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NEPHRON SPARING SURGERY FOR RENAL CELL CARCINOMA IN VON HIPPEL-LINDAU DISEASE

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ABSTRACT

Purpose: We evaluated the technical feasibility and followup outcomes of a nephron sparing operation for localized renal cell carcinoma and von Hippel-Lindau disease.

Materials and Methods: Our 5 patients underwent initial nephron sparing surgery followed by serial computerized tomography.

Results: All but 1 renal lesion was resected in 9 initial nephron sparing operations. Postoperative computerized tomography revealed 35 lesions of which 8 had enlarged. Four patients underwent secondary renal surgery and adequate renal function was preserved.

Conclusions: Even with the high risk of local recurrence nephron sparing surgery is an appropriate approach for these patients.

KEY WORDS: kidney; carcinoma, renal cell; hereditary diseases

von Hippel-Lindau disease, which is a phakomatosis, is genetically transmitted in autosomal dominant fashion with various penetrance reaching nearly 100% with advancing age.[1] Manifestations of this disease include retinal angioma, central nervous system hemangioblastoma, pheochromocytoma, renal cell carcinoma and cysts of the kidney, pancreas, liver and epididymis.[2] Renal cell carcinoma develops in approximately 25 to 45% of patients with this disease. Although nephron sparing operations have been advocated for the management of renal cell carcinoma in association with von Hippel-Lindau disease due to young patient age, common multicentricity and bilaterality, these carcinomas can sometimes metastasize and are a major cause of death. We report our experience with nephron sparing surgery in 5 patients with von Hippel-Lindau disease to justify the validity of this surgical approach for localized renal cell carcinoma. Furthermore, we evaluate and review the substantial role of serial computerized tomography (CT) of these patients at followup.

MATERIALS AND METHODS

From 1988 to 1991, 6 patients from 3 families with von Hippel-Lindau disease were treated at our institution for renal cell carcinoma. Of these patients 1 initially had advanced renal cell carcinoma, was not a candidate for nephron sparing surgery and is not included in the study. Median age of the remaining 4 women and 1 man at the diagnosis of renal cell carcinoma was 36 years (range 35 to 60). Four patients had bilateral synchronous renal cell carcinomas and 1 had unilateral multicentric cancer. All patients had a history of surgery for retinal angiomas and/or central nervous system hemangioblastomas.

The diagnosis of renal cell carcinoma was initially made by excretory urography, ultrasonography and CT of the abdomen. At diagnosis no patient had evidence of metastatic disease as determined by physical examination, chest x-ray or CT, or nuclear bone scanning and abdominal CT. Patients underwent preoperative selective renal angiography to identify other lesions and plan operative strategy. Nine initial nephron sparing operations were performed in the 5 patients.

Followup included physical examination, renal function tests, chest x-rays and CT, and abdominal ultrasonography or abdominal and pelvic CT to detect any occult recurrences or metastasis. In particular, serial abdominal and pelvic CT was performed at 3 to 6-month intervals after nephron sparing surgery. The size of the renal lesions detected on CT was measured by hand-held calipers. A qualitative description of the degree of enhancement of each lesion was recorded. The growth rate of each lesion was calculated as the length it had enlarged in 1 year. In addition, lesions were classified as cystic or solid according to Hounsfield value.

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RESULTS

Initial clinical information and treatment for renal cell carcinoma (table 1). Nephron sparing surgery was successful in these 5 patients. Patient T. K. with unilateral tumors underwent extracorporeal partial nephrectomy with autotransplantation of the renal remnant because of difficulty in the identification of deep intraparenchymal tumors. Bilateral renal surgery through subcostal transverse or midline incisions to allow bilateral exploration was performed in the remaining 4 patients of whom 3 underwent in situ partial nephrectomy and/or enucleation of 1 kidney, and extracorporeal partial nephrectomy with autotransplantation of the renal remnant in the contralateral kidney to explore and completely excise renal lesions (fig. 1). The intent of surgery was to excise tumors and cysts while sparing normal parenchyma. Formal regional lymph node dissection was not performed at partial nephrectomy. Initial mean preoperative serum creatinine level was 0.5 mg./dl. (range 0.4 to 0.7). No acute tubular necrosis developed and serum creatinine levels 1 month after initial nephron sparing surgery were within normal limits (mean 0.7 mg./dl., range 0.6 to 0.7).

A total of 16 right and 17 left tumors was resected. On gross pathological inspection the maximum tumor in each patient ranged from 3 to 7.5 cm. in diameter. Pathological evaluation of tumor specimens revealed pure clear cell carcinoma confined to the renal capsule (stage T2) in 4 patients and microscopic invasion into the adjunct kidney and perinephric fat (T3a) in 1. The highest histological grade of tumor in each patient was 1 in 2 and 2 in the remaining 3.

Followup examination and outcome. Median followup was 61 months (range 40 to 82). Patient T. K. with initially unilateral tumors had no local recurrence in the kidney treated

TABLE 1. *Patient characteristics at initial surgery*

Pt.—Sex—Age at Initial Diagnosis (yrs.)	No. Tumors		Maximum Tumor Size (cm.)	Surgical Method		Serum Creatinine (mg./dl.)		Maximum Pathological Grade/Stage
	Rt.	Lt.		Rt.	Lt.	Preop.	1 Mo. Postop.	
YN — F — 35	2	1	7.5	In situ partial nephrectomy	Extracorporeal with autotransplantation	0.5	0.6	1/T2
TK — M — 52	0	2	3		Extracorporeal with autotransplantation	0.7	0.7	2/T2
YK — F — 60	1	2	6	Extracorporeal with autotransplantation	In situ partial nephrectomy	0.5	0.6	2/T3
YI — F — 36	4	8	5	Extracorporeal with autotransplantation	In situ partial nephrectomy	0.5	0.7	1/T2
AK — F — 35	9	4	5	In situ partial nephrectomy	In situ partial nephrectomy	0.4	0.7	2/T2

Renal cell carcinoma was of the clear cell type in each patient.

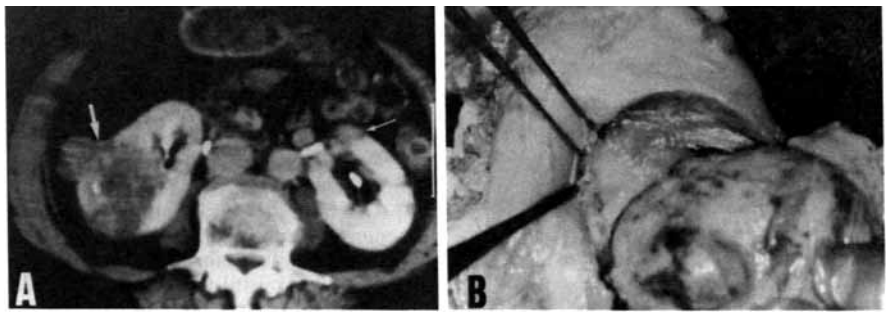

FIG. 1. CT of bilateral renal cell carcinoma in patient Y. K. *A*, right (large arrow) and left tumors (small arrow). *B*, large tumor in right kidney was resected by extracorporeal partial nephrectomy with autotransplantation of renal remnant.

by nephron sparing surgery and no new lesions although a cystic lesion developed in the contralateral kidney at 74 months postoperatively. In contrast, the remaining 4 patients with initially bilateral tumors had local recurrence (35 evaluable lesions). According to CT criteria 31 lesions (86%) were cystic and 5 were solid (14%). These lesions developed at a median followup of 24 months (range 1 to 57) after the initial nephron sparing operation. Of 31 cystic lesions 28 (90%) remained stable during followup and were less than 1 cm. in diameter. The remaining 8 lesions, including 3 cystic and 5 solid, enlarged for 7 to 45 months (fig. 2 and table 2). The 3 cystic lesions enlarged without any change in the density of the cystic fluid or wall thickness (fig. 3). Of the 5 solid lesions 4 (the remaining lesion was missed at initial surgery) began as tiny foci within the renal parenchyma and gradually grew. During growth the CT appearance did not change; attenuation of the lesion remained higher than that of water and it enhanced uniformly with contrast medium (fig. 4). Mean growth rate in the diameter of 8 lesions was 0.534 ± 0.217 cm. per year (range 0.264 to 0.9). There were no significant differences in mean growth rates between cystic and solid lesions (0.656 ± 0.259 cm. per year and 0.540 ± 0.206 cm. per year, respectively).

The 4 patients initially treated with bilateral nephron sparing surgery underwent repeat renal operations. Patients Y. K. and Y. I. underwent unilateral radical nephrectomy at 35 and 40 months postoperatively, respectively, and patients Y. N. and A. K. underwent repeat partial nephrectomy with complete removal of the local recurrences. In patient Y. N. in situ enucleations were done at 38 months postoperatively for the left kidney initially treated with extracorporeal partial nephrectomy with autotransplantation. In patient A. K. extracorporeal partial nephrectomy with autotransplantation was performed 77 months postoperatively for the right kidney initially treated with in situ partial nephrectomy. There was no distant metastasis in any case at repeat renal surgery. Pathological examination of the 6 enlarged resected lesions (3 solid and 3 cystic) revealed that 3 solid and 1 cystic

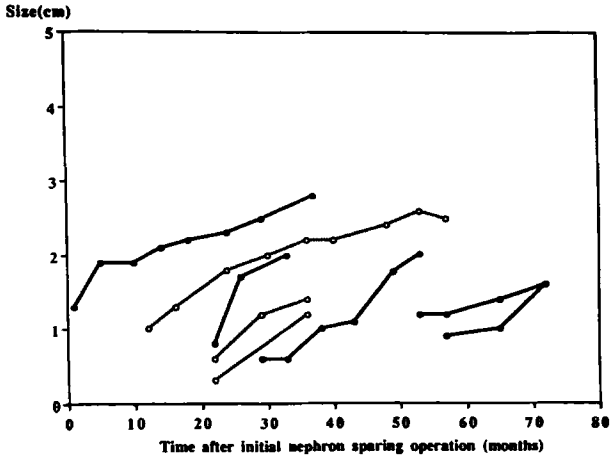

FIG. 2. Growth of solid (●—●—●) and cystic (···○···) renal lesions after initial nephron sparing operation.

tumors were grade 1 pure renal cell carcinoma and the remaining 2 cystic lesions were simple renal cysts not lined by clear cells.

Patients Y. K. and A. K. remain free of tumor at 40 and 61 months, respectively, after initial nephron sparing surgery. Patients Y. N. and Y. I. have recurrent local tumors in the contralateral kidney at 57 and 82 months postoperatively, respectively. Mean serum creatinine level at last followup was 1.1 mg./dl. (range 0.7 to 1.6). No patient has required dialysis at any stage of the disease.

DISCUSSION

Since the first report by Kernohan et al that the renal component of von Hippel-Lindau disease may be a malignant