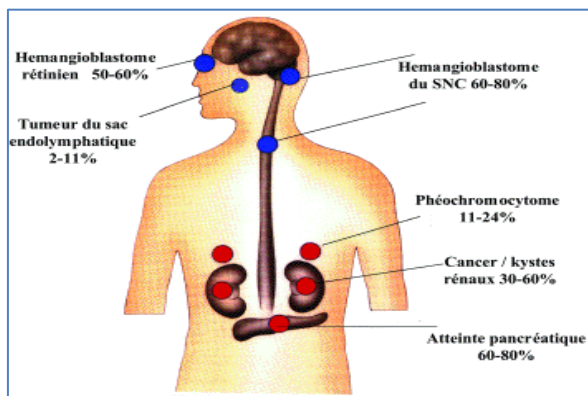


Fig-4

In adults, CRCC accounts for about 3% of all cancers and 85% of all primary renal malignancies [4], they are hereditary in about 5%, VHL accounts for 75% of the hereditary forms [5]. The CRCC and cysts in VHL disease are characterized by multicentricity and bilateral localization in > 75% of patients [6,7]. The median age at presentation is 10-20 years earlier than the age indicated for sporadic renal disease [8]. CRCC and cysts often remain asymptomatic for long periods [9,10]. The standard method for detecting renal involvement in patients with VHL is abdominal CT with contrast injection [11]. Treatment of VHL disease depends on the location, size of the tumor, and associated cyst. [12] currently, there are no definitive guidelines regarding the surgical timing approach for these multiple, bilateral tumors. However, the primary goal of treatment should be carcinological control, rather than cure, as well as preservation of functional parenchyma to avoid morbidity associated with renal or adrenal loss. A series of studies have reported that the majority of CRCCs in VHL have low pathological content [13], progressive growth [14] and do not metastasize to a diameter of 3 cm < [15]. Therefore, an isolated renal lesion can be maintained under regular surveillance until it reaches 3 cm in diameter [16].

Several authors have shown a correlation between increasing tumor size and the risk of metastasis in VHL, leading to a general recommendation to use a diameter of 3.0 cm for surgical resection [17, 18, 19-

20]. This strategy results in a recurrence-free survival rate of 76% at 5 years and 20% at 8 years [19].

In contrast, the study by Neumann *et al* [21] did not detect metastatic spread below a size of 7 cm in diameter. A literature review focusing on tumor diameter revealed that cases with metastasis are almost exclusively in the range of 45 to 110 mm [21, 17, 22, 23]. These conflicting data may indicate that the development of metastasis in VHL disease-associated CRCC is different from that of sporadic CRCC.

Partial nephrectomy and enucleation have evolved as effective alternatives to radical nephrectomy. [24]. Because CRCC lesions are often small and multiple enucleation may also be justified in order to preserve the renal parenchyma, Intraoperatively, co-existing cysts should be aspirated to facilitate subsequent follow-up. [25] Laparoscopic partial nephrectomy appears to be similar to open partial nephrectomy in carcinology. [26] Percutaneous radiofrequency thermoablation PRFA will be a promising treatment for patients who cannot undergo surgical procedures, not only for carcinological purposes, but also preservation of renal function, as much as possible. PRFA can cause thermal injury to neighboring organs such as the intestine that are 5 mm from the CRCC [27]. Radiofrequency ablation may be indicated for small renal tumors <4 cm, especially in metastatic CRCC. [28] Tyrosine kinase inhibitors such as Sunitinib and Pazopanib directed against VEGF and other pro-angiogenic pathways are an approved treatment for metastatic CRCC [29,30]. These promising results led to the opening of a pilot trial of Pazopanib in VHL patients with measurable lesions, which is actively underway [31].

Half-dose sorafenib is comparable to sunitinib in oncologic outcome and long-term stability, with relatively few complications. [32] Sunitinib has acquired an important role in the treatment of sporadic metastatic renal cell carcinoma. Several studies and clinical cases suggest that sunitinib may be effective in patients with metastatic renal cell carcinoma in VHL disease [33].

CONCLUSION

The management of patients with VHL disease requires a multidisciplinary approach that includes a genetic counselor, neurosurgeon, medical oncologist, urologic surgeon, and ophthalmologist in addition to robust psychosocial support and strict lifestyle for patients and their families. Treatment should be as conservative as possible. Anti-angiogenic therapy represents the most recent development in the management of CRCC in VHL disease

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