ADENOMA OF THE KIDNEY. REPORT OF A CASE WITH A DISCUSSION OF ITS RELATIONSHIP TO CARCINOMA (HYPERNEPHROMA)

C. D. CREEVY, M.D.

(From the Department of Surgery and the Cancer Institute, University of Minnesota)

INTRODUCTION

Adenoma of the kidney as a clinical entity is rather rare. In most of the recorded cases the diagnosis of adenoma is based upon histologic examination and in many instances is supported by the survival of the patient many years after the removal of the tumor. It is noteworthy that there is often a striking similarity between the cellular structure of carcinoma (hypernephroma) and adenoma of the kidney.

The case described below presented a small circumscribed tumor of the renal cortex with symptoms very early in its course, as a result of ulceration into an adjacent calyx. The histologic structure corresponds with that of typical carcinoma of the cortex (hypernephroma), but the macroscopic appearances suggest a benign tumor.

CASE REPORT

A.S., University Hospital No. 49211, an unmarried female of twenty-four, was admitted on Sept. 20, 1929. She complained of a recurrent and disabling pain in the left renal area of two months' duration, associated with gross hematuria. The tonsils, the appendix, and the gall-bladder had been removed elsewhere, before the onset of the present trouble.

Physical examination revealed a robust young woman with two laparotomy scars. The morphology of the blood was normal. The urine, whether voided naturally or obtained by catheterization, contained large numbers of red blood cells. The urea nitrogen of the blood was 15 mg. per 100 c.c. X-ray examination of the chest and of the urinary tract showed nothing unusual.

At cystoscopy, bloody urine issued from the left ureter. The indigo carmine excretion was normal and equal on the two sides, and the specimens of urine from the kidneys were free from pus and from tubercle bacilli. The right pyelogram was normal. That on the left showed partial obliteration of an upper minor calyx, which assumed a triangular
outline (Fig. 1). The significance of this minor change was not appreciated. A diagnosis of "essential hematuria" was made.

Lavage of the left kidney pelvis with silver nitrate was done repeatedly without benefit. On several subsequent occasions, pus but no tubercle bacilli were found in the urine from the left kidney. Several guinea-pig inoculations were made, with negative results. Three subsequent pyelograms were identical with the first. A course of x-ray therapy, as suggested by Hager, was given without relief.

On Nov. 29, 1929, the left kidney was exposed under spinal anesthesia. It was normal except for fetal lobulation. Decapsulation was done. Pain was relieved for one month, but then recurred, together with
hematuria. Repeated lavage of the pelvis and dilatation of the ureter were without results.

On June 19, 1930, the left kidney was again exposed. Except for a small aberrant vessel to the upper pole and fetal lobulation, it appeared normal. Nevertheless, nephrectomy was done. On section (Fig. 2)

![Image](image_url)  
**Fig. 2. The Kidney in Longitudinal Section Split at Its Medial Margin**  
The pyelographic findings (Fig. 1) are explained.

there was found beneath the upper major calyx a firm yellow encapsulated tumor which measured 3 cm. in diameter. The neoplasm had compressed the upper major calyx, obliterating its terminal portion and encroaching upon the pelvis, producing the deformity noted in the pyelogram. There was a small area of ulceration through the pelvic mucosa, which accounted for the hematuria.
Sections of the whole tumor (Fig. 3) showed cords of rather large clear cells with irregularly oval, dark-staining nuclei. The cytoplasm had a foamy appearance. The cells were arranged in tubules simulating those of the normal kidney. In some areas there were solid masses of cells without lumina. The stroma was scanty and consisted of fine connective-tissue cells with relatively few blood vessels. The entire tumor had a definite but rather thin fibrous capsule, adjoining which there was some compression of the normal kidney substance.

![Fig. 3. Photomicrograph of the Tumor, Low-power View](image)

Note the resemblance to adult renal tubules.

**Review of the Literature**

Renal adenoma has escaped most of the controversy which has involved the other epithelial neoplasms of the kidney. Sturm in 1875 differentiated the solitary adenoma of the otherwise normal kidney from the multiple adenomata of the arteriosclerotic organ. Weichselbaum and Greenisch subsequently separated alveolar and papillary types of the solitary form, while Ricker distinguished a tubular variety.

Ewing has described the solitary adenoma with which this paper is concerned as a small, encapsulated, grayish to yellow tumor,
situated usually in the cortex of the kidney. The papillary variety, which appears to develop in a cyst by proliferation of its lining epithelium, consists of connective-tissue papillae each covered by a layer of cuboidal or cylindrical epithelium the cells of which may be small, granular, and opaque, or large and clear with granules of doubly refractive lipid. The alveolar type is composed of large, cylindrical or cuboidal cells, which often contain fat droplets and are arranged in alveoli with lumina. The tubular variety consists of long irregular canals lined by small fat-free cells with large nuclei. The stroma is vascular.

The histogenesis of these tumors is not clear. It is generally conceded that the multiple adenomata represent a proliferative response to gradual vascular occlusion. Turley and Steel have sought to trace their origin to the glomeruli. Albarran has called attention to the presence in many kidneys of islands of imperfectly developed and displaced tubules, originating presumably in some aberration of fusion. He regards these as the precursors of adenomata.

The dividing line between benign and malignant adenoma on the one hand and carcinoma (hypernephroma) on the other is not sharply drawn. Ewing believes that transitions from benign to malignant adenoma are common and suggests that subsequently carcinoma may develop in these lesions. He states, however, that the question has not been settled. In some instances, adenomata have been reported as malignant solely upon a histologic basis (Squier, Judd and Grier); in others metastases have been found at autopsy (Eisenstaedt); while Frontz has recorded a case in which nephrectomy for an apparently benign papillary adenoma was followed by local recurrence.

Further evidence of the difficulty in separating sharply the various epithelial neoplasms of the kidney is to be found in the literature. Sudeck, as early as 1893, suggested that the Grawitz tumors (hypernephroma of Birch-Hirschfield) arose from pre-existing adenomata. He was led to this conclusion by the striking similarity between the cells of the two types of neoplasms. Oberzimer has recently emphasized this similarity.

Many observers have supported the theory that the so-called hypernephroma is in fact renal rather than adrenal in origin. Stoerck and Zehbe believed that hypernephroma arises in the adenomas of sclerotic kidneys. Sisson, Adami, and Wilson and Willis have all favored the idea of renal origin.
Adami proposed calling both renal and adrenal neoplasms mesotheliomata, explaining their varying cellular characteristics by their varying rate of growth. Wilson and Willis suggested that the Grawitz tumors arose in islands of renal blastema cells misplaced in the kidney cortex and stimulated to unrestrained growth by some factor such as trauma. Since during the course of embryonic development the histologic character of the kidney varies from that of very cellular connective tissue to that of highly differentiated epithelium, one could thus explain the relationship of tumors sometimes classed as sarcomata to those more obviously epithelial in origin. For these reasons, Bell, Young, and others have suggested that the comprehensive term "nephroma" be applied to epithelial neoplasms of the kidney.

Evidence tending to support the idea of a relationship between carcinoma (hypernephroma) and adenoma is found in a case of Nicholson. He recorded an instance in which a tumor of the kidney removed at operation had the typical histology of carcinoma. A recurrence developed six months later in the operative scar. At autopsy it was found that this recurrence had everywhere the characteristic microscopic form of a papillary adenoma.

This view has received strong confirmation from the case of Gray, who described a kidney tumor found at necropsy in which there were areas having the appearance of hypernephroma, others having the structure of papillary adenoma, and still others in which the cells and their arrangement suggested both tumors. These various areas graded imperceptibly into one another.

Foulds, Scholl and Braasch have called attention to the similarity between hypernephroma and alveolar carcinoma and have suggested that the former be called adenocarcinoma of the kidney. They hold that the alveolar carcinoma is simply a less differentiated and more malignant variant of the adenocarcinoma or hypernephroma, a contention recently supported by Judd and Grier.

Adenoma of the kidney as a clinical entity is uncommon. It was an accidental autopsy finding in 8 of 500 cases reviewed by Hefke at the Mayo Clinic. It was found but twice in a series of 57 neoplasms reported by Ljunggren and was absent from Hyman's series of 40 cases. Kretschmer and Doehring were able to collect but 17 instances from the literature in which an adenoma had attained sufficient size to permit a preoperative diagnosis of renal
neoplasm. In no instance has the diagnosis of renal adenoma been made preoperatively with certainty.

The literature has been reviewed by Kretschmer and Doehring and by Judd and Simon. Their data are of but little assistance in enabling one to make a clinical diagnosis without exploration. Reviewing their cases, one finds that the lesion occurred in the "cancer age." There was no sex predilection. The duration of symptoms varied from a few days to a maximum of eleven years. Pain was a feature in but half of the cases; hematuria occurred in a slightly higher percentage. The only symptom common to all was palpable tumor. This was to be expected, since all the writers were interested in large neoplasms. The largest tumor encountered by the author was that described by Gordon-Taylor, which weighed 22 pounds (10 kg.). The pyelographic findings in the few cases in which they were reported could be considered as diagnostic only of renal neoplasm. The usual treatment was nephrectomy. One patient was reported as well at five years, three each at nine years, and three at ten years after nephrectomy, while the patients of Kretschmer and Doehring and of Cunningham were well four and two years respectively after resection of the tumor.

A long postoperative survival is not convincing evidence of the benign nature of a tumor. Ljunggren was able to find in the literature and in his own series of Grawitz tumors eight patients who had died of recurrence or metastasis seven or more years after nephrectomy.

DISCUSSION

The case here reported presents several points of interest. It produced disabling symptoms before the pyelographic changes could be identified and so led to a long and unsatisfactory trial of the measures usually employed in the treatment of essential hematuria. Exploration revealed an apparently normal kidney which, upon removal, was found to contain a small tumor. The structure and situation of the tumor may shed some light upon the relationship of carcinoma (hypernephroma) and adenoma of the kidney.

The diagnosis of "essential hematuria" is most unsatisfactory. So vague a diagnosis should challenge the surgeon to follow his patient carefully in order to eliminate the possibility of error. In
this instance, long and painstaking study and conservative therapy led only to the conclusion that a definite lesion existed in the left kidney. The deformity in the pyelogram attracted attention early but was interpreted as sclerosis of inflammatory origin. Exploration of the kidney did not reveal the true nature of the lesion. In spite of the normal appearance of the kidney, it was removed. It should be emphasized that the removal of an apparently normal kidney is warranted only after careful and prolonged study, and after conservative therapy has failed.

The location of the tumor deep in the cortex led to early ulceration into the pelvis with bleeding, a symptom which attracted attention while the tumor was still very small. Its deep situation is against the idea of origin from adrenal rests since these are usually subcapsular.

The histologic structure corresponds exactly to that of typical hypernephroma or carcinoma of the cortex except that the individual cells are wholly "benign" in appearance. That is, the nuclei are small; nucleoli are lacking; there are no mitotic figures; the cell margins are distinct; their arrangement is orderly. Ewing's description of alveolar adenoma corresponds to the microscopic appearance of this lesion.

The situation of the tumor deep in the cortex, its small size, and complete encapsulation offer no suggestion of malignancy. Nevertheless, one cannot avoid the suspicion that, left to itself, this tumor would in time have developed into a typical malignant epithelial neoplasm of the kidney.

**Summary and Conclusions**

The occurrence of an unusually small tumor of the kidney with disproportionately severe symptoms has been reported. The symptoms were due to the proximity of the tumor to the renal pelvis. This situation produced a pyelographic deformity which was not recognized. Careful preoperative study and failure of conservative management indicated nephrectomy in spite of an externally normal kidney.

The gross appearance and situation of the tumor were those of an adenoma, while its histologic character was that of a typical carcinoma of the cortex, facts which suggest a close relationship between adenomata and the malignant epithelial tumors of the kidney.
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BIBLIOGRAPHY


RICKER: Quoted by Ewing.


