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UROLOGY 2

EDITED BY

MEREDITH F. CAMPBELL, M.S., M.D., F.A.C.S.

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Late Professor of Urology, New York University, and Consulting Urologist, Bellevue Hospital, New York

AND

J. HARTWELL HARRISON, M.D., F.A.C.S.

Cutler Professor of Surgery (Urology), Harvard Medical School, and Chief of Urology, Peter Bent Brigham Hospital, Boston

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VOLUME

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IX TUMORS OF THE UROGENITAL TRACT

X NEUROMUSCULAR DISEASE OF THE URINARY TRACT

XI EMBRYOLOGY AND ANOMALIES OF THE UROGENITAL TRACT

UROLOGY

VOLUME

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TUMORS OF THE UROGENITAL TRACT

CHAPTER 24 of self aword need

Tumors of the Kidney

Clyde L. Deming, M.D., and B. Marvin Harvard, M.D.

All tumors of the kidney are considered malignant until they are proved to be otherwise by direct vision and by histological examination. Actually, about 85 per cent of all renal tumors are neoplastic. The degree of malignancy varies with the specificity of tissue from which the tumor arises, because each tissue sets a standard of its own for biological growth and behavior. Tumors arise from any and all the components of the renal organ, from embryonic anlagen on, and in the kidney and from the connective tissue and nerve tissue about the hilum. The fact that the kidney passes through three stages of embryological development offers opportunities for the inclusion or accession of anlagen that manifest themselves later in tumefaction. The confusion between carcinoma and sarcoma has been prominent in many reports. It is true that mixed tumors do occur and that some tumors possess the characteristics of both epithelial and mesothelial elements. However, with the use of special stains for specific tissues, many of the controversies have been settled. Nevertheless, the complexity of the tissues composing renal neoplasms and the effect

of their biological behavior on the prognosis promote the keenest interest in the minds of the general practitioner, the urologist, the pathologist, and the on-

cologist.

Konig's gross description of kidney tumors in 1826 (cited by Carson, 1928) remains a monument to his keen observation. The credit for demonstrating tubular epithelial proliferation which destroyed and invaded the membrana propria and was followed by cancerous nodulation belongs to Robin in 1885. Weichselbaum and Greenish in 1883 described adenomas containing both papillary and alveolar types of growth. To Eberth in 1872 we owe much of our early knowledge concerning the tumors of the wolffian body. Wilms, in 1882, gave a classic description of the embryoma that was designated by his name but that will now be termed nephroblastoma. Birch-Hirschfeld coined the term "hypernephroma" in 1883. Tuffier (1914) recognized alterations in sex characteristics in suprarenal tumors in contradistinction to the hypernephroma. The extensive writings of Albarran and Imbert (1903) and the four volumes of Wolff (1928) represent masterpieces on this subject. The British clinics, especially the London Cancer Clinic, have contributed greatly. In America, Ewing commanded respect for his understanding of renal neoplasms. From the Mayo Clinic, the Rockefeller Institute, and from many individuals has come valuable information. The Armed Forces Institute of Pathology has recently done much to correlate and crystallize the present knowledge of renal tumors.

Incidence. Although kidney tumors occur throughout the span of life, they are seen most frequently in the first and sixth decades. They are the least common in the teen-age group. In Deming's series of 150 cases, 13.5 per cent were encountered in children under ten years of age. Rarely are they recorded in the second decade of life, and there are scattered reports of cases found in the third and fourth decades. The average age is 56 years for the females and 58 years for the males. The right and left sides are about equally involved. The male sex is favored by a ratio of 2 to 1 in the adenocarcinomas, but in some of the benign tumors such as the fibroma the female shows the advantage of a ratio of 4 to 1. In children both sexes are equally involved. The races are equally subject to renal tumors, and the geographical distribution does not show any variation.

Etiology. The cause of renal tumors remains an unsolved problem. In this brief background summary it becomes apparent that many factors may possibly be involved in the development of a kidney tumor. Local trauma, though often calling attention to the presence of the lesion, cannot be implicated as a cause. Steiner's studies appear to indicate that neither race nor geography plays a significant role in causing kidney cancer. Heredity as a factor has been suggested (Brinton), but reported cases are few (Riches) and may merely represent chance occurrence. Gross' (1963) concept of oncogenic viruses existing in a latent state in one individual and being transmitted unknown to another-for example, from parent to child-may

represent a plausible explanation for those tumors thought to be hereditary. It must be remembered, however, that other common factors in a family background such as hygiene and diet must be considered here. That adenocarcinomas of the kidney can be produced in experimental animals by viruses has been proved conclusively by Lucké (1938, 1952), Oberling, Chesterman and Negroni, and many others. It has long been known that papillomas of the bladder can be caused by viruses and, because the epithelium of the renal pelvis is histologically and biologically indistinguishable from that of the bladder, presumably papillary tumors of the renal pelvis may also be caused by viruses. Kirkman and Bacon (1952) clearly demonstrated that bilateral renal adenocarcinomas can be induced in hamsters by administration of synthetic estrogen (stilbestrol). Bloom and Wallace, in support of their belief that there is a gonadal factor in the production of renal adenocarcinoma, point out that the tumor is found more often in men, that the majority of such tumors found in women occur after the menopause, and that spontaneous regression of renal adenocarcinomas has been reported eight times more often in men than in women; further, that the estrogen-induced hamster tumors occur primarily in males or castrated females and that tritium labeled stilbestrol administered to hamsters was found to be concentrated in significantly higher quantities in the kidneys of the male than in the female animals. One is constrained to observe, however, that hormonally induced cancers in hamsters are almost invariably bilateral, whereas in humans bilateral renal adenocarcinoma is extremely rare. Chemical carcinogens have long been known to cause cancer in experimental animals. The early work of Ilfeld and later studies by Leary and by Hieger have implicated cholesterol, either alone or in combination with some other substance, as being the possible source of both epidermoid carcinoma and renal cortical adenomas. Methylcholanthrene

has also been used to produce epidermoid carcinomas and sarcomas in the kidneys of rodents. These are but two of 30 substances listed by Pavone-Macaluso as having been studied by various investigators for their carcinogenic effect on the kidneys of laboratory animals. Recently, Staszewski has shown an increased incidence of bladder tumors in male smokers; presumably this observation may be expanded to include all urothelium. Ionizing radiation (Koletsky and Gustafson; Rosen and co-workers; Berdjis) has been shown to cause renal adenomas, adenocarcinomas, and transitional cell tumors in rats, whereas Rosen and Cole found that the incidence of tumors was further increased following unilateral nephrectomy before irradiation.

Classification. CLINICAL. The tumors of the kidney are divided into two categories-the benign and the malignant.

Benign tumors. The benign tumors with few exceptions are small, often multiple, and usually are found at autopsy. Because these are small and cause few or no symptoms, they were given little significance. However, they are of importance because some are precursors for malignant growths. A few benign growths develop into large tumors and give rise to symptoms such that they cannot be differentiated clinically from malignant tumors. The nodule's may be fibromas, lipomas, angiomas, adenomas, adrenal rests, and cysts. There are many types of cysts, single, multiple, small, and large, only a few of which are malignant. The benign tumors may be found in the capsule, cortex, medulla, or pelvis of the kidney. They do not metastasize.

Malignant tumors. These comprise about 80 to 85 per cent of the renal tumors that give clinical manifestations. They occur all during life but are most prevalent in the first and sixth decades. The epithelial tumors of the cortex and pelvis, such as the adenocarcinomas and papillary carcinomas, are found mostly

(Esmarch: Stevenson and von Haam) in adults, whereas the nephroblastoma is the most common tumor in the first decade. Sarcomas and the mixed sarcomas, such as fibrosarcoma, liposarcoma, and leiomyosarcoma, are rare but of a high degree of malignancy. Some of the adenocarcinomas grow slowly, but most of the malignant tumors grow relatively fast and develop into large tumor masses. There are several reports showing that a kidney may contain two different primary malignancies. malignant tumors metastasize readily by way of the blood stream and lymphatics, and some by invasion.

> HISTOLOGICAL. Great confusion has existed over the cellular structure of some of the malignant tumors. For instance, the epithelial tumors of the cortex are known by the names of adenocarcinoma, Grawitz tumor, hypernephroma, hypernephroid carcinoma, renal cell carcinoma, and alveolar cancer, all producing the same symptoms, having the same biological behavior, and causing death. In this description they are classified as adenocarcinoma with some variations. The Wilms tumor is not termed nephroma but nephroblastoma. Benign tumors give less difficulty in recognition by cell structure. Mixed tumors containing two or three cell structures have caused much difference of opinion, but special stains now aid in their differentiation. The classification in Table 24-1 is one now used most frequently by the clinican and pathologist and is based on the cell structure, origin, and biological behavior. The first day and and

Symptoms. Renal tumors, benign or malignant, do not cause any one sign or symptom emblematical of their existence. Forty-five per cent of all renal tumors do not give any symptom and are accidentally discovered on routine playsical examination. The old triad of tumor, pain, and hematuria is indicative of a late phase in the development of any malignant renal tumor. In poorly nourished individuals, small irregularities on the anterior surface of the kidneys may be distinguished by palpation. Tumor can be felt in 55 per cent of the

TABLE 24-1 Classification of Renal Tumors

1. Tumors of the Renal Capsule Fibroma Leiomyoma Lipoma Lipoma Discognosisi bas semos Mixed Mixed

2. Tumors of the Mature Renal Parenchyma manufaction ed lo zon

Adenoma Adenocarcinoma
(Hypernephroma) (Renal cell cancer)

(Alveolar carcinoma) 3. Tumors of the Immature Renal Parenchyma

Nephroblastoma (Wilms) Embryonic carcinoma Sarcoma

4. Epithelial Tumors of the Renal Pelvis Transitional cell papilloma Transitional cell carcinoma Squamous cell carcinoma

Adenocarcinoma

5. Cysts
Solitary
Unilateral multiple
Calyceal

galvad Pyogenic Small 941 gambuborg

ents bas Calcified ad Instantion ames ad Tubular ectasia Tuberous sclerosis Cystadenoma

Papillary cystadenoma smoles de Dermoid and smoudger bemie

Pararenal and perirenal cysts

Hydrocele renalis Lymphatic Wolffian Malignant Malignant

6 Vascular Tumors Hemangioma Hemangioma

Hamartoma Lymphangioma 7. Neurogenic

Neuroblastoma Sympathecoblastoma Schwannoma

8. Heteroplastic Tissue Tumors

Adipose officers rient to Latous desvai Smooth muscle Adrenal rests Endometriosis Cartilage Daid to somebioni bessen Bone Smokers; presumably the snod

9. Mesenchymal Derivatives

Connective Tissue Fibroma Fibrosarcoma fiscal and special transfer Osteogenic sarcoma

Adipose Tissue of the temporal and and another than the temporal and the t Lipoma er di riomut des lamolite Liposarcoma Muscle Tissue Leiomyoma Manual Park Months 100 Leiomyosarcoma

Rhabdomyosarcoma 10. Pararenal and Perirenal Solid Tumors

Sarcomas

Liposarcoma Liposarcoma Fibrosarcoma

Lymphangiosarcoma

more with lew exceptions and Lymphoblastoma Neuroblastoma Hodgkin's disease 11. Secondary Tumors

Cancer successed someroomi lo ens Blastoma World Statement of Programs Granuloma doleveb adaworg meined Thymoma and or sair pure but whom Testicular and towns yell sail

patients with renal neoplasms, but many times the tumors develop on the posterior surface of the kidney or at the upper pole where it is impossible to palpate a nodule or irregularity. Thick abdominal walls also prevent the palpation of a tumor mass. Pain is present in 50 per cent of the cases. It may be a dull, nondescript type of pain localized in the flank, or it may be sharp and excruciating due to distention of the renal capsule or to the passage of blood clots down the ureter. A patient may see bloody urine or complain of inability to urinate. Such patients develop a large

blood clot in the bladder that obstructs urination and directs attention toward the bladder rather than to the kidney as a source for the blood. The tumors of the kidney pelvis bleed early, whereas the parenchymatous tumors bleed when they penetrate the pelvis of the kidney; or, in some cases, as Patch has pointed out, the enlarging tumor causes a rupture of veins in the pelvis of the kidney rather than the tumor per se. Blood clots may take the gross form of a cast of the ureter, indicating upper urinary tract bleeding. Bleeding is usually periodic and may be initiated by quite ordinary maneuvers, such as a slight injury or even raising the hands above the head.

Gastric symptoms with varying degrees of nausea and vomiting occur. Patients with these complaints often pass through the gastroenterologist's hands with negative findings in the radiograms of the gastrointestinal tract. Nevertheless, these patients refuse to eat and continue to lose weight. General malaise, lassitude, loss of strength, and secondary anemia develop. Large tumors in children may cause obstipation and constipation.

Elevation of temperature not associated with infection is a common finding and, indeed, may be the only presenting sign. It has been variously estimated to occur in as few as 6 per cent (Melicow and Uson) to as many as 56 per cent (McCague) of patients. Weinstein et al., reviewing 1238 cases, found it elevated in 11 per cent of them. The temperature may be irregular, ranging up to 104° F., or may become more or less stable around 101 to 102° F. In children the temperature may be higher than in adults. The fever may be from intratumoral hemorrhage with absorption of hematin, toxic products of the tumor, absorption of degradation products of tumor necrosis, or metastases to the brain involving the heat center.

BLOOD PICTURE, In nonmalignant tumors, and in the early phases of malignant tumors, the hematocrit is normal. In longstanding malignant tumors and in patients who lose a large amount of blood, various stages of secondary anemia develop. An elevation of leukocytes is seen in patients who have an associated infection in the kidney, in those who have had intratumoral hemorrhage, and especially in children with nephroblastomas who suddenly develop a local spread. The leukocytosis ranges from 12,000 to 44,000 even in the absence of infection. Patients with metastases are subject to severe grades of anemia. The erythrocyte sedimentation rate (ESR) is often elevated, particularly in those patients with metastases and in whom fever is present, but a positive C-reactive protein is felt by some to be a better index of tumor activity (Holm and Pompeius). Polycythemia is present in about 3 per cent of patients with adenocarcinoma.

BLOOD PRESSURE. This is elevated in many cases of renal tumor. It is estimated to occur in 75 to 90 per cent of patients with nephroblastoma, but in adults the incidence appears to be little more than that which one would ordinarily expect for the age group in which the tumor occurs. In children the pressure returns to normal in nearly all patients after nephrectomy (Williams, 1964), but except in certain clearly defined cases (Roberts; Lampe and Crovatto) the response in adults is not as great (Gordon). The mechanism of hypertension in renal tumors is unknown, although it may be obvious in cases in which arteriovenous fistulae exist within the tumor or there is tumor obstruction of the renal artery. Whether the tumor itself secretes a substance which can cause a rise in blood pressure, or by its pressure on the renal arterial tree causes increased renin production, is speculative, anob ad bluoda mista noel

Presenting finding. Varicocele may be the presenting finding of a renal tumor and is produced by pressure of the tumor on the spermatic vein or stasis of the spermatic vein caused by the growth of the tumor into the renal vein. Such findings are reported in the child and in the adult, but they are not very common, nor are they produced by any one particular type of tumor. Large tumors in children may cause "pot belly" and distention of the accessory veins of the abdominal wall. Such experiences are now rare because renal tumors are discovered earlier than formerly, owing to frequent health examinations made in clinics and by school physicians. Occasionally a metastatic lesion from a renal malignancy may be the initial symptom. A secondary brain tumor producing neurological evidence of its presence, a metastatic chest lesion causing dyspnea and cough, or a pathological fracture of a long bone are too often the introductory symptoms of a

renal tumor, whereas the primary lesion is silent. Fever, as noted previously, may be the presenting sign. The dictum that renal tumors do not possess any charac-

teristic symptom is true.

Diagnosis. The determination of the presence of a renal tumor is usually not a difficult procedure either in the adult or in the infant patient. The visualization or the palpation in the kidney region of a tumor mass connected with the kidney is presumptive but not conclusive evidence of a renal tumor. The tumor must be demonstrated by roentgenograms produced by intravenous injection of radiopaque medium or by cystoscopy and retrograde injection of the contrast medium. A filling defect in one or more of the calyces, together with a palpable tumor or an enlarged kidney outline by x-ray, gives ample assurance of the tumor's existence. If the patient has renal pain and shows blood in the urine accompanied by typical xray findings, one can be quite positive of the diagnosis. Tumor cells may be found in the urine, and the Papanicolaou stain should be done if any doubt exists about the diagnosis.

Occasionally tumors obstruct the pelvis of the kidneys so that no shadows of radiopaque medium can be seen in the kidney pelvis even when intravenous or retrograde attempts are made to visualize the kidney. Tumors of the kidney pelvis usually bleed and may form wormlike clots, which are casts of the ureter. The large, parenchymatous tumors may bleed profusely, continuously, or interruptedly. One should not depend too implicitly on the intravenous x-ray series but should execute retrograde examination for accurate renal studies of the urine together with phenolsulphonphthalein functional tests of the kidneys. Very rarely a tumor is found in a congenital single kidney; and, again, both kidneys may have tumor involvement, or the so-called good organ may show pathologic changes. A differentiation of tumors of the liver, gallbladder, spleen, pancreas, intestine and omentum, and retrorenal areas must be considered.

Lateral and oblique radiograms are helpful. Sometimes a gastrointestinal and gallbladder x-ray series is necessary.

Malignant tumors are firm, round or lobulated, and only slightly tender. Cystic tumors are usually soft. The tumor shadow will be seen to move with the kidney in the early development of the renal neoplasm, but when a malignant tumor has spread beyond the renal capsule, it becomes fixed to the adjacent tissues. Tumors at the upper pole of the kidney cannot always be palpated and can only be demonstrated with difficulty. Retroperitoneal coccygeal carbon dioxide insufflation is recommended in these difficult cases to outline the upper pole of the kidney. Injection of the gas in this way is not painful, nor does it in any way injure the patient. The technique may be combined with urography or arteriography (Harvard, 1964). Only very rarely and in very obese patients is the surgeon required to perform an exploratory operation to conclude the diagnosis. If the tumor is small, a biopsy

of a nodule may be justified.

If a patient bleeds from the kidney and the examiner is in doubt, repeated urograms are urged every one to three weeks until a diagnosis is made. Stones and blood clots may be mistaken for tumors. An infarct of a major calyx sometimes gives a permanent defect of the kidney pelvis. The usual spreading of the calyces and elongation of an isthmus are indicative of a tumor mass. One should study both kidney pelves for similarity of pyelograms. There are a few characteristics that suggest certain types of tumors. In the infant a large, smooth, rapidly growing tumor is usually a nephroblastoma. Sarcomas may present a spotty appearance in the radiogram, which is due to incorporated fatty tissue. Calculi occur in the pelvis with pelvic tumors and also with sarcomas. Calcific deposits are occasionally seen in adenocarcinoma and dermoids. Solitary cyst of the kidney is usually smooth in outline. Polycystic kidney disease is bilateral and accompanied by elevated blood pressure and nonprotein nitrogen