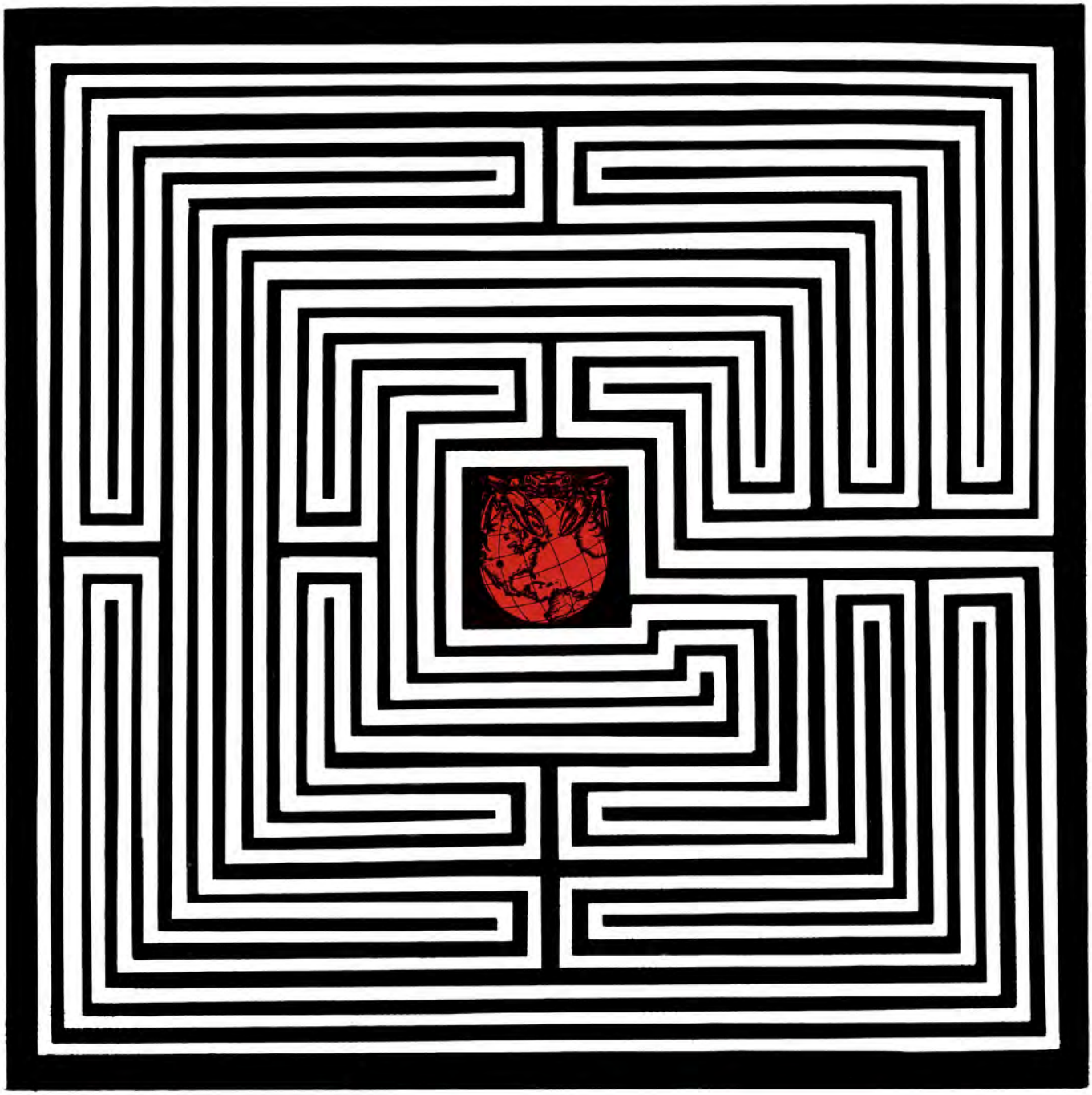

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Sisters of Charity

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VOLUME FOUR AUGUST, 1972 NUMBER FIVE

Juan A. del Regato, *Editor*

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J. A. del Regato, M.D.

Anthony F. Lalli, M.D.

Walter C. Bauer, M.D.

James F. Glenn, M.D.

TUMORS OF THE URINARY TRACT

The 23rd annual CANCER SEMINAR was given to a selection of tumors of interest to the urologists as well as to radiologists and pathologists. In the few years that have elapsed, since our previous CANCER SEMINAR on this subject, there have been substantial changes in our views. First, the new methods, such as selective angiography, are now able to stand analysis and comparison with other diagnostic procedures. Second, some of our concepts in histopathology have been imperceptibly changing to a point not yet realized by all of us: witness, the first three cases of this CANCER SEMINAR.

Those who read these proceedings would be rewarded by the unusual radiodiagnostic sagacity of our guest radiologist, Dr. Anthony Lalli; it is amazing what information may be drawn from insufficient radiographic documents by a knowledgeable inquirer. The masterful academic discussions of histopathologic details, despite the unassuming conversational style of Dr. Walter Bauer, are a distinct contribution to this CANCER SEMINAR. We owe to him also the excellent quality of the carefully taken photomicrographs and their legends. The discussion of each case by an academic urologic surgeon of the caliber of Dr. James Glenn, rounds the proceedings with the pragmatic view of one who, in the last analysis, must understand the diagnostic interpretations and their consequences and make the fateful decisions which they imply.

To the hundreds of radiologists, pathologists and surgeons who through the years have offered us their cases for discussion, we owe special thanks. Our guest speakers put a great deal of time and effort in addition to their talent in these proceedings which are known throughout the oncologic world: our 23 published issues bear their co-authorship. These proceedings find their justification in the many thousands who have attended them through the years and the many more who testify to their interest in reading them.

J. A. del Regato, M.D.
Colorado Springs, Colorado
September, 1972

1. *Fetal Hamartoma of the Kidney*

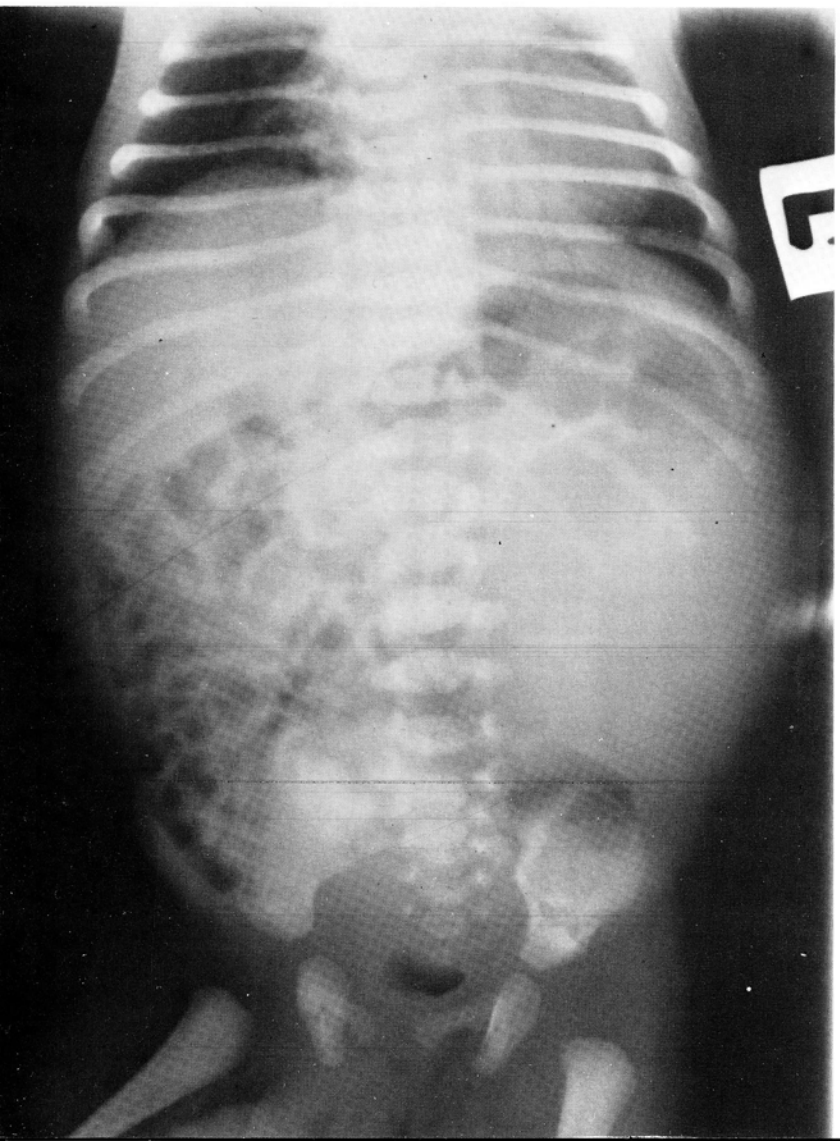
Contributed by **A. O. Severance, M.D.** and **H. Elmendorf, M.D.,** San Antonio, Texas

THE PATIENT was a just-born infant boy in August, 1970, when a large left upper abdominal quadrant mass was noted.

Dr. Lalli: This film of the abdomen presents a large mass of tissue density in the left flank with most of the air-containing bowel displaced to the right. Contrast medium has not been used at this time and we have the information that when it was used, there was cephalad displacement of the left kidney. This would suggest that we are dealing with an extrarenal mass, although it is possible to have tangentially connected cysts and tumors, particularly in adults, which cause displacement of the kidney. We note furthermore that there is no calcification in this mass.

This is an excellent age group for identifying congenital lesions such as hydronephrosis, in which transillumination of the abdomen might lend some help; in this instance, it could be that there is a duplex anomaly with congenital obstruction of one-half of the duplication, presumably the lower half. This is less common than obstruction of the upper half, but does occur. It is unlikely that this represents multicystic kidney disease, since that tends to involve the entire kidney and the urogram would probably show no function. I am not considering Wilms' tumor because I am led to believe that this is extrarenal. However, tangentially attached Wilms' tumor is a possibility. I am unable to identify calcifications within the mass, these being found approximately 50% of the time in neuroblastomas. A lateral projection after urography and an angiogram would be most helpful. Neuroblastomas are the most common abdominal malignant tumor of this age group. Wilms' is the second most common. Two diagnoses that I am willing to consider are retroperitoneal teratoma and ganglioneuroma. While the teratoma might contain calcifications or skeletal parts or teeth, none can be identified on this film. The ganglioneuroma is to be considered because of its location, frequently being found inferior to the kidney and causing displacement of the kidney and the ureter. But this lesion is more common in older children and adults. There are no skeletal abnormalities and it would be unlikely that this should represent an intra-abdominal meningocele. I do not believe that it should be a simple serous cyst of the kidney, as these are unusual in this age group. Multilocular cysts do occur in infants but are rare. The nature of this discussion, however, encourages one to consider rare entities.

Fig. 1—Large mass in the left flank with bowel displaced to the right.



Dr. Lalli's impression: 1) NEUROBLASTOMA 2) LOWER POLE NEPHROBLASTOMA.

Roentgenologic impressions submitted by mail:

Wilms' tumor	25
Neuroblastoma	16
Retroperitoneal tumor	15
Hydronephrosis of lower segment	14
Teratoma	11
Others	26

Dr. Lalli: The radiologists have clung to the same two primary diagnostic possibilities that I have discussed, but the order is slightly different than I would have preferred. Retroperitoneal tumor would include such things as the lymphangioma and the ganglioneuroma. The hydronephrosis of the lower segment is important to consider. Teretoma of the kidney I am going to discuss more completely in one of the subsequent cases: I would look for fetal parts, forms or calcifications to help me with that diagnosis.

Dr. Regato: Dr. L. O. Martinez, of Miami, submitted an impression of hydronephrosis of the lower segment in a case of duplication of the calyceal system. Dr. Milton Elkin, of New York, also considered this diagnosis but concluded that Wilms' tumor was a better bet. Dr. R. B. McMullen, of Denver, made a diagnosis of Wilms' tumor.

Operative findings: On August 28, 1970, a left radical nephrectomy was carried out. The specimen measured 8x6.5x6 cm and weighed 155 gm; it contained a tumor that had almost completely replaced the kidney leaving only a narrow rim of parenchyma. The tumor was rubbery in consistency and yellow in color and contained cystic areas 1.5 cm in diameter containing clear fluid.

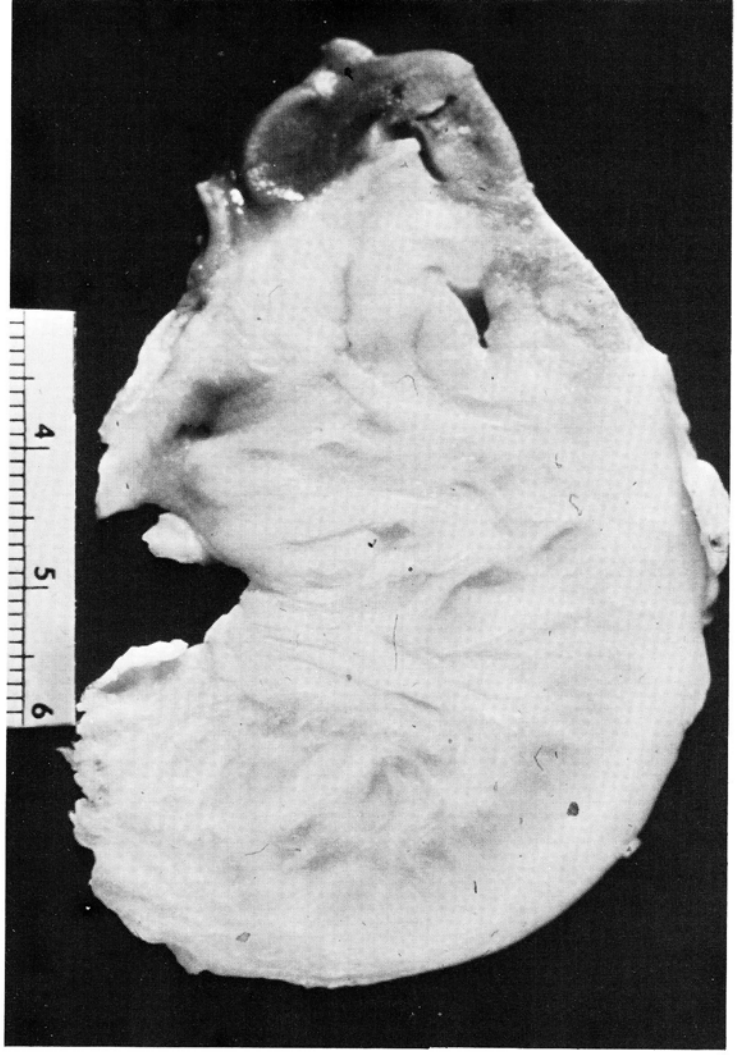


Fig. 2—Surgical specimen showing replacement of renal parenchyma by whitish tissue.

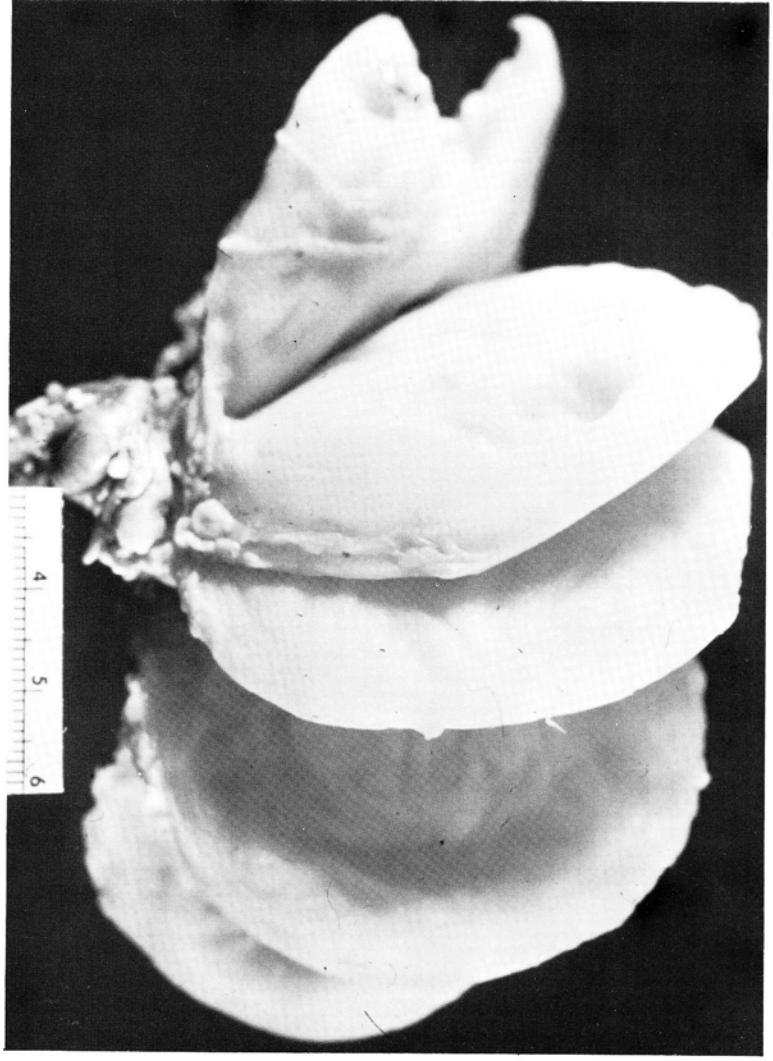


Fig. 3—Cross sections reveal homogeneity and interlacing appearance.

Dr. Bauer: This infant's kidney shows a large tumor with a homogeneous histologic pattern; that of interlacing fascicles of elongated mesenchymal cells. The fascicles are quite cellular with plump spindle-shaped cells having abundant wavy or fibrillar cytoplasm and elongated nuclei with smoothly rounded or blunt ends. The cells appear quite active with mitotic figures easily seen. The origin of the cells would seem to be fibroblastic or leiomyomatous or a mixture of the two. A Masson trichrome stain suggests a definite smooth muscle component. Although the many mitotic figures would indicate fairly rapid growth. The tumor does not appear malignant to me; rather it has the vigorous cellular appearance of immature or developing tissue. No striated muscle, adipose tissue, angiomatous component or cartilage is seen.

The growth pattern of this lesion is quite striking. There is no capsule or sharp delimiting zone about it. Finger-like projections insinuate themselves between areas of adjacent kidney parenchyma to form a peripheral transition zone containing isolated islands of renal tissue and interconnecting bands of tumor. There in no destruction of tubules or glomeruli and little evidence of compression atrophy. Isolated areas of dysplastic kidney may be found but these are very small and few in number. There is a gradual transition from a peripheral interdigitating zone to the center of the lesion where renal tissue is absent. The lesion contains a moderate number of mature blood vessels whose relation to the surrounding cells does not suggest a site of origin for the smooth muscle cells of the tumor. At the periphery a plexus of thin walled venous and lymphatic channels is quite evident.

Differential diagnosis: Hamartoma, leiomyomatous (fetal), angiomyolipomatous, leiomyoma, atypical Wilms' tumor.

I think we can quickly dispose of angiomyolipomatous hamartoma for the absence of any angiomatous or lipomatous component, the lack of relation to the renal capsule and the wrong age group.

In the past five years considerable attention has been given to tumors of the neonatal kidney that originally were classified as an atypical form of Wilms' tumor, but are now thought to represent a hamartoma of mesoblastic origin. They all show two features shared by our seminar case; a cellular pattern of interlacing fascicles of relatively immature smooth muscle cells or fibroblasts and a nonencapsulated growth pattern. They look nothing so much like uterine leiomyomas. I believe this case is a good example of this lesion so well described by Wigger in 1969. Among pediatric pathologists these lesions are considered smooth muscle hamartomas resulting from maldevelopment of fetal renal mesenchyma. Except for the immature appearance of the cells, they appear very much like cellular leiomyomas.

Intrarenal leiomyomas have been reported; there is an excellent review by Gordon et al. Excluding the small,

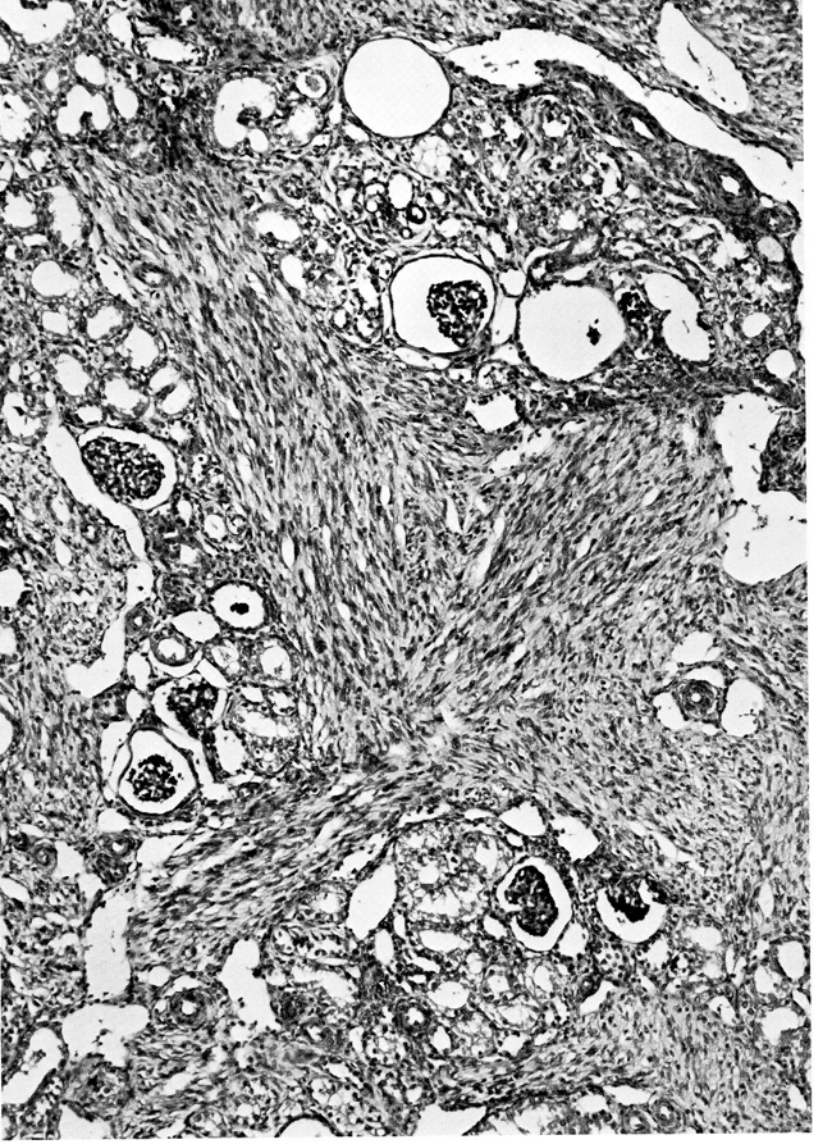


Fig. 4—The periphery of the tumor. Note the absence of circumscription and the separation of kidney tissue by fascicles without destruction or atrophy. X100 W.U. Ill. 72-5390.

often multiple, leiomyomas of the kidney seen so commonly at autopsy, the solitary, symptomatic leiomyoma is rather uncommon. They differ from the seminar case in that they occur in an older age group, mostly in females; are always encapsulated and are very large, occasionally gigantic in size (Clinton-Thomas). In spite of this the possibility of a relationship between leiomyomatous (fetal) hamartoma and solitary leiomyoma will remain until such time as the complete natural history of each lesion is ascertained.

However one chooses to regard this lesion there is one aspect of great clinical significance. That is, that these lesions are benign and should not be called Wilms' tumor or congenital nephroblastoma. It would appear that the excellent prognosis of Wilms' tumor under the age of one year is related to the confusion of this lesion with nephroblastoma. Wigger has stated that all congenital Wilms' tumors reported in detail in the literature are in fact benign leiomyomatous hamartomas. Other authors are in essential agreement on this point and it is important that a histologic diagnosis be made before radiation or chemotherapy is given to infants suspected of having Wilms' tumor.

In this case I will defer to the pediatric pathologists and choose the name "fetal hamartoma" for the diagnosis.

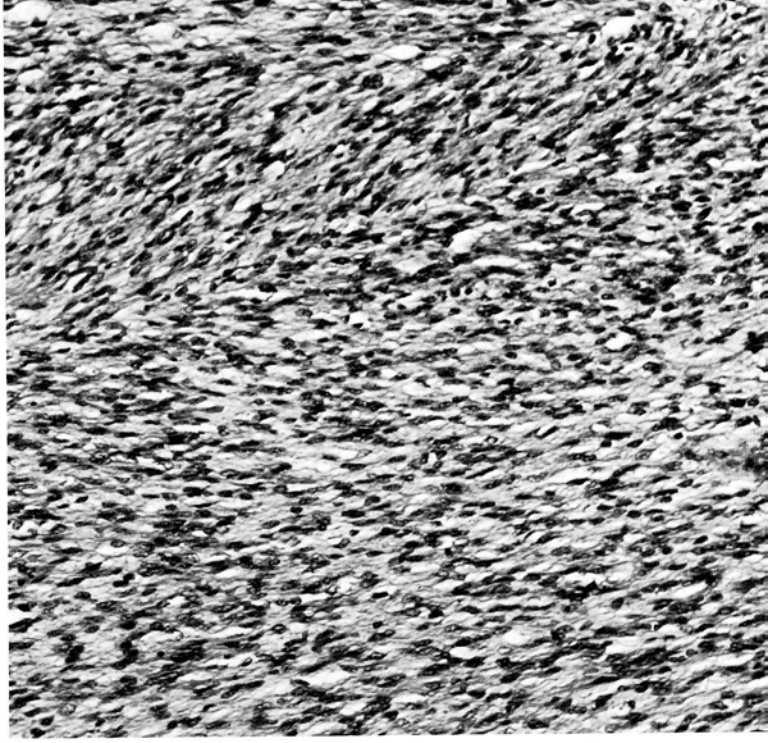


Fig. 5—Cellular fascicles of plump spindle cells with fibrillar cytoplasm. X150 W.U. Ill. 72-5391.

Dr. Bauer's diagnosis: FETAL HAMARTOMA.

Histopathologic diagnoses submitted by mail:

Nephroblastoma (Wilms')	42
Leiomyosarcoma	35
Angiomyolipoma	29
Leiomyoma	10
Fetal hamartoma	22
Congenital nephroma	11
Sarcoma	12
Fibroma	10
Others	10

Dr. Bauer: A good number of the pathologists considered this as a malignant tumor. I suppose the number of mitotic figures and the cellularity of this stroma were features which they translated as signs of malignancy. However, almost an equal number have made diagnoses of benign lesions of one form or another and 22 agreed with the terminology that I used. Angiomyolipoma and leiomyoma I have discussed; my reasons for the choice of the term I think I have covered.

Dr. Regato: Drs. M. Cammoun, of Tunis, and A. O. Severance, of San Antonio, also made a diagnosis of congenital mesoblastic nephroma or fetal mesenchymal hamartoma. Dr. John B. Frerichs, of El Paso, and Y. LeGal, of Strasbourg, offered leiomyosarcoma. Dr. Leo Lowbeer, of Tulsa, preferred nephroblastoma with predominant fibrosarcomatous elements. Dr. M. Berthrong, of Colorado Springs, called it an angiolipomyoma.

Subsequent history: In September, 1970, the infant had to be re-operated upon due to intestinal obstruction caused by adhesions that were released. On September 4, 1971 he was reported well and without evidence of recurrence.

Dr. Glenn: Dr. Lalli presented a differential diagnosis of a number of tumors all retroperitoneal and all of urologic origin. The next step, diagnostically, is an intravenous pyelogram; uroradiologic techniques have advanced so much in the last ten years that there is little doubt that we could have established a reasonable diagnosis with the intravenous urogram. Most Wilms' tumors will exhibit function (95 to 98 per cent) on an intravenous

pyelogram when sufficient contrast medium is employed; this was not true prior to the advent of the better urographic agents and the high dose uroradiography. This is also true of neuroblastoma; the multicystic kidney with atresia of the ureter most often does not function radiographically; neither does a massively hydronephrotic kidney exhibt function. I would deplore the use of retrograde pyelography in a situation like this; I don't think it would add very much; the morbidity of angiography in the new born may be about as high as that of a surgical exploration: some complications can be expected by way of thrombosis.

Apparently this tumor came out very well, was well encapsulated, had no extension, had no nodes. We have had experience with nine tumors of this category which we have classified as mesenchymatous or mesoblastic Wilms' tumors. I quite agree with Dr. Bauer in that they are different from the usual Wilms' tumor. I was a little surprised at the term hamartoma; a hamartoma of the kidney classically does exhibit fat and vessels in considerable degree. But I can see that it could be called a hamartomatous type of tumor. The prognosis in this mesoblastic group is infinitely better than it is in the other types of Wilms'; it raises a very serious question as to whether we should employ post-operative Actinomycin D or irradiation. Two years ago I operated on a 10-month old baby who had a tumor identical to this except that a finger of tumor extended through the renal vein and well up into the vena cava; we did use Actinomycin D and he got a severe reaction which was extremely frightening and confusing in the immediate post-operative period. Of the nine cases that we had, eight are alive and well, one died of surgical complications. None has had recurrent disease; we must regard these as reasonably benign and withhold the vigorous therapy that might attend the treatment of the usual Wilms'.

P. H. Cooper, M.D., Los Angeles, California: Dr. Jerry Waisman and I were able to find 34 cases of this lesion in the literature: 17 had been treated by surgery alone, two of them died of post-operative complications; there has never been a case of metastasis reported. We have written a paper specifically to suggest the withholding of pre-operative or post-operative Dactinomycin and radiation therapy until a complete histologic examination is available. We also are wondering, and would probably have to review some records to find out, what proportion of diagnosed Wilms' tumors in the first month of life would turn out to be this sort of lesion. We found that Wilms' tumors diagnosed in the first year of life yield approximately an 80 percent survival. We suspect that this early neonatal lesion is probably confusing these figures considerably.

Dr. Regato: The matter of pre-operative irradiation in Wilms' tumors disturbs us also. We do advocate pre-operative irradiation in Wilms' tumors but this does require that the histologic diagnosis be well established; the irradiation of these small children is hazardous and should not be done without ascertaining that what is being irradiated is a Wilms' tumor. Obviously, the majority of these lesions are clinically suspected of being Wilms' tumors but, when pre-operative irradiation is to be instituted, there should be histologic assurance; the point made about their predominance in the first year of life is a good one. The other point made is also a good one, that in current statistics these cases may be giving false comfort to a variety of therapeutic approaches.

E. B. Price, Jr., M.D., Denver, Colorado: I would like to make two points: 1) there is a great overlap between lesions that we pathologists call hamartoma and renal dysplasia or renal dysgenesis. 2) in my experience, a solid mass in the retroperitoneal region of a newborn child is more likely to be benign than malignant; it will be either a congenital hydronephrosis, fetal hamartoma or renal dysgenesis, all of which, together, are more common than either Wilms' tumor or neuroblastoma in the newborn. A hamartoma is simply normal tissue (fat, muscle, vessels) either present in excess amount or jumbled up; Wilms' tumor is a misnomer for this lesion; a Wilms' tumor is derived from primitive immature nephroblastic tissue and no pathologist is justified in making a diagnosis of Wilms' tumor unless there is immature nephrogenic tissue in the lesion.

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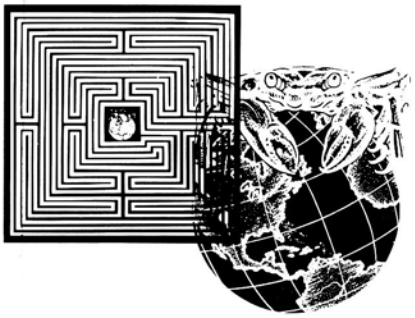


2. *Benign Teratoma of the Kidney*

Contributed by **Walter C. Bauer, M.D.,** St. Louis, Missouri

THE PATIENT was a 5-month old infant girl in December, 1970, when a large mass was palpated in the left side of the abdomen; it extended from the costal margin to the brim of the pelvis and from the left flank to beyond the midline. Hemoglobin was 13.2 gm %.

Dr. Lalli: The urogram demonstrates the presence of an enormous mass in the left flank displacing the stomach cephalad and the other abdominal viscera primarily to the right and across the midline. A preliminary film not being available, I must conclude that this mass is primarily due to calcifications and that there is probably no function of this left kidney for I cannot identify anything which I could call a calix. The right kidney appears to be normal, as does the skeleton.

The differential diagnosis here must rest primarily with three possibilities, the first being *Wilms' tumor* because we have a mass involving an entire kidney and crossing the midline in a five-month old infant. The presence of the calcifications is against Wilms' tumor, since calcifications of this type are identified more commonly in Wilms' tumors discovered in older children, suggesting perhaps that they are elderly Wilms' tumors. The presence of the calcifications in the abdominal mass recommends *neuroblastoma,* although the calcifications in this entity are usually punctate and not flaky. However, that is usually an extrarenal mass, which can invade the kidney, but never in my experience to this extent. The shape and appearance of some of these things that I believe are calcifications suggest the possibility of *teratoma* which has involved the kidney and become malignant.

Dr. Lalli's impression: 1) WILMS' TUMOR 2) Unusual NEUROBLASTOMA.

Roentgenologic impressions submitted by mail:

Neuroblastoma	59
Wilms' tumor	22
Sympathicoblastoma	8
Teratoma	7
Others	10

Dr. Lalli: Most of my radiologic colleagues wanted to call this a neuroblastoma. I can't argue with their diagnosis; I think that they were using the calcification of the mass as the criterion. A few clung with me.

Dr. Regato: Dr. Harry Z. Mellins, of Boston, Dr. L. Kun, of Colorado Springs, and Dr. J. Maxey Dell, of Gainesville, Florida, also suggested neuroblastoma. Dr. J. L. Eller, of Denver, suggested teratoma.

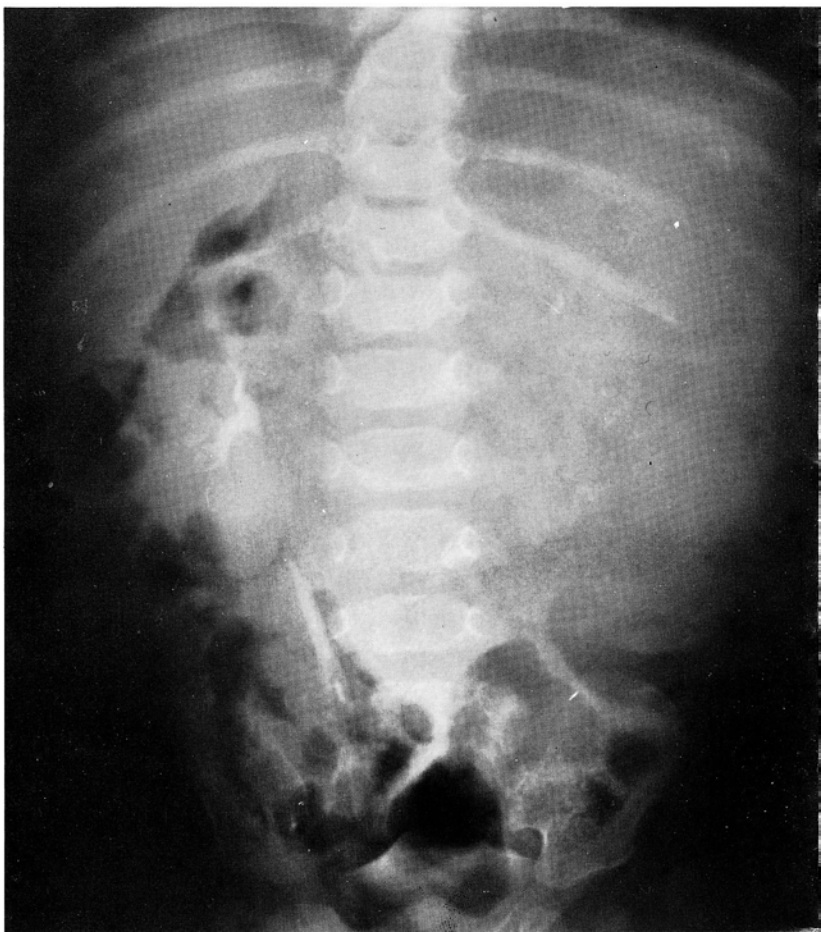
Operative findings: On December 24, 1970, a left nephrectomy was carried out. The specimen measured 12.5 x10x8 cm and weighed 650 gm. The kidney capsule was intact and almost the entire kidney was replaced by a gray-white mass with cartilaginous as well as cystic areas containing clear fluid.

Dr. Bauer: The sections of this cystic intrarenal lesion show many different types of embryonic and developing tissues whose distribution is in a haphazard arrangement. Thus one finds nodules of cartilage in relation to respiratory epithelium, foci of developing smooth and striated muscle, mucous and secretory glandular structures, nonkeratinizing epithelium resembling bladder mucosa, and wide variety of other tissues including sympathetic ganglia and bone. The appearance and arrangement is similar to teratomas in other locations and that is my diagnosis. Some sections show a considerable amount of developing neural tissue and may present a disturbing picture suggestive of undifferentiated malignancy. However, taken in context of the rest of the case the disorganized developing neural tissue should be recognized as such and therefore is not an indication of malignancy in a teratoma. The adjacent compressed kidney was normal.

Differential diagnosis: Benign teratoma of the kidney, benign teratoma of the retroperitoneal region.

Teratomas in the renal fossa are not common and are thought to involve the kidney only by displacing it. Attached to the renal fascia they are considered primarily retroperitoneal in origin. Teratomas within the kidney are very rare; Kissane mentions thirteen reported cases of which only about nine are considered genuine. In this regard the gross findings of the present case are very important in that they demonstrate convincingly an intrarenal location.

Fig. 1—Huge mass in the left flank presenting flaky calcifications.



Dr. Bauer's diagnosis: BENIGN TERATOMA.

Histopathologic diagnoses submitted by mail:

Nephroblastoma (Wilms')	64
(with teratoid areas 18)	
Teratoma, unclassified	71
malignant	30
benign	8
Kidney, man, kidney!	1
Others	15

Dr. Bauer: Most of us did think this was a teratoma; one-third thought that it had some malignant features, probably because of the immature nervous system elements in the particular slide they may have gotten. I don't believe that this looks microscopically like a Wilms' tumor.

Dr. Regato: Drs. Mark J. DeMeo, of Santa Rosa, California, and Ray E. Stanford, of Fort Dix, New Jersey, also made a diagnosis of benign teratoma. Drs. G. Vogt, of Tunis, and J. F. Fennessey, of Detroit, considered it as malignant. Drs. G. Gricouroff, of Paris, and Giles D. Toll, of Denver, submitted nephroblastoma with teratoid elements. Drs. M. C. Wheelock, of Miami, Florida, and D. L. Dawson, of Colorado Springs, called it a malignant teratoma. Dr. F. Cabanne, of Dijon, France, designated it as a malignant desembryoma with a predominant neuroblastic contingent.

Subsequent history: Post-operatively she was given Dactinomycin, but it had to be discontinued. In September, 1971, the patient was reported doing well.

Dr. Glenn: The calcification seen here would prompt me to think that this was certainly not a Wilms' tumor, though it could happen. The absence of function would predispose me against the diagnosis of Wilms' tumor or neuroblastoma, since most of those do function, while the extension across the midline could be found in either neuroblastoma or Wilms'.

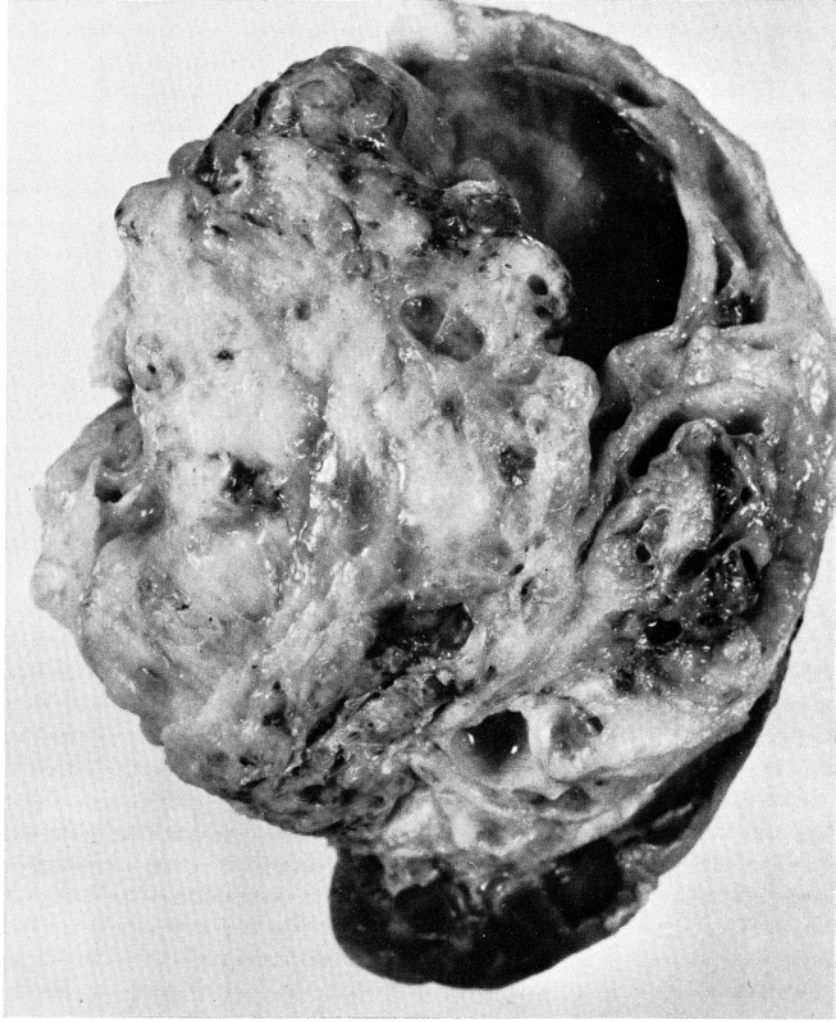
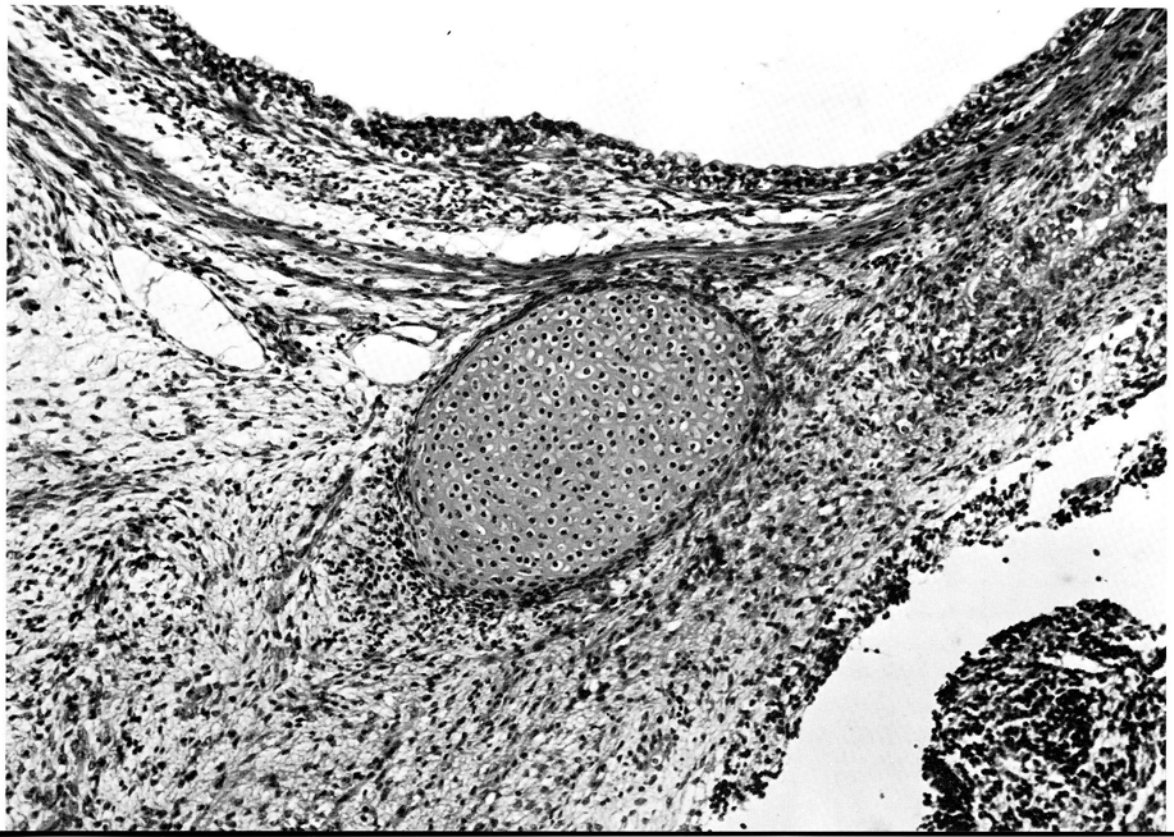


Fig. 2—Gross specimen with almost complete replacement of the left kidney by cystic lesion.

Fig. 3—A focus of developing cartilage is seen next to a cystic structure with an epithelial lining. Smooth muscle cells form part of the cyst wall. A focus of developing neural tissue is seen at the lower right. X150 W.U. Ill. 72-5212.



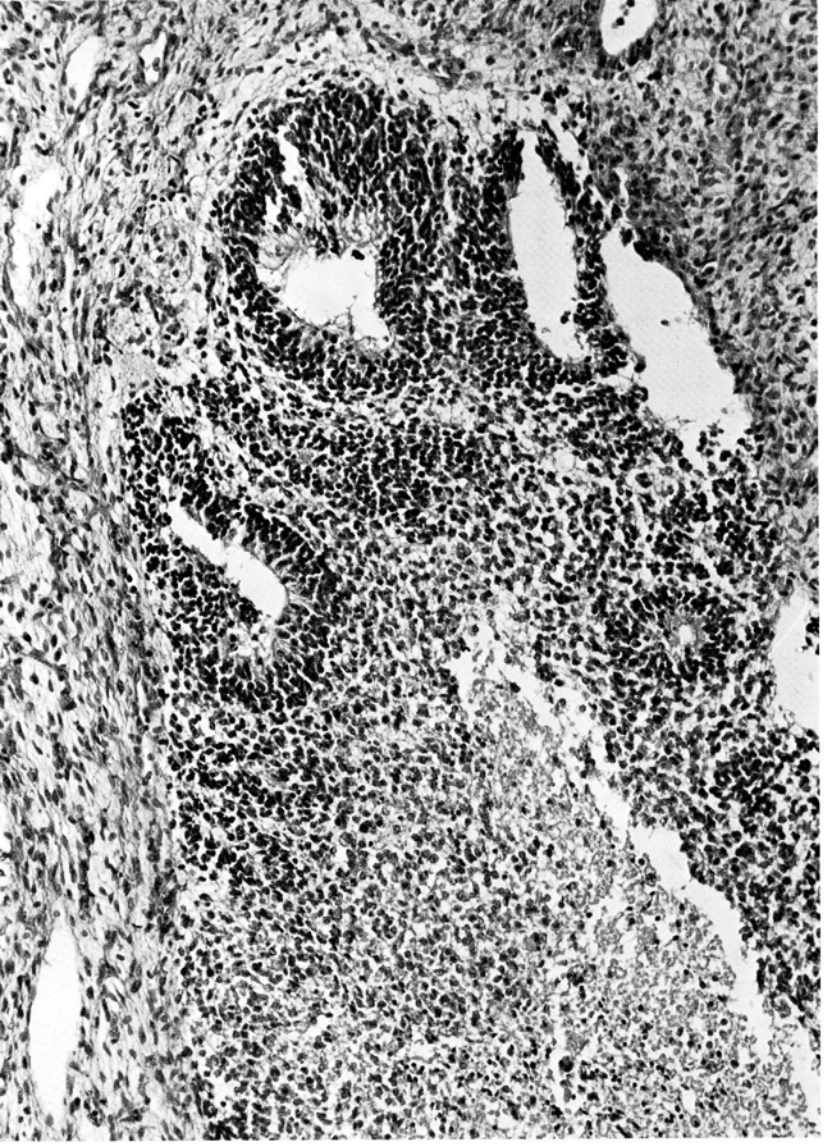


Fig. 4—An area of developing nervous tissue with attempted neural tube formation and necrosis. The disordered appearance of such areas should not be taken for malignancy. X150 W.U. Ill. 72-5214.

I would have approached this child as if he had a malignant renal tumor, which would mean transabdominal exploration. Approaching a benign lesion, such as hydronephrosis, we might go extraperitoneally. Having removed this tumor and found that it was well encapsulated, I would draw some confidence from this. I don't think this is a kidney tumor; I certainly don't think it is a Wilms' tumor. I would have to respect the histologic evaluation as a teratoma, but I have never seen an intrarenal teratoma. I have seen many retroperitoneal teratomas that displace the kidney. I would wonder if perhaps the initial impression that this was a retroperitoneal teratoma and not truly renal teratoma, was not correct. In any event the prognosis here is excellent, whether it is intrarenal or retroperitoneal displacing the kidney. The interesting thing about it is not the surgery or the radiologic appearance or even its histology, but the fact that this is such a primitive and diffuse type of tumor. We have seen this sort of thing in our laboratory experimentally. One wonders if this is not the result of some prenatal influence, perhaps a viral infection. We are seeing cases that we recognize as viral nephritis in the newborn and I would wonder if perhaps an infectious origin might stimulate teratomatous formations.

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3. *Congenital Mesoblastic Nephroma*

Contributed by **Fritz Lin, M.D.,** Kansas City, Kansas

THE PATIENT was a 6-weeks old infant girl in October, 1970, when a firm, rounded, abdominal mass was palpated in the left side of the abdomen. Laboratory examinations revealed no additional abnormality.

Dr. Lalli: We are beguiled by three children, all with left flank masses. But in this instance we are given a urogram of fair quality demonstrating unmistakably that there is a mass which appears to occupy primarily the lower half of the left kidney, the mass being approximately 3.5 cm in diameter, causing displacement of the calices and attenuation of the infundibula. Absolute amputation of calices is not identified.

In an adult this appearance suggests either cyst or tumor. In a child, this should indicate only tumor. One of these three children must have a Wilms' tumor and this child is the best candidate. I say this because there is an intrarenal mass and because it does not contain calcifications. The differential diagnosis in this instance, of course, does include the rare multilocular cyst, rare renal lesions such as neuromas, fibromas and such. It would be most unusual for a child in this age group to have a renal cell carcinoma and it would be unlikely that this represents a lesion such as hemangiopericytoma or hamartoma of the angiomyolipomatous type. The urographic distinction among these lesions is impossible.

Dr. Lalli's impression: 1) WILMS' TUMOR 2) MULTILOCULAR CYST.

Roentgenologic impressions submitted by mail:

Wilms' tumor	63
Renal cyst	7
Teratoma	4
Neuroblastoma	3
Others	25

Dr. Lalli: It seems that most of the radiologists were with me on this one. A renal cyst would be an extremely rare thing in these circumstances. A diagnosis of cyst in such a very young patient I will consider out of keeping with what we should expect. Teratoma is always a possibility and so is the intrarenal neuroblastoma, but I certainly would not make those my first diagnoses.

Dr. Regato: Dr. Wendell Stampfli, of Salida, Colorado, offered an impression of Wilms' embryoma. Drs. Mostafa Batata, of New York, and J. Mira, of Colorado Springs, also proposed a diagnosis of Wilms' tumor.

Operative findings: On October 30, 1970, an abdominal transverse incision was done to gain access to the kidney anteriorly; a mass 4 cm in diameter was found on the surface of the left kidney and nephrectomy was carried out. The specimen measured 8 x 5.5 x 4 cm and weighed 78 gm. The lower pole of the kidney contained a mass 5 cm in diameter distorting the calyces, without apparent invasion but extending on the perinephric tissues.

Dr. Bauer: The photograph of the gross specimen has a white-yellow-gray rather translucent surface. I do not see any cystic areas. It looks as though there were some adhesions over the outside of the tumor which occupies an intrarenal position. The tumor appears well demarcated in some areas and in others it is intermixed with the renal substance.

The histological findings in this case are very much like those of Case 1; namely those of a nonencapsulated cellular mesenchymal tumor composed of plump smooth muscle or fibroblastic cells growing in an interlacing fascicular pattern. At the interface with the infant kidney there is an intimate mixture of entwining bands of tumor with well developed renal tissue. Again, no skeletal muscle, cartilage, adipose or angiomatous tissue is found.

One difference from Case 1 may be noted and emphasized. In the peripheral zone of the lesion one can find circumscribed areas of disorganized tubules that appear immature, primitive or dysplastic. These areas, usually small, are separated from the tumor bundles by a zone of loose stroma whose cells are often arranged in a concentric fashion around the tubules. The abnormal tubules are usually small with a narrow lumen and are lined with closely packed, regularly spaced cells that are low cuboidal or tall columnar. They appear undifferentiated with respect to the tubular portion of the nephron. Their arrangement one to another and to the adjacent tumor and kidney is haphazard.

These differences from Case 1 are those emphasized by Bolande et al in descriptions of neonatal or congenital mesenchymal tumors of the kidney that are otherwise the same as those described by Wigger (see Case 1). These areas of immature tubules are regarded as dysplastic and an intrinsic part of the tumor. This leads to a slightly different approach to histogenesis in that the maldevelopment of nephrogenic blastoma is considered to involve nephroblastic epithelium as well as stroma. Therefore a relationship to Wilms' tumor is suggested. Kay et

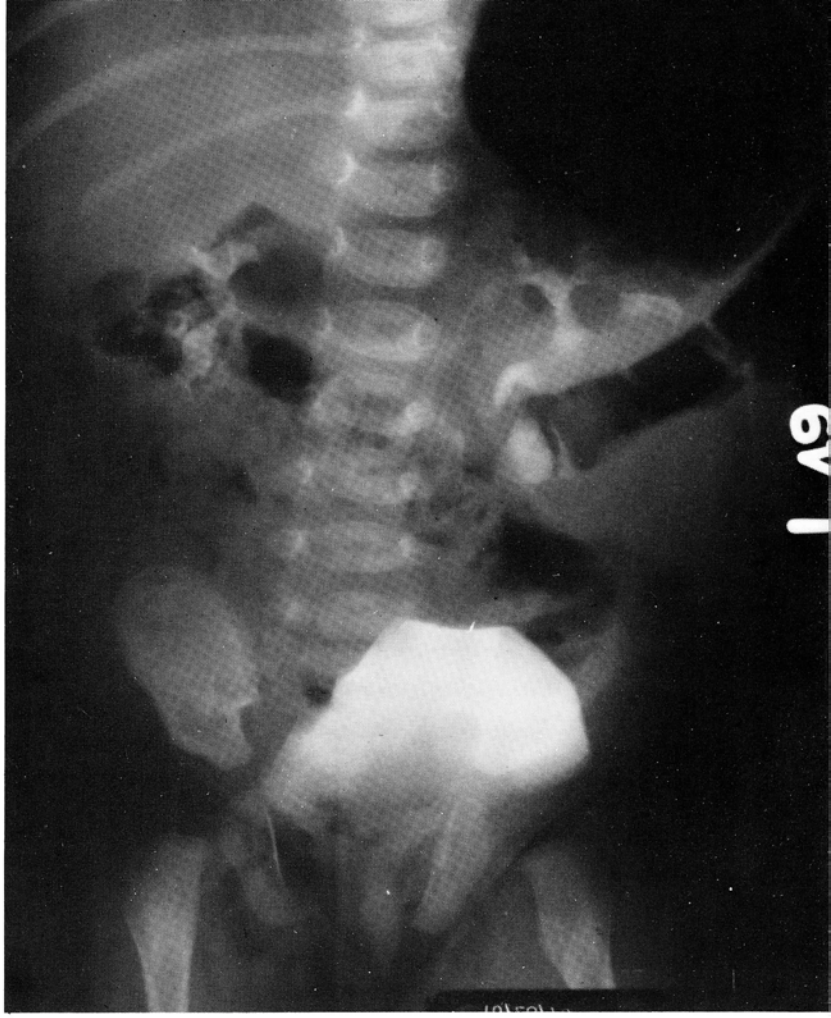
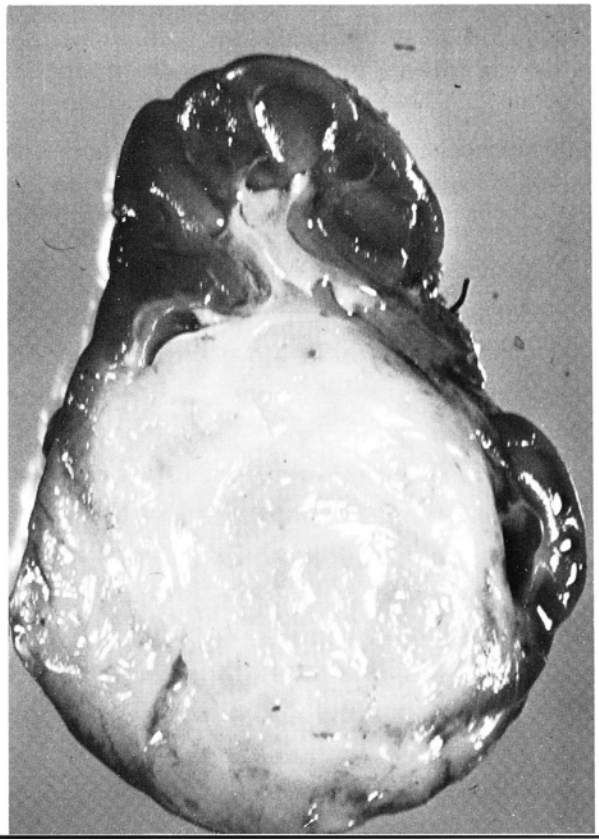


Fig. 1—Urogram showing mass occupying the lower half of the left kidney with displacement of calices.

Fig. 2—Surgical specimen revealing a rather translucent surface and some demarcation.



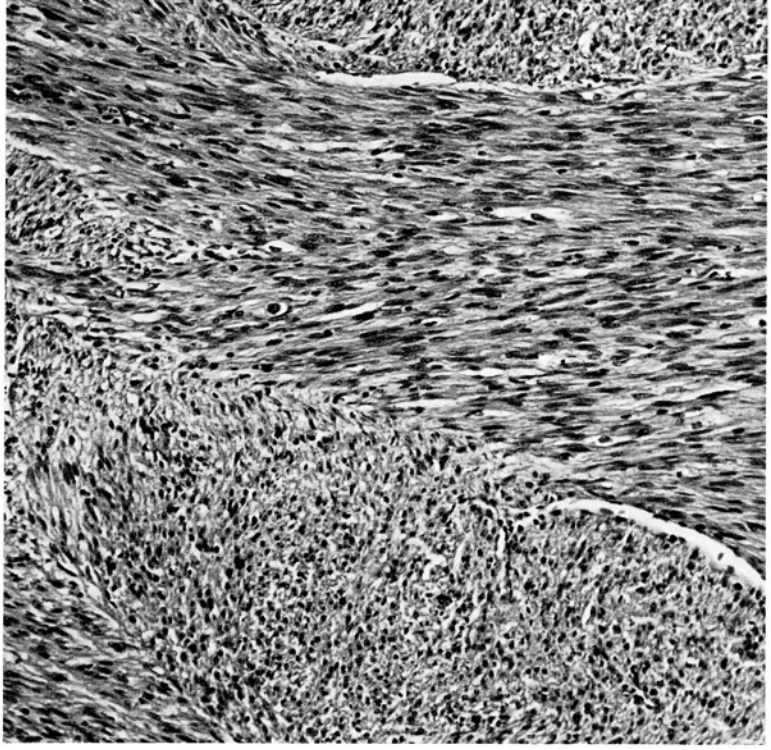


Fig. 3—Elongated cells with a fibrillar cytoplasm arranged in interlacing fascicles. X150 W. U. Ill. 72-5392.

al and Burkholder et al have placed similar interpretations on such immature tubular areas in their reported cases.

Another histogenetic consideration might be that these bizarre tubular areas represent maldeveloped renal tissue isolated and entrapped within the expanding and infiltrating tumor. As such they are not part of the tumor, but rather the consequence of the growth of an infiltrating tumor within a developing organ. This view would hold that these lesions are not nephroblastomatous and unrelated to Wilms' tumor.

This rather rarefied discussion relates to the practical question of whether or not these tumors, however named, may be dangerous to the patient. So far, there have been about twenty of these cases reported in the literature in which the patients have been followed beyond the time period designated by Collins' Law as curative. In every case the children are alive without evidence of tumor except for those who have died following aggressive radiation or chemotherapy. With our present understanding it seems that the greatest risk to life lies with the therapy than with the biologic behavior of the tumor.

In addition to the peculiarity of the tubules there is one more bizarre finding in this case; that is a columnar metaplasia involving all or a portion of the parietal layer of Bowmans capsule. It is found only in the interface zone between tumor and renal cortex where glomeruli are in close proximity to tumor cells. It is interesting that this rare and striking finding has been found in the kidneys of patients with various types of malignancies. The most recent report is that of Reidbord in which the metaplasia occurred in a patient dying of esophageal carcinoma with hepatic metastases. I do not know how to relate these reports to the seminar case, but it is possible that our intrarenal tumor exerts some inductive or dedifferentiating effect on adjacent glomeruli; an atavistic effect shared rarely by other neoplasms.

Dr. Bauer's diagnosis: CONGENITAL MESOBLASTIC NEPHROMA.

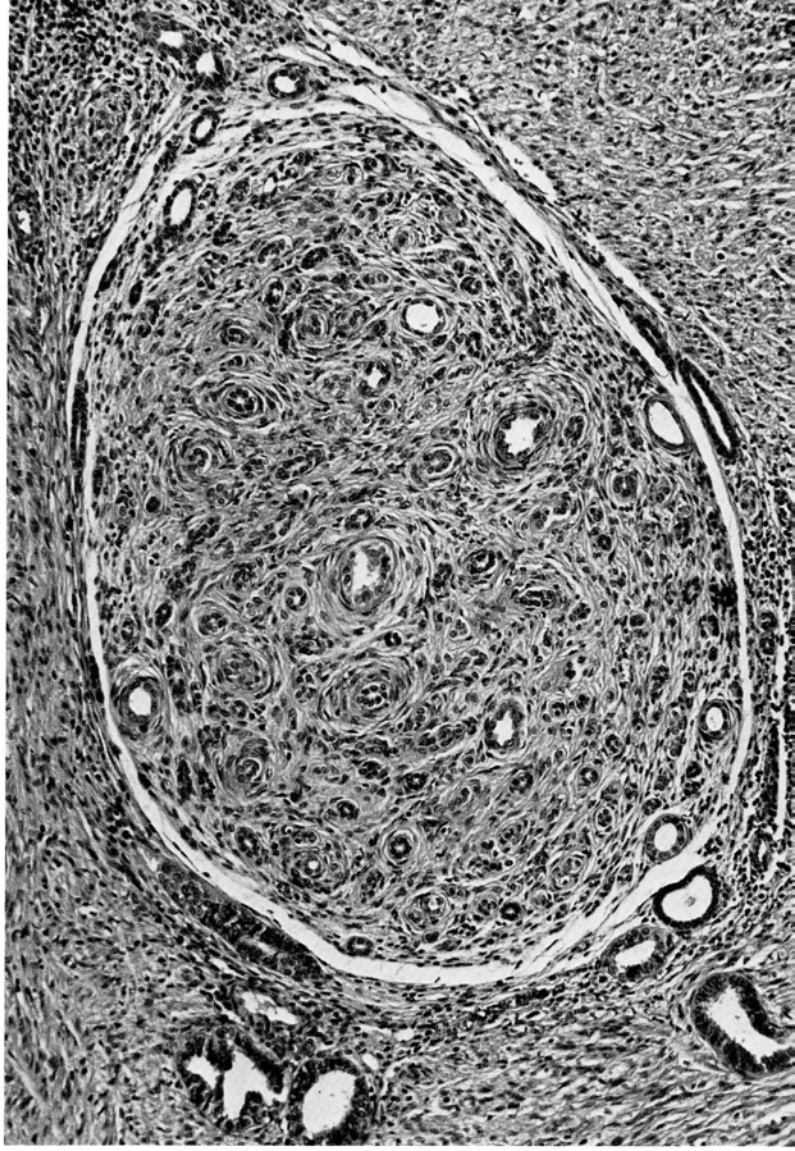


Fig. 4—An isolated group of distorted tubules separated by loose stroma whose cells are arranged in a concentric pattern. This island of tubules is surrounded by tumor. X150 W. U. Ill. 72-5393.

Histopathologic diagnoses submitted by mail:

Nephroblastoma (Wilms')	45
Leiomyoma	36
Leiomyosarcoma	25
Fetal mesenchymal hamartoma (congenital mesoblastic nephroma)	30
Fibroma	20
Others	22

Dr. Bauer: When you have three children in a row in a Seminar like this one, you should think that you ought to turn up a Wilms' tumor, or a neuroblastoma. I was advised by wiser heads than my own that you ought to stick with the slides and leave out psychology.

Dr. Regato: Drs. C. F. Farinacci, of San Antonio, and M. Cammoun, of Tunis, also made a diagnosis of congenital mesoblastic nephroma. Drs. Carlo Sirtori, of Milan, D. R. Dickson, of Santa Barbara, California, and R. D. Schultz, of Sioux Falls, preferred nephroblastoma. Drs. K. R. Holloman, of Denver, and D. B. Troxel, of Lafayette, California, offered a diagnosis of leiomyoma. Dr. L. B. Henley, of Fort Sam Houston, diagnosed leiomyosarcoma.

Subsequent history: In June, 1971, the patient was reported well. On October 14, 1971, the patient showed no evidence of recurrence or metastasis. The roentgenogram of the chest was reported negative.

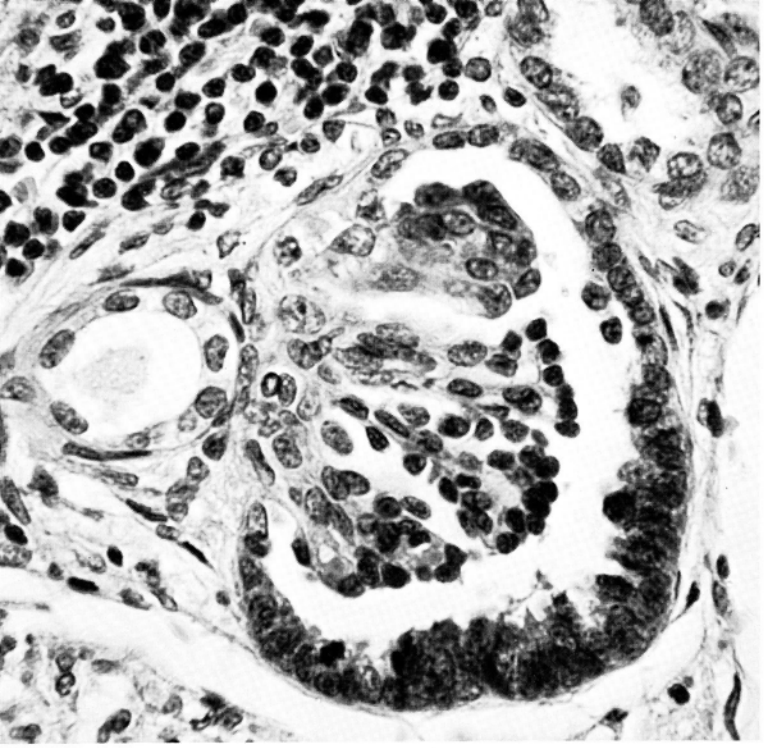


Fig. 5—A glomerulus showing metaplasia of the parietal layer of Bowman's capsule. X600 W. U. Ill. 78-5394.

Dr. Glenn: Dr. Lalli and I would have had no difficulty in plotting our course. This is a classical Wilms' tumor, if you will, by radiologic examination. I don't think that any surgeon would have had any difference of opinion about that. I don't think there is any diagnostic confusion or that there would be differences about appropriate surgical management. We are perhaps in a morass of confusion as to how we ought to classify these things and how we ought to begin to think about them from the long term therapeutic point of view. In the first edition of Campbell's Urology, Dr. Clyde Deming wrote the section on renal tumors. He gave some 15 different categories of renal tumor on the basis of microscopic variations. Frankly, I think this is histologic hairsplitting; from the clinical point of view it helps us very little to proceed to these minutiae because they merely cloud the issue. I have difficulty in accepting extensive classifications; for my purposes all renal tumors can be fairly and conveniently classified into four major groupings: First, there are the nephroblastomas, the types of tumor seen in Case 1 and Case 3 of this Cancer Seminar. Secondly, adult tumors, under the categorization of nephrocarcinoma, accepting the histologic variations that can occur and may have some bearing upon prognosis. Thirdly, the transitional cell tumors of the kidney. Fourthly, a miscellaneous category that would embrace the teratomatous tumors that Dr. Bauer discussed in Case 2, the fibrosarcomas of the capsule, lipomas of the kidney, and so on. I would like to see Case 1 and Case 3 of this Seminar categorized under Wilms' tumor and accept the fact that there can be histologic variations. This last case has a one-year follow-up since surgery; that is beyond the period at risk for recurrence of the tumor in a six-week old patient. I would like to see us come to some agreement on categorization of nephroblastomas to include this wide spectrum of neoplasms.

Dr. Regato: We must admit that unless these diagnoses are generally agreed to, the radiodiagnosticians lack the guidelines and confirmation of differential interpretations which are the basis of accuracy and sustained usefulness. A radiodiagnostician is guided by what is found after his examination and also by his pathologist's opinion as to the findings.

Dr. Glenn: This tumor did show, as Dr. Bauer showed us, several discrete areas of differentiation of tumor and yet the total pattern is one of disorganization. You can induce this same sort of disorganization of the fetal kidney in the hamster by administration of estrogens; it is that simple. The kidney has many propensities; it has cells of multiple origin. I find it convenient to believe that this is the potential of the nephroblastoma group.

Dr. Bauer: I usually don't find myself on the side of the splitters, particularly if it doesn't make any difference to the patient. But I would like to see if I couldn't convince Dr. Glenn to modify his approach a little bit: I think that the one great contribution that morphologists have made is to recognize that there are benign lesions that occur in the newborn, or just after birth, which are not Wilms' tumors, which don't behave like Wilms' tumors and which do not necessitate the vigorous clinical application of poisons in the post-nephrectomy period. The reason for discussing these cases is to make the pathologists aware of them; they are not very common and therefore they need to be carefully studied. It is quite clear that we now need to accurately describe them, to do electromicroscopy, to freeze these tissues for histochemical and immunofluorescent studies and perhaps even make extracts of some of these tumors to see if they contain growth factors which can explain some of these normally metaplastic areas in the adjacent normal kidney. Careful follow-up of these cases is also needed.

Dr. Glenn: It is important to identify these tumors which do appear to have less malignant behavior. I would be happy to modify my categorization if, at some point, we are able to say that these are mesenchymal tumors which do not have the malignant potential of the usual Wilms' tumor.

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4. *Transitional-Cell Carcinoma of the Renal Pelvis*

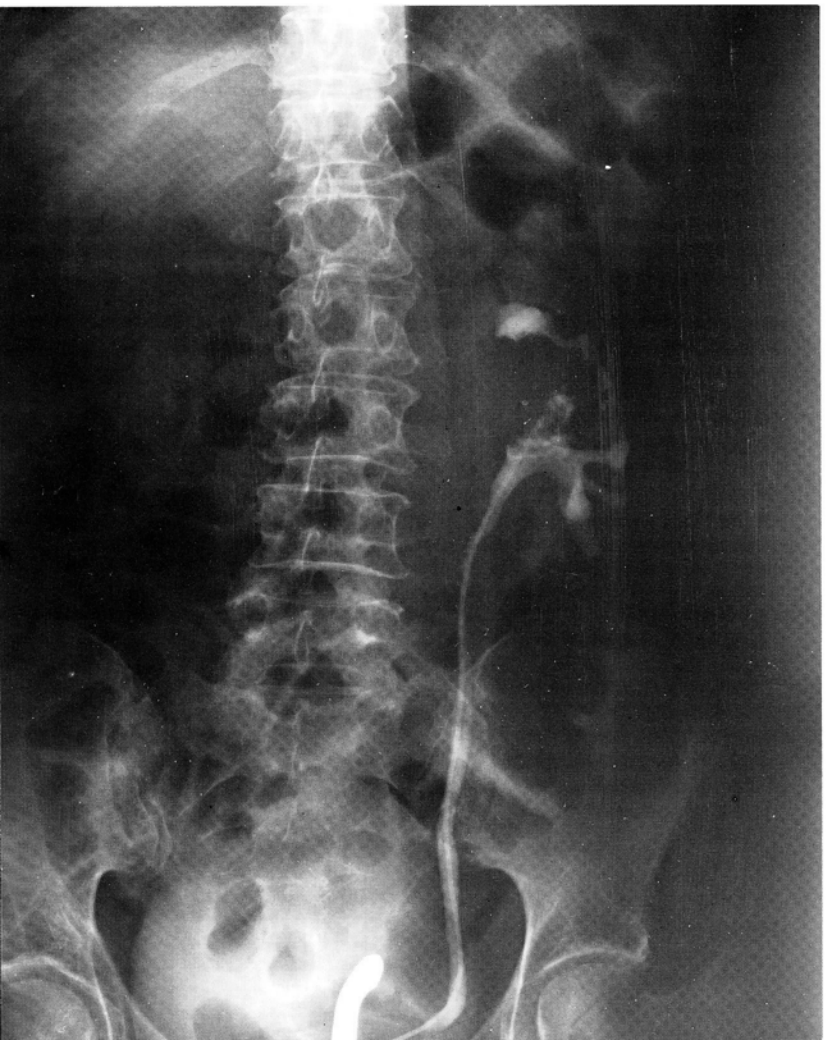
Contributed by **Carlos Perez-Mesa, M.D.,** Columbia, Missouri

THE PATIENT was a 57-year old woman in March, 1968, when she complained of left flank pain of two months duration. Examination revealed two palpable non-tender masses, 15 cm and 6 cm in diameter in the left lower abdominal quadrant; in addition there was a left supraclavicular mass 5 cm in diameter. The hemoglobin, white cell count and differential were normal; there was moderate albuminuria.

Dr. Lalli: These cases become more difficult and we are now given a retrograde pyelogram on the left. The examination is of fairly good quality and demonstrates the presence unmistakably of a mass in the upper half of the left kidney which is distorting the upper portion of the left renal pelvis and the infundibulum. On close examination one finds that there is contrast medium which appears to be covering an irregularity of the mass in the upper pole infundibulum. This suggests the possibility of a foliated surface to the mass.

This has to be a tumor. The question is what type and how can it be associated with the supraclavicular and lower abdominal masses. One of these masses is enormous, 15 cm in diameter, and gives no evidence of its presence on this film. It is also almost impossible to associate these masses with the mass in the kidney. One of the possibilities would be to have a carcinoma of the colon which has invaded the kidney. Primary amyloidosis does not invade the kidney and secondary amyloidosis would show generalized renal replacement. Inflammatory lesions such as tumefactive xanthogranulomatous pyelonephritis must also be considered but would be less likely in the absence of calcifications and in the presence of function of the affected kidney. Presumably calcifications were not observed in the kidney on the preliminary film. It is unlikely also that it represents a tuberculoma. Renal cell carcinoma and squamous cell carcinoma can invade the collecting system, mimicking transitional cell carcinoma, and can metastasize widely but not commonly to soft tissue parts. Squamous cell carcinomas have been reported primarily in instances of obstructive uropathy with contained calculi in the renal pelvis. Primary lymphoma of the kidney is most unusual with lymphomatous involvement usually appearing late in the history of the patient with lymphoma.

Fig. 1—Retrograde pyelogram with mass in the upper half of the left kidney.



Dr. Lalli's impression: 1) TRANSITIONAL-CELL CARCINOMA of upper pole infundibulum. 2) RENAL-CELL CARCINOMA.

Roentgenologic impressions submitted by mail:

Metastatic tumor	43
Carcinoma pelvic epithelium	19
Malignant lymphoma	18
Renal carcinoma	12
Others	21

Dr. Lalli: Few of my radiologic colleagues did agree with my first diagnosis and fewer yet with my second. I think that these are indeed the four pertinent diagnoses to consider; I would have simply altered the order in which I would have listed them.

Dr. Regato: Dr. Milton Elkin, of New York, and Dr. L. O. Martinez, of Miami, Florida, also submitted an impression of transitional-cell carcinoma of the kidney pelvis with invasion of the renal parenchyma.

Operative findings: On March 29, 1968, a left nephrectomy was done. The specimen measured 17 x 12 x 9 cm and weighed 540 gm; it was occupied by a mass 7 x 10 cm, gray in color, which contained numerous small cysts with mucous material and which extended to the surface of the pelvis.

Dr. Bauer: The low power view of this large tumor shows involvement of both the pelvis and peripelvic tissues and the renal parenchyma itself. The tumor infiltrating the peripelvic tissues is a fairly well differentiated transitional cell carcinoma which can be shown to be in-continuity with the pelvic epithelium; thus confirming its origin from the renal pelvis. The carcinoma is physically contiguous with the intra-renal tumor masses and although its histological appearance has changed somewhat, I believe it to be the same tumor. The intra-renal masses show considerable separation of the cancer cells into intertwining bands and strands with a thin mucoid material in between. All degrees of this acantho-

lysis may be found ranging from small areas of cell separation in solid masses to free floating tumor strands in mucoid areas. Gland-like spaces appear in a few areas, but this finding was certainly not the predominant pattern. The mucoid material stained a deep blue with Alcian-blue—PAS indicative of an acidic mucoprotein and it was extracellular in location. Acidic mucoproteins are found with normal urothelium and it should come as no surprise to find it in carcinomas derived from pelvic epithelium.

Differential diagnosis: Transitional cell carcinoma of the renal pelvis; metastatic carcinomas, perhaps breast, colon or ovary.

I did not consider metastatic carcinoma a serious possibility in that the origin from the renal pelvis was quite evident in the slides I examined. A considerable number of pelvic carcinomas show extensive intra-renal invasion and this case is a good example of that growth.

As pointed out by Becker the roentgenographic findings may be unusual in such cases with non-visualization on excretory urography.

Dr. Bauer's diagnosis: TRANSITIONAL-CELL CARCINOMA OF THE RENAL PELVIS.

Histopathologic diagnoses submitted by mail:

Transitional-cell carcinoma of renal pelvis	81
Renal-cell adenocarcinoma	38
Metastatic carcinoma	12
Sarcomas	16
Others	21

Dr. Bauer: Some of my colleagues thought this was a renal-cell adenocarcinoma; I suppose that it could be an anaplastic or a dysplastic type of adenocarcinoma with predominantly a spindle cell component, however, the topographical features of this case are much against that. I have discussed metastatic carcinoma and sarcoma.

Dr. Regato: Drs. W. J. Holaday, of Columbus, Ohio, and H. A. Azar, of Kansas City, Kansas, offered also a diagnosis of transitional-cell carcinoma; Dr. J. B. Frerichs, of El Paso, commented that the tumor has a peculiar non-artifactual "pulled-apart" pattern. Dr. W. M. Russell, of Las Vegas, Nevada, favored an adenocarcinoma; Dr. E. M. Donowho, of Fort Sam Houston, called it metastatic adenocarcinoma.

The AFIP had been consulted in this case (Accession No. 1277197): a diagnosis of transitional-cell carcinoma, grade 2, was rendered; the additional comments pointed at the presence of areas resembling adenocarcinoma with vascular and lymphatic invasion.

C. Perez-Mesa, Columbia, Missouri: I had the opportunity to prepare a whole-organ section of the specimen in which there is clear evidence that tumor was arising from the urothelial covering of the renal pelvis and infiltrated the entire thickness of the organ, reaching its capsule. The histological pattern was variegated showing areas of mucin producing adenocarcinoma, non-keratinizing epidermoid carcinoma and of transitional cell type which was the predominant microscopic feature. The variations in the histological composition of tumors arising from the urothelium has been recognized for a long time. The specimen (Fig. 2) showed numerous enlarged lymph nodes as well as invasion in some of the major vessels of the hilum. Perhaps the abdominal mass alluded in the clinical history represented metastases in a lymph node located along the aorta.

The patient died at home 2 months after surgery; no autopsy was performed.

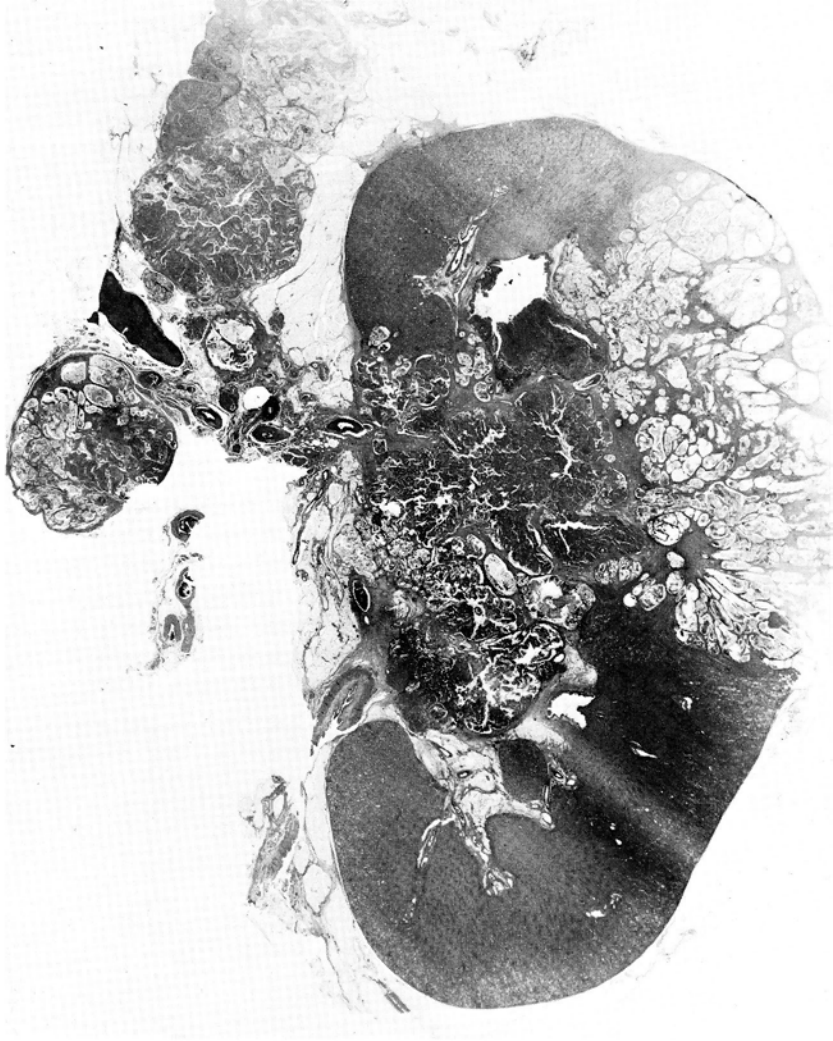


Fig. 2—Giant slide containing the entire specimen shown in low power (Dr. C. Perez-Mesa).

Dr. Glenn: This seems to be a straightforward transitional carcinoma of the renal pelvis, but there are a number of features about it that are interesting: I think that those evanescent masses were due to gas which was gone by the time that she went to the department of radiology. Ordinarily a transitional-cell tumor of the renal pelvis will not metastasize in that fashion and will not present with masses in the lower abdomen; I have no idea what this was. The supraclavicular node was apparently a typical metastatic lesion. I think this is a case where a retrograde is very definitely indicated. A transitional-cell tumor of this magnitude involving the renal parenchyma and perhaps even the renal pedicle will show a nonfunctioning kidney irrespective of dosimetry or contrast material used. I don't think that tomography or angiography would be appropriate in this case; tumors of the urothelium are not well identified by angiographic techniques, in contrast to the solid tumors. The submitted roentgenogram shows a notching in the upper portion of the ureter which is very suggestive of spread of tumor down the lumen of the ureter; this is characteristic for transitional-cell carcinoma. Dr. Perez-Mesa has indicated that the ureter was involved.

What should we do with this lady? She had albuminuria and I would feel certain that she was having hematuria as well. She already has a supraclavicular metastasis; are we justified in undertaking what we know to be a palliative operation. I should think that this is a clinical judgment that only the surgeon can make. He has to decide whether he thinks the advantages of palliation exceed the

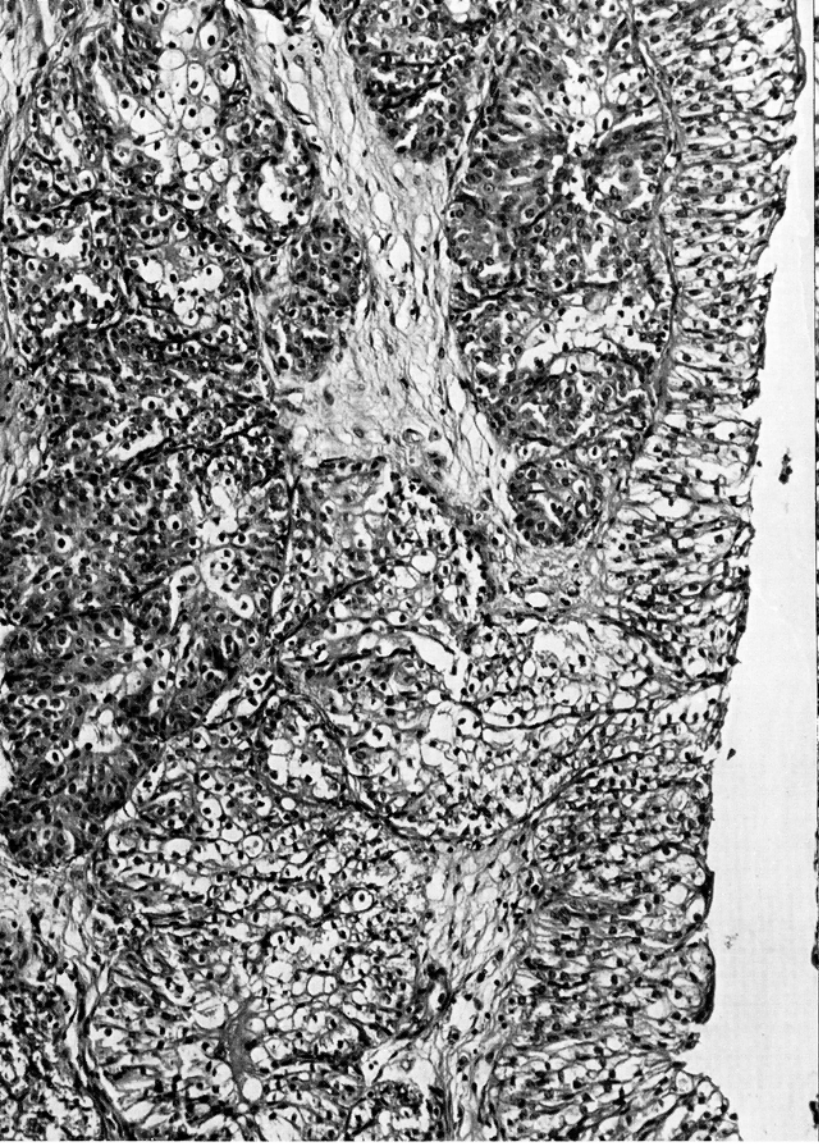


Fig. 3—This view of the renal pelvis shows infiltrating well-differentiated transitional cell carcinoma in continuity with the overlying pelvic epithelium. X150 W.U. Ill. 72-5218.

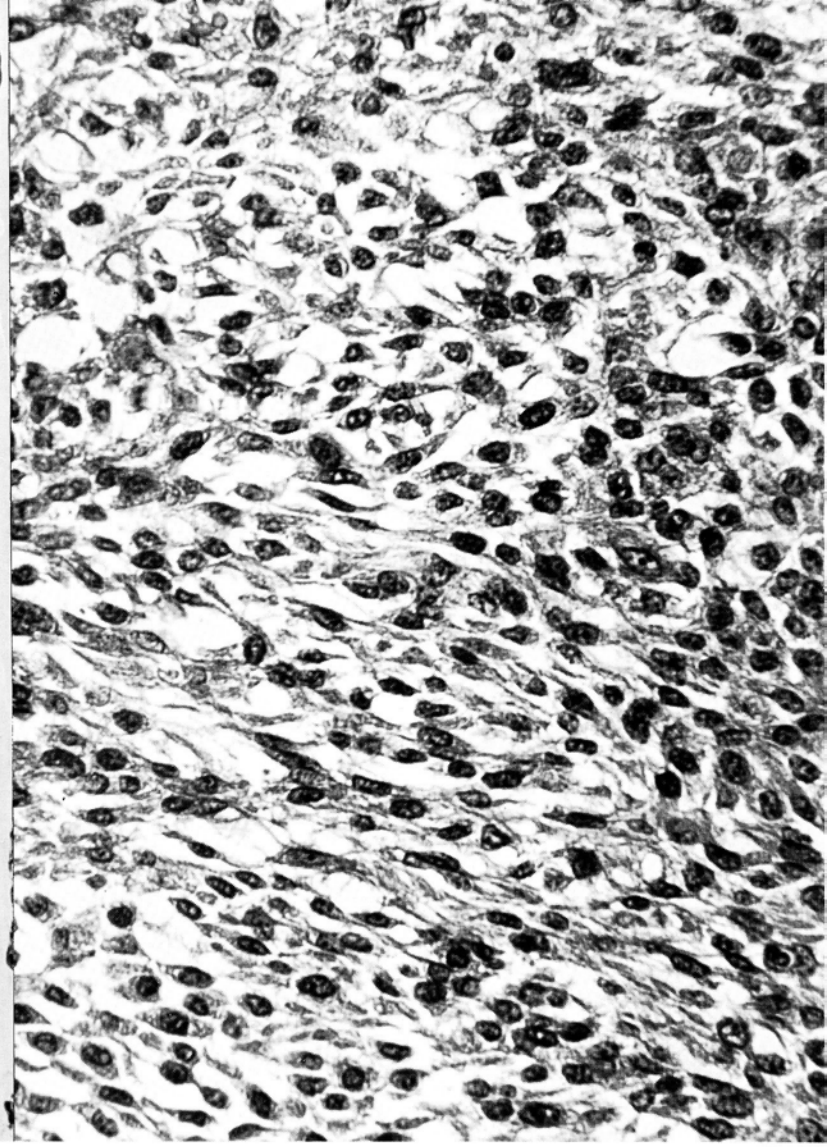


Fig. 4.—A higher power view of the carcinoma in an intrarenal location showing considerable acantholysis resulting in a peculiar spindle-shaped pattern. X350 W.U. Ill. 72-5219.

risks involved in major surgery. If you are going to do surgery, you need to do a nephro-ureterectomy as was done here. Under the circumstances probably I would have done the same thing. This can be done through an eleventh rib incision; you do not need a thoraco-abdominal approach. With the patient in a 45 degree position and an extended incision from the terminal portion of the eleventh rib down into the lower quadrant, the entire kidney, the Gerota's fascia and the ureter can be removed all the way down to the bladder.

Dr. Regato: Actually the specimen that was removed in this case was 17 x 12 x 9 cm and I am sure that that is probably what they were feeling. They say in the iliac fossa which suggests the pelvis; they should have said in the left lower abdominal quadrant.

Dr. Lalli: I don't think that Dr. Glenn and I are in disagreement about the value of a retrograde pyelogram. The point that I was making is that if urography has failed, then you go to retrograde pyelogram. I am sure that the radiologist in Columbia, Missouri, tried to do an intravenous urogram first and couldn't show what was there, then he did a retrograde pyelogram.

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5. *Renal Adenocarcinoma*

Contributed by **J. Pettigrew, M.D., R. Beadles, M.D.** and **M. Berthrong, M.D.,**
Colorado Springs, Colorado

THE PATIENT was a 60-year old man in August, 1971, when he complained of weight loss and dyspnea; a diagnosis of emphysema had been made; there was no history of hematuria or pollakiuria. On examination there was no abnormality on palpation of the abdomen. Blood studies and urine analysis were within normal limits.

Dr. Lalli: The angiogram shows very poorly defined vessels and what appears to be an hepatic artery, which is overlying a portion of the right kidney and appearing to supply vessels to a poorly vascularized mass in the suprarenal region. It is almost impossible to separate this as a mass either within the kidney or outside the kidney.

This may be an adrenal carcinoma which is involving the upper pole of the kidney, a true hypernephroma. There is not an enormous amount of vascularity such as we would associate with a renal-cell carcinoma nor sufficient to suggest pheochromocytoma. There is a suggestion that the right kidney is displaced caudad which would also lend weight to this being an extrarenal mass. The small amount of vascularity prevents serious consideration of an inflammatory lesion. Metastatic lesion to the adrenals such as a bronchial carcinoma or metastatic lesion to the upper pole of the right kidney of the same sort must also be considered. The fact that the patient has a diagnosis of emphysema is also one to suggest the possibility of metastatic bronchial neoplasm.

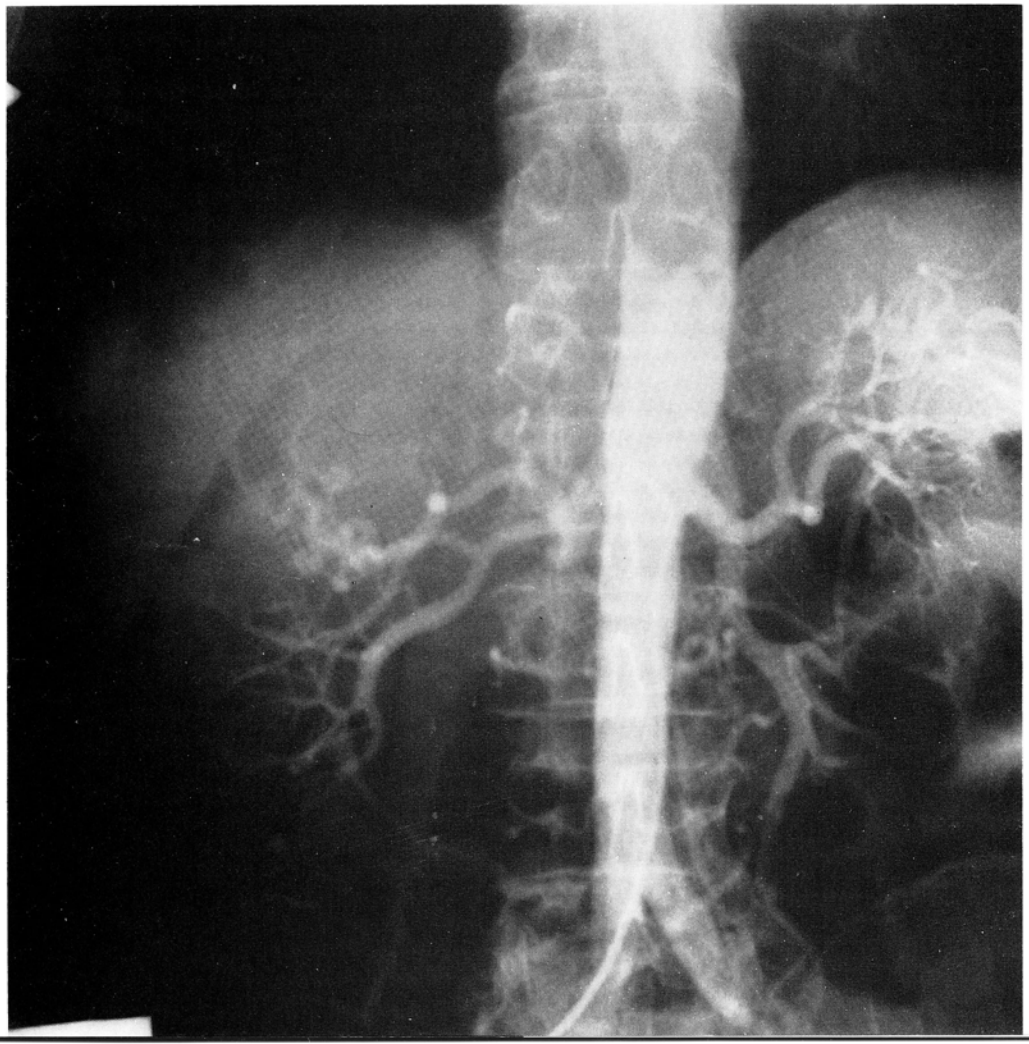
Dr. Lalli's impression: 1) Primary ADRENAL CARCINOMA 2) METASTATIC CARCINOMA involving the right adrenal.

Roentgenologic impressions submitted by mail:

Renal carcinoma	46
Metastatic carcinoma	16
Adrenal tumor	10
Others	31

Dr. Lalli: I find myself in a small group talking about adrenal tumors; the majority suggested that this was a renal carcinoma arising presumably in the upper pole of the kidney and that is an eminently reasonable diagnosis to make. Metastatic carcinoma either to the adrenal or to the upper pole of the kidney is also a very reasonable diagnosis to make; however, it is unusual for us, as radiologists, to be able to make that diagnosis. Metastases arising from lesions in the lung have been docu-

Fig. 1—Angiogram showing poorly defined vessels overlying the right kidney.



mented to be the most common tumor of the kidney, and so, from an autopsy statistical standpoint, one would be justified to make this particular diagnosis. Adrenal tumors are much less frequent than renal carcinomas and so, you would be making a safe bet with this particular diagnosis.

Dr. Regato: Dr. Mostafa Batata, of New York suggested an occult primary with metastases to the kidney. Dr. Wendell Stampfli, of Salida, submitted hypernephroma. Dr. J. Pettigrew, of Colorado Springs, favored an adenoma.

Operative findings: On August 30, 1971, the right kidney was explored. A small mass 1.5 x 2 cm was found sitting on the upper pole; it presented some superficially enlarged veins. Frozen section diagnosis was adenoma. A pursestring suture was placed around the upper pole and the mass was dissected from the kidney.

Dr. Bauer: The slides show a sharply localized tumor in the kidney composed of cells with predominantly granular pink cytoplasm. In most areas the tumor cells are arranged in trabeculae, plates or columns. The nuclei in most areas are slightly enlarged with a regular spherical conformation. Nucleoli are usually single and often prominent. Erythrophagocytosis by tumor cells is evident. In some areas the tumor cells lose their regular growth pattern and take on a disorganized look. The cells are larger, more variable in size and outline. The nuclei have multiple and enlarged nucleoli. In the central regions of the tumor there is evidence of degeneration with threads or islands of surviving cells in a loose or collapsed stroma. No vessel invasion was noted.

Differential diagnosis: Adenocarcinoma of the kidney, adenocarcinoma of the adrenal, metastatic adenocarcinoma (adrenal, liver).

I believe this is a fairly well differentiated adenocarcinoma, granular cell type, of the kidney with a trabecular growth pattern that brings to mind the possibility of adrenal or liver cancer. Apparently the cancer did not involve the adrenal. Metastases from the liver might be expected to be multiple. I would therefore think it primary in the kidney.

Dr. Bauer's diagnosis: ADENOCARCINOMA OF THE KIDNEY.

Histopathologic diagnoses submitted by mail:

Renal-cell carcinoma	110
Adenoma (cortical, tubular, granular, eosinophilic)	46
Metastatic carcinoma	10
Adrenal tumor	8
Others	5

Dr. Bauer: A large majority of pathologists agree that this was a renal cell carcinoma and about half as many thought that this was an adenoma. It seems to me that the cellular features of this case are sufficient to indicate malignancy; I am not always sure that I can tell the difference between an adenocarcinoma of the kidney and an adenoma. When you have well differentiated areas that resemble adenoma and other areas that appear carcinomatous, there is the possiblity that there is an adenocarcinoma arising in an adenoma; I suppose that could be a consideration in this case.

Dr. Regato: Drs. A. O. Severance, of San Antonio, and Y. LeGal, of Strasbourg, also submitted a diagnosis of renal-cell adenocarcinoma. Dr. Leo Lowbeer, of Tulsa, diagnosed a hypernephroid cortical adenoma with questionable incipient malignant changes. Dr. C. R. Vest, of

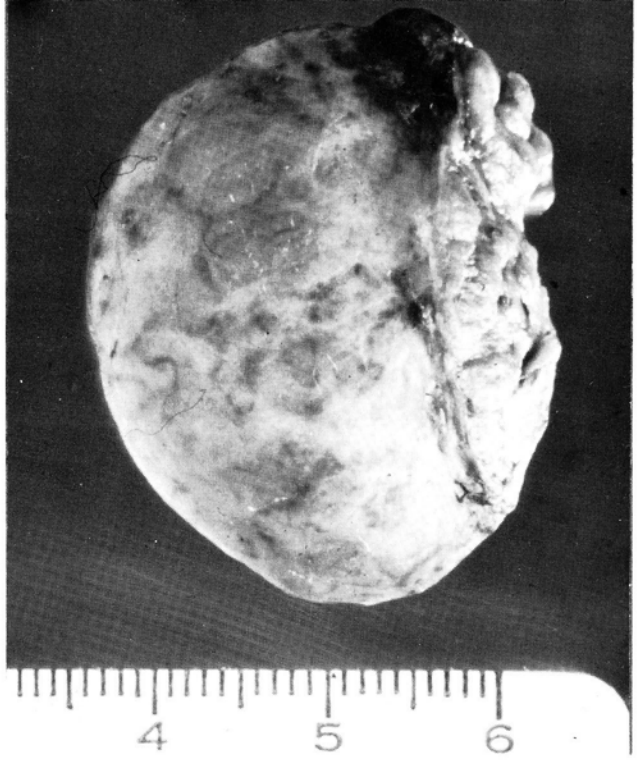
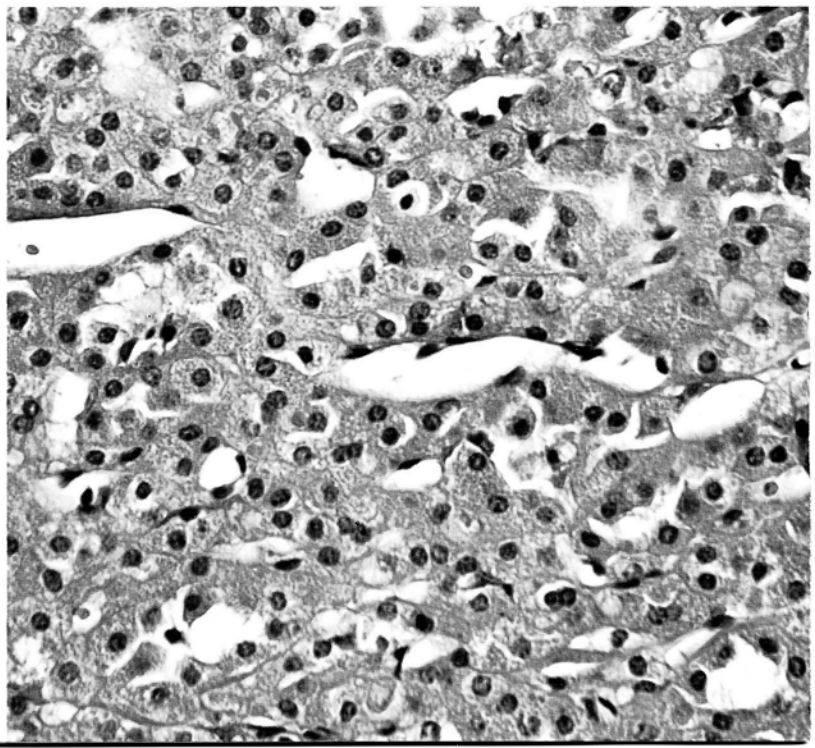


Fig. 2—Gross appearance of the tumor excised from the right kidney.

Fort Sam Houston, called it an adrenal cortical adenoma and Dr. E. V. Price, of Denver, a granular cell type of renal-cell adenoma. Dr. G. H. Moore, of Colorado Springs, made a diagnosis of well differentiated renal adenocarcinoma.

Subsequent history: No further surgery was done. On October 14, 1971, the patient had regained eight pounds and had regained strength. Examination failed to reveal any evidence of recurrence or metastasis.

Fig. 3—Granular cell adenocarcinoma in a solid trabecular pattern. X350 W.U. Ill. 72-5397.



Gene H. Moore, M.D., Colorado Springs: At operation, Dr. Beadles called the attending pathologist to the operating room. Actually the tumor was almost pedunculated, it was also in excess of 3 cm as the gross photograph shows. The frozen section diagnosis that was given Dr. Beadles was that of a well differentiated renal tubular cell structure; the size alone would indicate to most of us that it was probably a carcinoma. The striking thing was that is was almost a pedunculated structure, rather than embedded within the mass of the kidney. The adrenal gland was not grossly involved.

Dr. Glenn: Selective arteriography is certainly highly desirable in this situation. Dr. Bauer has pointed out the similarity of this tumor pattern to adrenal tissue; the term hypernephroma derived from the original work of Growitz and others in the late 1800's, at which time they thought that these tumors were indeed of adrenal origin, arising from adrenal rests beneath the renal capsule. The term hypernephroma should be put to rest; we should get out of the literature all together.

There are two important advances in the management of renal-cell carcinoma that deserve mention. The first is the development of angiographic techniques and the second is the judicious utilization of radiotherapy: perhaps Dr. del Regato will speak to this subsequently. With good angiography our limits of confidence in making a diagnosis of a renal mass are now in the realm of 97 per cent; there is the 3 per cent margin of error which includes both false positives and false negatives. We have been guilty of removing kidneys with benign lesions in a few occasions out of 160 operations for suspected renal carcinoma; that is a relatively slight price to pay when you consider the potential for the cure of those with cancer. The size of the lesion is of little consequence to me. The literature is replete with the arbitrary statements that if a lesion is less than 2 cm it is benign and if it is more than 3 cm, it is a carcinoma; we depend more on the angiographic pattern than we do on the size of the lesion. Given an angiogram with a distinctly malignant pattern, we would have proceeded in this instance with a radical nephrectomy as distinct from an exploration of the kidney. One does not open Gerota's fascia, one does not visualize the kidney, one does not do a biopsy, one does a complete cleanout from the diaphragm to the brim of the pelvis and this is done either through a thoracoabdominal incision, a transabdominal incision, or a modified flank incision, the eleventh rib approach. With radical surgery carried out in this fashion, the cure rates have been markedly improved: radical nephrectomy has doubled our five-year survivals up to 50 per cent. In the case of a lesion that is localized, like this one, with no metastatic nodes, the expected result should be about 80 per cent five-year survival. But you must believe the angiogram and you must commit yourself before surgery, not at surgery. I don't think there is any real equivocation about the histologic diagnosis in this case; it would seem to me that this is within the realm of the spectrum of adult renal cell carcinoma.

H. Braunstein, M.D., San Bernardino, California: A very high proportion of this type of tumor cannot be classified histologically with any certainty; thus, pathologists are obliged to give some weight to the criterion of size. This is based upon the work that was done by Dr. Bell, many years ago; he demonstrated that tumors which were less than a certain size practically never produced metastases, whereas tumors which exceeded a certain size did metastasize with some frequency. We did this waltz previously at another Cancer Seminar, with Dr. Franks. We had two cases very similar to this one, the first of which Dr. Franks classified as an adenoma; when he was asked whether he paid any attention to size, he said no. Later on an almost identical tumor, he classified it as a carcinoma; when he was asked why he called it a carcinoma, he said "because it was so big." So, size is of some consequence. I do not think many of us would be completely confident in a significant proportion of these and classify them unequivocally as benign or malignant; therefore we are forced to fall back on this criterion of size as an approach which does have a valid basis on statistical data.

S. Kazmi, M.D., Evanston, Illinois: I would like to ask Dr. Glenn if, in the approach of a suspected malignant tumor, he would open the Gerota's fascia and take a biopsy?

Dr. Glenn: Absolutely not. With a good angiogram and the conviction that this is a malignant tumor, you are obligated to do a good cancer operation; a good cancer operation is not the exposure and the biopsy of the tumor.

Dr. Kazmi: After you have cut the vessels, is there any danger if you open the Gerota's fascia and take a piece out for frozen section?

Dr. Glenn: It is hard to say never. Last week I operated on a resident who presented with hypertension and a 3 cm lesion in the upper pole of the kidney which our radiologist felt represented carcinoma. In view of his hypertension, in view of the extensive vascularity of the lesion, in view of his age of 28 years, I did a radical nephrectomy. After I had the specimen on the table, I opened Gerota's fascia and took a peek at it, but not before; it turned out to be a hamartoma.

J. J. Kepes, M.D., Kansas City, Kansas: I would like to comment on the relationship between tumor size and histological, as well as biological, characteristics. It has been stated that renal cortical tumors with a diameter under 3 cm are likely to be benign and the larger ones malignant. I would accept one half of this supposition, namely that very large tumors of renal tubular origin are likely to be malignant: a yellow tumor with a 20 cm diameter is not likely to be a benign adenoma. On the other hand if we say that a tumor that is smaller than three, two or even 0.5 cm is by definition benign, we are running contrary to what we know about cancer in general. Carcinomas must also start somewhere and at one stage they are small, even microscopic in size. This should be true for renal cell carcinomas also unless we assume that they always develop from pre-existing adenomas up to 3 cm in size, and never from normal kidney tissue. I am not aware of any proof in the literature for this latter assumption.

M. McGavran, M.D., Hershey, Pennsylvania: I am somewhat concerned about claims that have been made by Dr. Glenn for 97 per cent accuracy. I would be particularly glad to have Dr. Lalli give us his considerate opinion about how accurate renal angiography is, not only in specialized centers, but across the land.

Dr. Lalli: Very frankly, I think that angiography ought to be done by individuals who have experience, not only in manipulating the catheters, but interpreting the examinations that they produce. We have had a chance to see many angiograms, performed sometimes in very small institutions, which are of absolutely excellent quality; we

have to balance those with some which are, unfortunately, not of very good quality. It is not the size of the institution, it is the devotion, interest and training of the radiologist who is carrying out this sort of an examination. The papers published on the accuracy of angiography in the diagnosis of renal-cell carcinoma give a range of 90 to 98 per cent. If you add the claims of those who advocate nephrotomography which in some instances is said to improve on angiography, you have a difficult argument to beat.

The following is our concept of work-up of a patient with a renal mass: The patient should have a well-executed excretory urogram performed where you have facilities for doing tomography, if necessary; if you are interested you should have oblique views, using good ureteral compression, reinjecting the patient with more contrast medium and then evaluating that total examination with the patient's clinical history. If you decide that this is probably cancer of the kidney, you should then do an angiogram and proceed to doing the surgery. If, having done these examinations you have reached the conclusion that you are probably dealing with a benign cyst, then the kindest and, to my way of thinking, most intelligent procedure, is to turn the patient over and under fluoroscopic guidance, stick a needle into this mass. If you find that the mass contains clear fluid, you are usually very much assured that it is a cyst, you send the fluid to the cytologist for examination, you empty the cyst completely; in most instances this should solve the problem. I don't think the patient should be hospitalized, I don't think that he should have in all instances, an angiogram, I don't think that he should have a renal exploration. I am perhaps over-stating my case, but I believe that this is the kindest and best way to handle the problem; there are so many cases of renal cyst, and many of these patients are not good operative risks. It seems to me that sometimes we are guilty of academic masturbation, rather than offering good care of the patient.

Dr. Regato: Surgeons beware! With the advent of arteriography the radiologists have become adept at operating room procedures; they make incisions, insert needles, and now they are doing biopsies. There is, I am certain, the good of this, but the potential danger of it, also.

L. Lowbeer, M.D., Tulsa, Oklahoma: I believe the concept of size in relation to malignancy is true for certain tumors of low biologic activity, such as rectal carcinoids, such as carcinomas or carcinoids of the appendix, and mucin producing carcinomas of the breast, which notoriously have a good prognosis, if they are very small. But it is not true for a number of other small carcinomas which are extremely aggressive, such as a carcinoma of the stomach, which can be minute and cause enormous metastasis to the skeleton, or carcinomas of the bronchus.

Dr. Regato: In the Fall of 1965, Dr. Glenn and I had the privilege of being invited to an International Conference on Renal Neoplasia which was called in Brazil. We were asked to present the point of view of radiotherapy in reference to renal carcinoma. Dr. Eric Riches, the famous urologist from London, was also at the conference; he presented his experience which had shown him the usefulness of post-operative radiotherapy in a small group of non-randomized cases; he had noted improvement in results when nodes had been found involved and radiotherapy had been carried out. Sir Eric was fortunate to have done this work in association with Sir Brian Windeyer, one of the most capable radiotherapists in England. We concurred in his view and also pointed out that when *post-operative* radiotherapy proves to be of any value, *pre-operative* radiotherapy is likely to be of greater value. Dr. Patrick Cavanaugh, of Duke University, and myself presented at that conference our view that a scientific trial of pre-operative radiotherapy should be planned to ascertain whether or not this would improve results. We also discussed our views in reference to technological and dosimetric factors (King). This proposal has been taken over and followed through by Dr. Claire Cox, Professor of Urology, at Bowman Gray. Dr. Cox has in operation a national cooperative program with a well protocoled plan for pre-operative radiotherapy and also another one for post-operative radiotherapy; both associated with adequate surgery; this is being carried out very well with an accruence of a sufficient number of patients. Awaiting statistical confirmation, we feel, indeed, that pre-operative radiotherapy is well indicated in a case where a diagnosis of carcinoma of the kidney is made with sufficient degree of certainty. When that is not the case, an exploration should be done for biopsy because it would not be right to irradiate a nonmalignant kidney for lack of evidence. On the other hand, as very often happens, the kidney in question will be removed anyway, for it is not a functional kidney. The argument raised by Dr. Glenn against biopsy would not apply when the tumor is questionably operable or the biopsy is going to be followed by adequate pre-operative irradiation.

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6. *Undifferentiated (Neurogenic?) Malignant Tumor of the Kidney*

Contributed by **A. O. Severance, M.D.** and **H. Elmendorf, M.D.**, San Antonio, Texas

THE PATIENT was a 22-year old woman in March, 1970, when she gave a three years history of obstipation and left sided abdominal pain, 12 lbs. weight loss in one year and bloody stools for four weeks. Examination revealed a freely movable palpable mass 8 x 10 cm in the left upper abdominal quadrant.

Dr. Lalli: The abdominal angiogram shows a normal appearance of the right kidney. There is a very low position of the intra-aortic catheter and we see a very peculiarly distributed mass of vessels not characteristic for renal cell carcinoma tending to a palisade distribution. There is a complete obliteration of the left kidney and probably no function to be demonstrated on urography. There is no surviving normal renal parenchyma except for the small bits seen very high on the left side in the abdomen. The mass is also quite large, extending down to the level of the fourth lumbar vertebra.

The diagnoses to be considered include an unusual neoplasm arising in the kidney and involving the colon or a neoplasm in the colon invading and completely replacing the kidney. The latter is considered most unusual so we will focus our attention on the first. Both the age of the patient and the pattern of the vascularity is generally against a renal cell carcinoma. The peculiar vascularity suggests lesions such as malignant hemangiopericytoma replacing the kidney and involving the colon or an unusual sarcoma of the kidney such as a fibrosarcoma. The palisading of the vessels recommends lymphoma to me as does her age group, but as I said before primary lymphoma of the kidney is very rare, but so is my appearance as the discussant at this conference. It would be my conclusion that we are definitely dealing with a malignant neoplasm arising in the kidney of unusual type, that a late appearing Wilms' tumor must be considered.

Dr. Lalli's impression: 1) Atypical NEPHROBLASTOMA extending to the colon. 2) RENAL SARCOMA

Roentgenologic impressions submitted by mail:

Renal carcinoma	43
Malignant lymphoma	18
Wilms' tumor	8
Carcinoma of the colon	6
Others	27

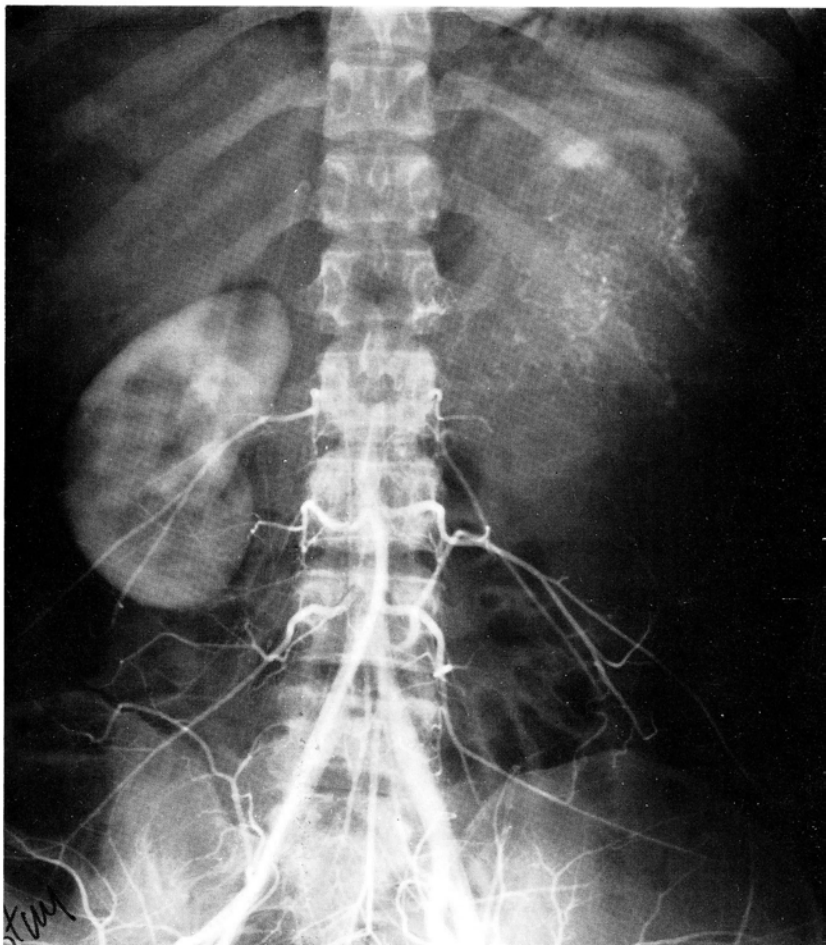
Dr. Lalli: Obviously, I am in the minority. Most of the participants were betting on renal carcinoma, the most common malignant tumor in this age group. The malignant lymphoma is a very defensible diagnosis from the angiographic point of view, although from the statistical point of view, it is extremely unlikely. Carcinoma of the colon invading and replacing this much kidney would be to me very rare.

Dr. Regato: Dr. Harry Z. Mellins, of Boston, suggested a metastatic tumor with possible primary in the ovary. Dr. Milton Elkin, of New York, commented that this cluster of peculiar tumor vessels is apt to be seen in unusual types of tumors.

Operative findings: On March 13, 1970, a left nephrectomy was done. The specimen measured 21 x 15 x 13 cm and weighed 1560 gm; most of the kidney was replaced by a tumor which invaded the pelvis.

Dr. Bauer: The sections of this very large tumor show almost total replacement of kidney tissue by a poorly differentiated small-cell malignant tumor. Only a remnant of renal cortex is present with widely separated surviving glomeruli. The pattern of the tumor is one of solid masses of small cells with little cytoplasm, poorly defined cellular outlines and round to slightly elongated nuclei. The chromatin distribution in the nuclei is fairly homogeneous with some tendency to aggregation at the nuclear mem-

Fig. 1—Abdominal angiogram showing no function and probably complete obliteration of the left kidney with peculiar vessel distribution.



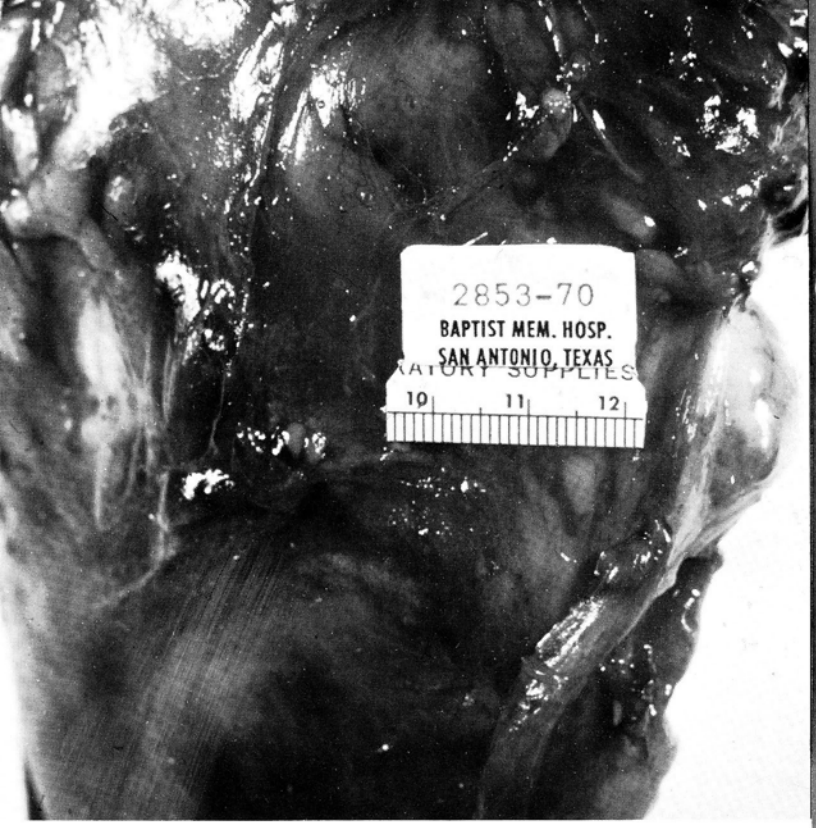


Fig. 2—Detail of outer surface of surgical specimen.

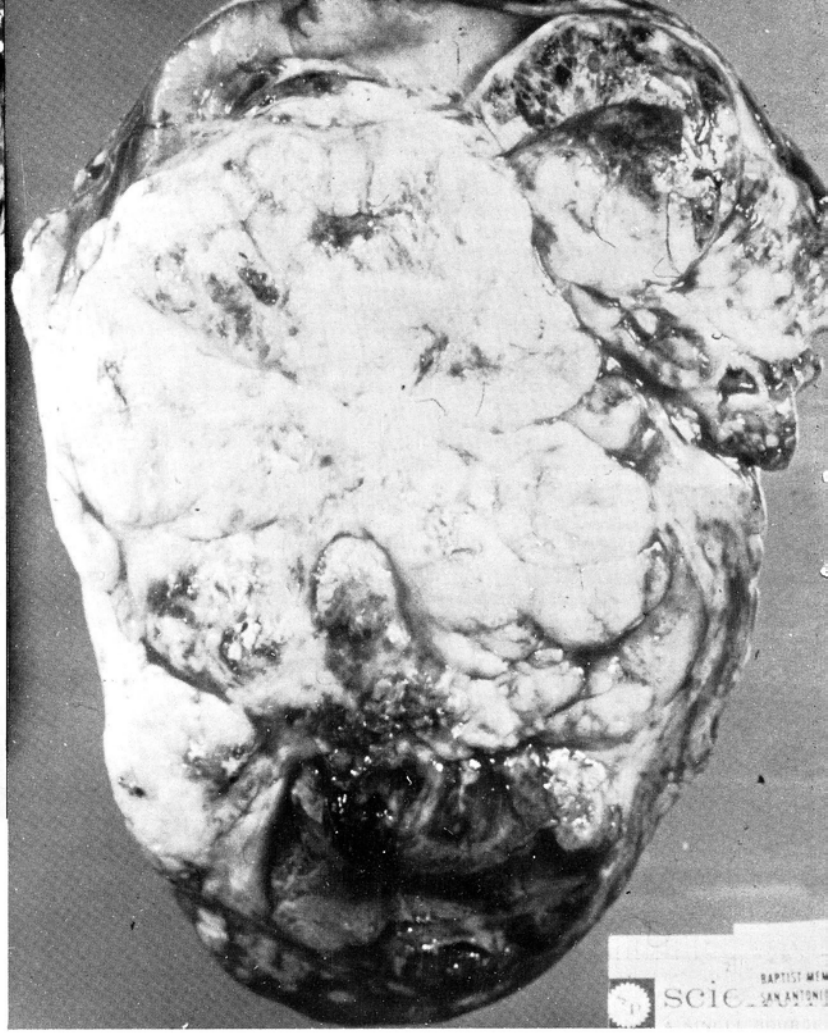


Fig. 3—Cross section showing necrotic mass and little remaining kidney.

brane. There is a tendency toward uniformity of nuclei that makes every field look the same as every other field. Nucleoli are rather small and inconspicuous. Mitoses are frequent and degenerating cells are common.

The state of fixation in many areas of the tumor precludes any evaluation of the cytoplasm, but in one or two areas judged to be better preserved, there does seem to be a fibrillar matrix between cells. No convincing arrangement of cells into rosettes or pseudorosettes or other configurations was detected. The tumor extends beyond the confines of the renal capsule where invasion of small vascular channels was easily found.

Differential diagnosis: Neurogenous (neuroblastoma) tumor; lymphoma; undifferentiated carcinoma, metastatic (lung, anus, rectum, ovary, kidney, salivary gland and thyroid); metastatic Ewing tumor; metastatic carcinoid; metastatic melanoma; Wilms' tumor.

It is very difficult for me to make a specific histological diagnosis in this case and the best that I can do is to present a list of possibilities. We have no evidence from the history and clinical findings of a primary tumor in another site with metastases to the kidney. I personally do not feel that the appearance of the tumor suggests any of the primary sites listed above but they certainly must be considered as possibilities. And I also probably left out some that others would want to consider. I am impressed with the fibrillar matrix that is seen in some areas. This leads me to consider a neurogenous origin and would be against the possibility of lymphoma. The round or oval shape of the nuclei sway me away from this diagnosis also. I am familiar with two other cases that are somewhat similar to this case. One is an ancient case from our own files that Dr. Ackerman thought was neurogenous in origin. The second one is Case 3 from the 1964 (Arean) Penrose CANCER SEMINAR which was interpreted as neuroblastoma by Dr. Franks. In both of those cases the cells were a little more elongated and areas suggestive of alignment in rosette formation were found; unfortunately I was not able to find convincing areas in this case.

Electron microscopy might prove very helpful in determining the type of this tumor. We have had some success with just such undifferentiated appearing tumors. Urinary catacholeamine determinations would also be of interest in this case.

In view of the nature of the tumor and the vascular invasion I expect the prognosis will be poor. Perhaps the follow-up or the autopsy findings will tell us more about the origin of the tumor. At this point I am unable to make a specific diagnosis but, in the spirit of this seminar, I would favor a tumor of neurogenous origin.

Dr. Bauer's diagnosis: UNDIFFERENTIATED (Neurogenic?) MALIGNANT TUMOR.

Histopathologic diagnoses submitted by mail:

Neuroblastoma	50
Nephroblastoma (Wilms')	47
Malignant lymphoma	27
Sarcoma	25
Renal carcinoma	15
Others	26

Dr. Bauer: I see that I have some support. A number of pathologists are still going with Wilms' tumors. Malignant lymphoma is a good possibility. Some sort of sarcoma, a rhabdomyosarcoma of embryonal type or undifferentiated type, might fit. I have discussed Ewing's sarcoma and renal-cell carcinoma.

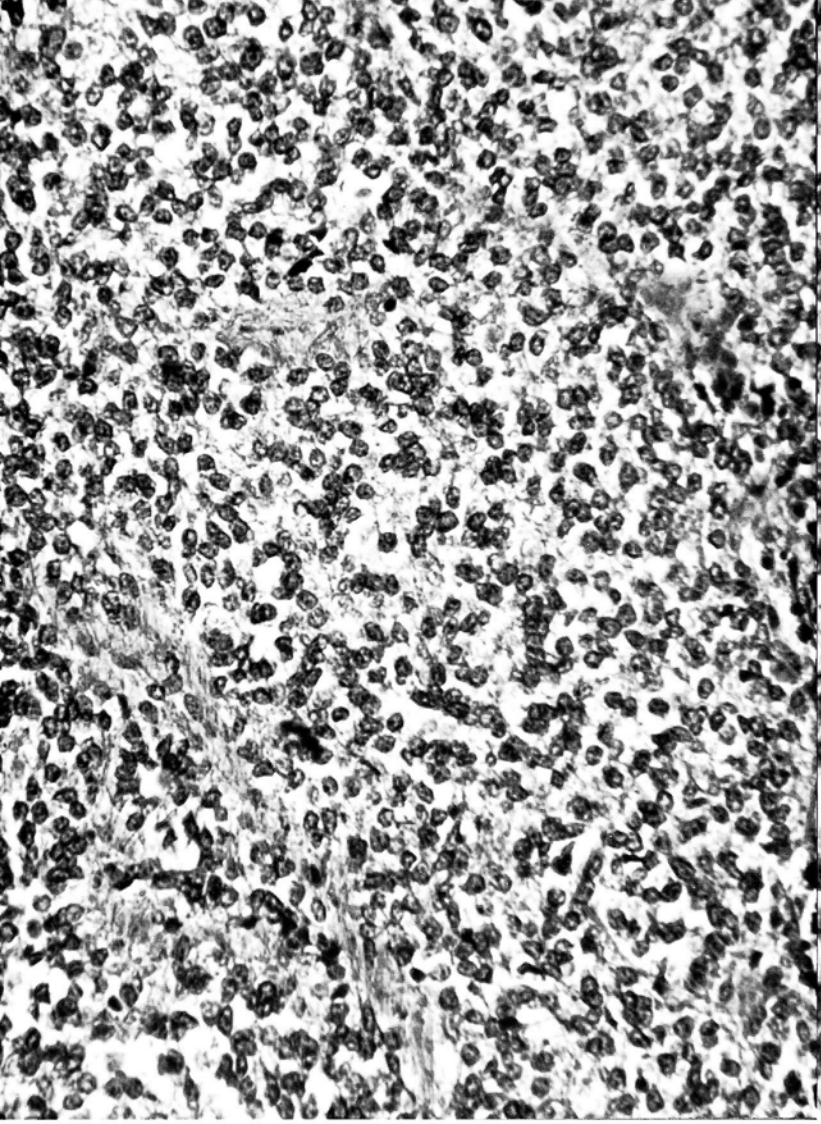


Fig. 4—Uniform cells comprise this malignant tumor. In a few areas the cytoplasm appeared fibrillar suggesting a neurogenous origin. X350 W. U. Ill. 72-5226.

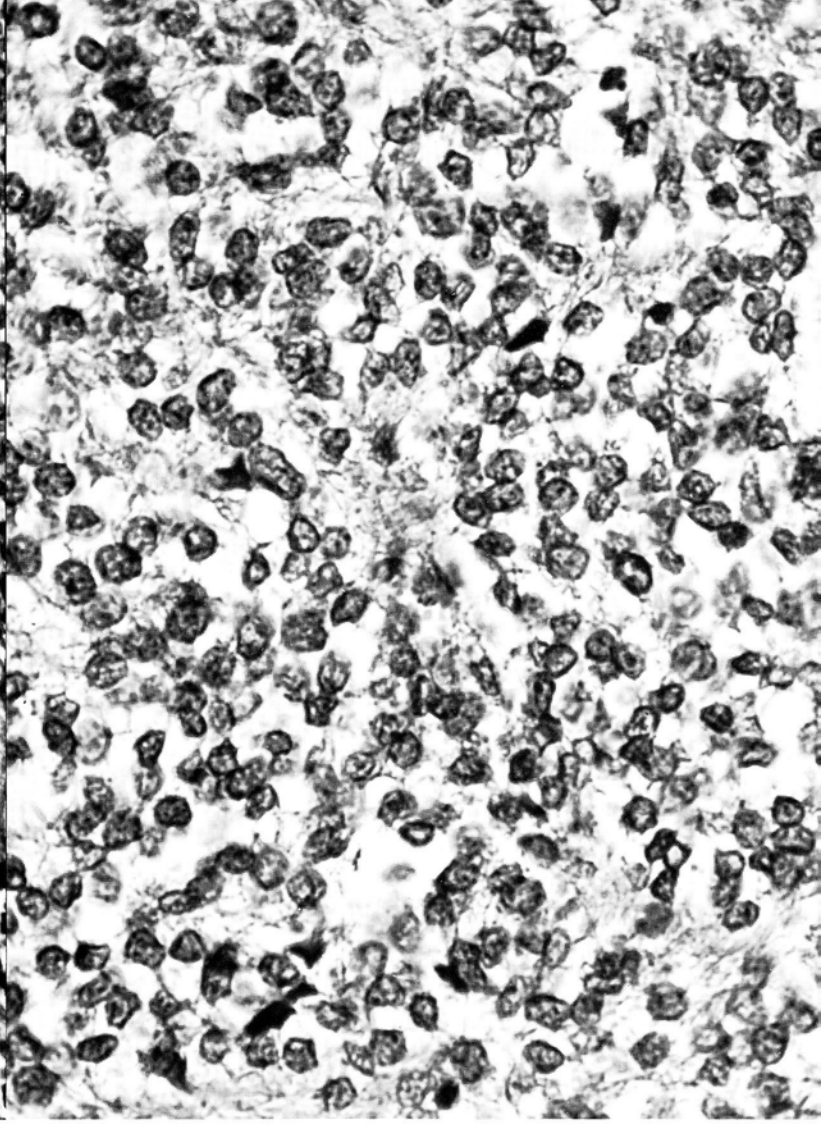


Fig. 5—A higher power field showing homogeneous chromatin distribution, inconspicuous necleoli and fibrillar cytoplasm. Occasionally large nuclei and nucleoli are seen. X720 W.U. Ill. 72-6227.

Dr. Regato: Dr. A. O. Severance, of San Antonio, offered a diagnosis of undifferentiated carcinoma; Dr. G. Gricouroff, of Paris, preferred undifferentiated sarcoma. Drs. G. Vogt, of Tunis, C. Maso, of Chicago, and M. J. DeMeo, of Santa Rosa, California, made a diagnosis of neuroblastoma, while Drs. D. R. Dickson, of Santa Barbara, California, and E. C. Farkas, of Sioux Falls, preferred nephroblastoma.

The AFIP had been consulted about this case (Accession No. 1345119). Dr. Mostofi rendered an opinion of malignant undifferentiated tumor, possibly transitional-cell carcinoma, because of the sheets of small round or spindle cells. Other diagnostic possibilities considered less likely by "the staff" were: undifferentiated renal-cell carcinoma, neuroblastoma or lymphoma.

Subsequent history: No VMA or HVMA excretion tests were done in this patient. Following operation she received post-operative radiotherapy. In August, 1970, she presented a swelling of the orbit and was put on chemotherapy. On December 14, 1970 she expired. She had radiographic evidence of metastases in the lungs and in the superior maxillary and pelvic bones.

A. O. Severance, M.D., San Antonio, Texas: This tumor involved the pelvis of the kidney and the wall of the ureter; it did invade the renal vein and you did see a thrombus of tumor in the renal vein. We did special stains and, for what it is worth, there was fat positive material and also PAS positive material in the tumor cells. I did a reticulin stain and it appeared to me that it had an epithelial pattern. In looking at this tumor, I thought the same things that you did; but I couldn't see any rosettes and I was unable to identify that little fine staining material which you see around the tumor cells in a good neuroblastoma, so I chose not to use that diagnosis. I could not find the pattern of a Wilms' tumor, and so I didn't like that diagnosis. I didn't think it was a lymphoma. I came up with the idea that it was a malignant tumor of epithelial origin and called it an undifferentiated carcinoma probably of renal-cell type. And then I did what you said, I punted. I sent the whole specimen to Mostofi. First, I sent him a slide and he said "this looks like a transitional cell carcinoma of the pelvis," then I sent him the whole specimen and he did a lot of side stepping, you know, like a football player: it could be an atypical Wilms' tumor, it could be a neuroblastoma; he left question marks after both of them and he said other people at AFIP thought it might be an undifferentiated carcinoma; that is all the answer I got. So, take your choice; to me it is an undifferentiated carcinoma. An autopsy was not obtained even though the patient died in our hospital.

Dr. Glenn: Dr. Severance, did the tumor involve the colon?

Dr. Severance: Not to my knowledge; I think there was a red herring here.

Dr. Glenn: The retro-orbital reappearance of the tumor, of course, speaks very strongly for it being of neurogenic origin, a neuroblastoma. Perhaps that is the best route to follow. Some years ago, a young woman died in our hospital; she had a history of melena and of a urofecal fistula. One of my general surgical colleagues and I were asked to discuss this at a CPC. We both called our files and went down to the record library; we have on file, at Duke, two cases of renal carcinoma which invaded the colon and two cases of colon carcinoma which invaded the kidney; we discussed this in an erudite fashion and my diagnosis was carcinoma of the colon invading the kidney, his diagnosis was carcinoma of the kidney invading the colon. It turned out that the woman had an adrenal cortical carcinoma, non-functioning, which had eroded both kidney and colon. I think the situation here is pretty much the same. I would be very happy with Dr. Bauer's diagnosis of possible neurogenic undifferentiated tumor.

Dr. Regato: Within limitations of this exercise, if you do not say that the patient had melena, you are withdrawing information, and if you say that she had blood in the stools you are throwing in a red herring.

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7. *Medullary Cystic Disease (Sponge Kidney)*

Contributed by **Joseph Kuzma, M.D.,** Milwaukee, Wisconsin

THE PATIENT was a 40-year old woman in March, 1968, when she complained of right sacro-iliac pain and hematuria. Examination revealed a symmetrically enlarged uterus but no fetal sounds, gross hematuria from right ureter and mild albuminuria.

Dr. Lalli: One wonders why this translumbar aortogram was done, in 1968, in a 40 year old lady. Was there some problem associated with the femoral approach? The right kidney does appear to be smooth in outline and a little wider than I would expect it to be. The middle branch of the intrarenal artery appears to be attenuated and obstructed in the middle portion of the kidney, but this is very difficult to see. In addition there appear to be several small vessels which extend beyond the boundary of the kidney in the upper pole, also an uncertain observation. I identify a normal adrenal artery on the right. In addition there is a strangely curvilinear practically serpiginous course of an artery immediately lateral to the fifth lumbar vertebra. I don't know whether this represents a tremendously dilated ureteral artery. The internal iliac arteries are very large.

Associating this appearance with the presence of a large uterus is difficult and may be impossible. It is unlikely that markedly dilated ureteral arteries are responsible for the hematuria but they may feed a metastasis. I am inclined to think that the lady has a malignant uterine tumor involving the right ureter with questionable involvement of the right kidney, producing the peculiarly attenuated right renal artery and suggesting tumor encasement with extension in the upper pole. Diagnostic possibilities include leiomyosarcoma and choriocarcinoma. Malignant degeneration of a teratoma must also be considered but is less likely. Because of the paucity of vascularity is is unlikely to represent a primary renal cell carcinoma. Choriocarcinoma should be very vascular. I feel that the radiologic evidence in this case is disturbingly small, and I am therefore hesitant to put forth these diagnoses.

Dr. Lalli's impression: 1) UTERINE LEIOMYOSARCOMA with involvement of ureter 2) OVARIAN CHORIOCARCINOMA with retroperitoneal metastases.

Roentgenologic impressions submitted by mail:

Renal infarct	24
Transitional-cell carcinoma	23
Ovarian tumor	12
Endometriosis	9
I don't know what she's got!	1
Others	31

Dr. Lalli: Those radiologists who suggested renal infarct were probably basing that diagnosis on the size of the right kidney. The angiogram with its paucity of vascularity would not permit me to make this diagnosis. Transitional cell carcinoma is diagnosed on the basis of the fact that there was no tumor vessel demonstrated in the kidney; most of us seem to think that transitional cell carcinomas are very difficult to diagnose angiographically because they have very small vessels and no tumor blushes. Dr. Joshua Becker, of New York, is soon going to publish a paper which refutes this; apparently if you take good films and you are a really sharp radiologist you can even suggest a diagnosis of transitional cell carcinoma of the renal pelvis on an angiogram. Endometriosis can involve the ureter and cause obstructive uropathy and hematuria. We have no radiologic evidence to say that she had any obstructive uropathy.

Dr. Regato: Dr. Frank Wilson, of Colorado Springs, suggested choriocarcinoma. Dr. R. B. McMullen, of Denver, preferred endometrial carcinoma with ureteral extension.

Operative findings: On April 18, 1968, a right nephrectomy was performed. The kidney measured 10x6x4 cm and showed external areas of congestion. Cut section revealed a cystic cavity 2x1.5 cm situated in the lower pole containing red-yellowish fluid. The medullary area presented numerous small cysts varying in size up to 3 mm; the pyramids appeared involved and there were tan areas noted in the papillae.

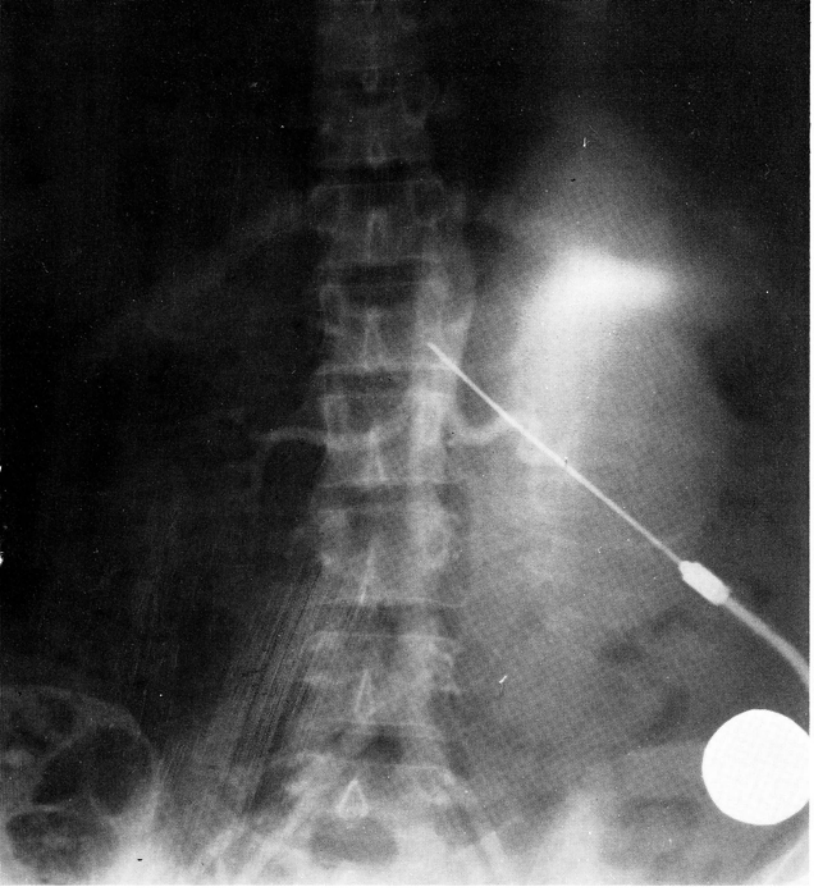


Fig. 1—Translumbar aortogram revealing some abnormality of the ureteral arteries.

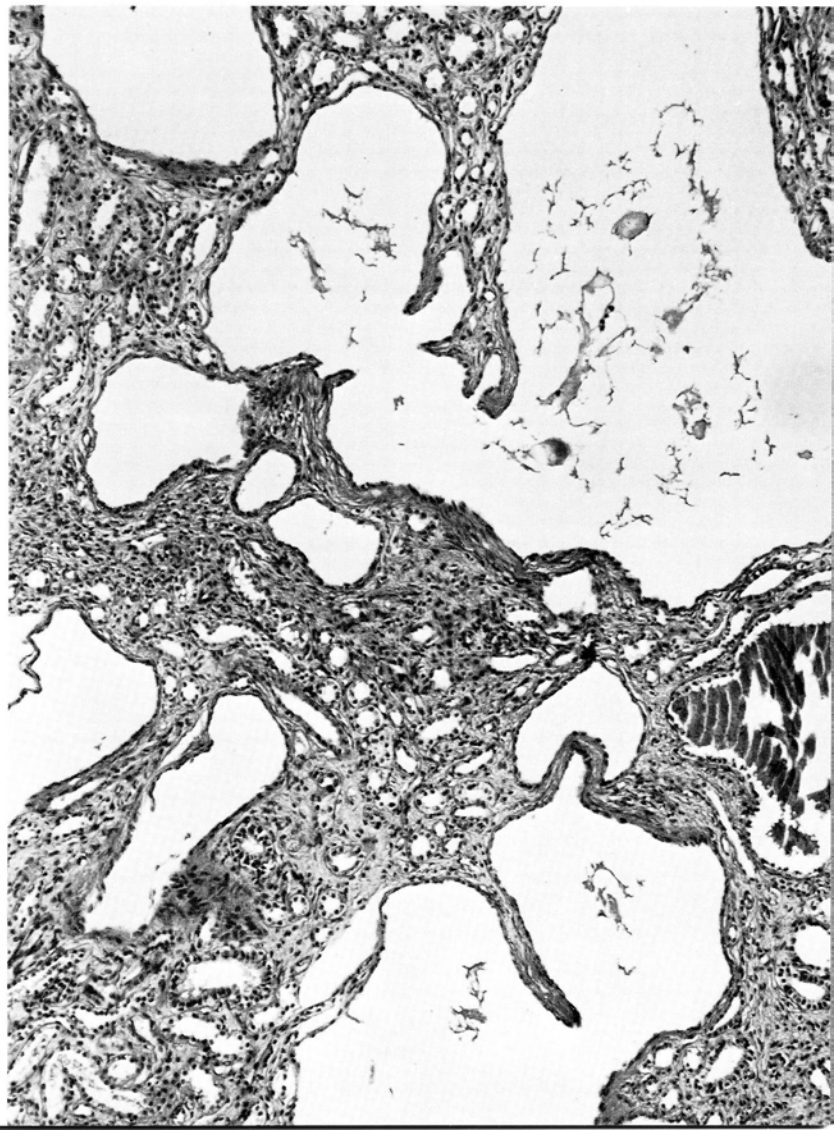
ity. Patients with medullary sponge kidney are usually without complaints but when symptoms occur, flank pain and hematuria are common. Disturbances of renal function are not a prime characteristic of the condition. The first manifestations usually occur in the fourth or sixth decades. Males are affected more often than women and there is no familial tendency.

Uremic medullary cystic disease is a less common disease affecting adolescents and young adults. The disease is familial with minor functional renal abnormalities demonstrable in asymptomatic members of the family. The clinical manifestations are those of renal failure with polyuria, polydipsia, growth failure, anemia and a progressive fatal azotemia. Whereas sponge kidneys are usually of normal size those of uremic cystic disease are contracted and granular with extensive tubular atrophy, glomerular and interstitial fibrosis. Most of the cysts are concentrated at the cortico-medullary junction but some are also found in the cortex while in sponge kidney they are pretty well limited to the medulla.

The findings in our case fit best with medullary sponge kidney. The flank pain and hematuria are probably due to the intrarenal bleeding caused by microliths and calculi associated with the cysts.

The diagnosis can be made roentgenographically as Dr. Lalli has pointed out in his publications and I

Fig. 2—Multiple delicate thin-walled cysts in the medullary region of the kidney. X90 W.U. Ill. 72-5603.



Dr. Bauer: The multiple small cysts scattered throughout the medullary region are seen to be delicate thin-walled cavities with minimal fibrosis or atrophy of renal tissue about the periphery. Their outline is roughly circular but often there are thin fibrous projections into or across the lumen. The cells lining the cysts are low cuboidal and they bear a striking resemblance to the epithelium of collecting tubules. The larger cysts have an extremely flattened, often indistinct, lining. Proteinaceous material mixed with casted off lining cells fill the lumen of some cysts; a few others show red cells in addition. Red cell and hemoglobin casts are found in the distal portion of convoluted tubules. Microliths or focal granular calcifications are seen in the interstitium of the pyramids infrequently. In a single instance a microlith was associated with a medullary cyst with evidence of erosion of the cyst wall. A few red cells and an overlying cap of fresh fibrin marked the breach of the cyst wall.

The cysts are limited to the pyramids; the remainder of the kidney appeared relatively unremarkable. Some of the glomeruli are somewhat hypercellular causing one to wonder whether the patient might also have a glomerulonephritis but I finally decided against this possibility.

Differential diagnosis: Medullary cystic disease (sponge kidney); medullary cystic disease with uremia and anemia.

This interesting case presents a problem of differentiating cystic diseases in which the medullary area is the principle site of involvement. I believe we have two choices, (1) medullary sponge kidney (2) uremic medullary cystic kidney. While the microscopic appearance of the cysts are very similar in the two entities I believe there are other aspects of our case that favor the first possibil-

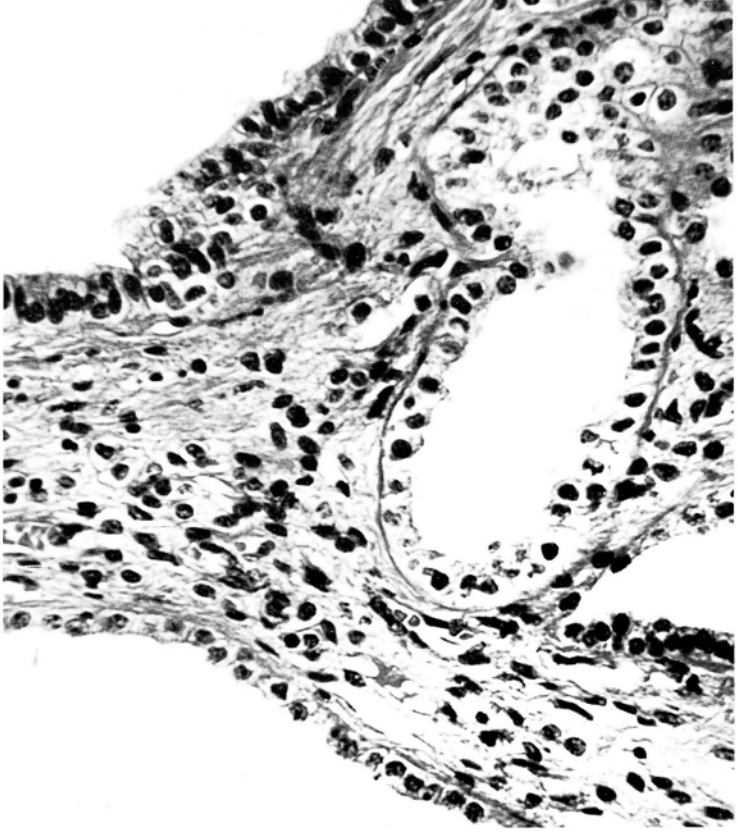


Fig. 3—Similarity of the epithelial lining of the cysts at top and bottom left with the epithelium of the collecting tubule on lower half. X300 W.U. Ill. 72-5602.

am confident he would have been able to make it in this case had films from an excretory urogram been available to him. There is great importance to the clinical recognition of this condition because it is bilateral in about 75 percent of cases and the disease follows a benign course. Symptoms are usually due to complications caused by stones, microliths and secondary pyelonephritis. These should be treated medically; surgery being reserved only for those cases unresponsive to conservative management. One wonders just how severe the bleeding was in this case.

Dr. Bauer's diagnosis: MEDULLARY CYSTIC DISEASE (SPONGE KIDNEY).

Histopathologic diagnoses submitted by mail:

Medullary cystic disease	61
Polycystic kidney	30
Glomerulonephritis	35
Lymph-, hemangioma	23
Single renal cyst	10
Others	27

Dr. Bauer: A good many of us agreed that this is a polycystic kidney. Glomerulonephritis is an interesting diagnosis. I, too, wondered whether or not this patient might not have glomerulonephritis and part of the bleeding could be explained by that. I looked at these glomeruli a long time and I thought there was something wrong with them; they did appear cellular, and focal glomerular loops did show some thickening of the basement membrane. I have relegated the glomerular changes to secondary importance. If one interpreted the cystic spaces as vascular or lymph channels, one can understand the diagnosis of lymph or hemangioma; but they are lined with tubular epithelium and are not that sort of thing.

Dr. Regato: Drs. H. A. Azar, of Kansas City, Kansas, and R. E. Stanford, of Fort Dix, New Jersey, also made a diagnosis of medullary cystic disease of the kidney.

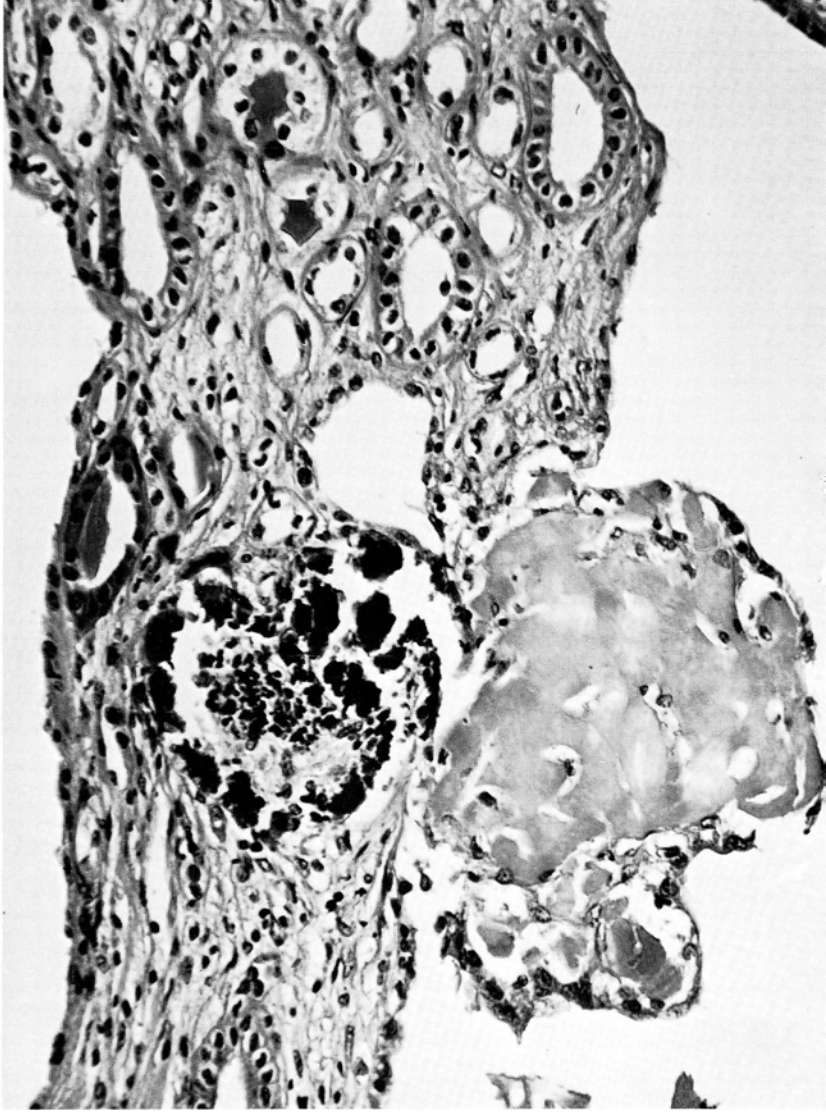


Fig. 4—A granular microlith in the cyst wall with an overlying cap of fibrin. X275 W.U. Ill. 72-5601.

Dr. L. Lowbeer, of Tulsa, diagnosed polycystic kidney, grade 3. Drs. R. D. Schultz, of Sioux Falls, and W. M. Russell, of Las Vegas, Nevada, preferred glomerulonephritis. Drs. Magda and John Kepes submitted a diagnosis of acute glomerulonephritis with medullary cysts. Dr. D. F. Wiench, of Fort Sam Houston, offered lymphangioma and Dr. W. J. Holaday, of Columbus, Ohio, preferred hemangioma. Dr. M. Berthrong, of Colorado Springs, made a diagnosis of medullary sponge disease.

Subsequent history: Five months after operation the patient delivered a normal baby. In September, 1971, she appeared well except for hypertension 150/104, headaches and sciatic pains.

Dr. Glenn: It would have been nice had we known that this lady was pregnant.

Dr. Regato: They said that she had a symmetrical mass in the midline and that there were no fetal sounds. So that is what I gave you.

Dr. Glenn: Suspecting that this woman was pregnant, I would have been reluctant to undertake vigorous diagnostic studies unless, of course, the woman was having such severe bleeding and pain and disability that it was necessary to intervene. Certainly an arteriogram would have been the last thing I would have thought of under the circumstances. We would have probably elected a high dose pyelogram.

The cysts that Dr. Bauer has shown us are so small that it is quite possible we would have missed the diagnosis, even with the finest of radiographic technique. Nephrectomy would have been one of my most remote considerations. It seems unfortunate that the kidney was removed because I strongly suspect that this lady has the lesion on the other side also. Certainly there is nothing in the angiogram to suggest tumor. There is a diagnosis that should have been entertained very early and that is the possibility of ovarian vein thrombosis and the ovarian vein syndrome, which can produce pain, can produce an enlarged kidney and can produce the bleeding. As to what to do about it, I really don't know. I wonder whether pregnancy with its physiologic hydroureteronephrosis, the progestational changes, the possibility of ovarian vein syndrome would accentuate the intraparenchymal hydronephrosis which is what a meduallary cystic kidney represents.

Dr. Bauer: I don't believe I can answer that question. I don't know of another case in which pregnancy has been a factor.

J. Kuzma, M.D., Milwaukee, Wisconsin: We thought it was a medullary sponge kidney of the type that is not associated with uremia. Our clinicians take the point of view that a patient, in good general condition, with unilateral hematuria, is highly suspect of having a malignant tumor of the kidney; the urologist did the translumbar aortogram and the radiologists agreed that there was a suspicious tumor; on that basis they took the kidney out.

Dr. Lalli: Medullary sponge kidney disease can only be diagnosed preoperatively by a well executed urogram. You can't do it angiographically, you can't do it by retrograde pyelography. It is justified to do partial nephrectomies when you have localized medullary sponge kidney disease.

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8. *Multilocular Cystic Nephroma*

Contributed by **Frank J. Glassy, M.D.,** Sacramento, California

THE PATIENT was a 49-year old woman in June, 1970, when on routine examination a symptomless non-tender mass was palpated, in deep inspiration, in the left upper abdominal quadrant. There was a history of numerous skin moles and cysts removed in the past. EKG, blood pressure, urine and hemoglobin were found within normal limits.

Dr. Lalli: The subtraction film of the left renal angiogram demonstrates that there are large capsular vessels extending laterally at the midportion of the left kidney and in the lower pole, describing by their course a mass approximately as large as the kidney. In addition there is a loss of definition of the left renal outline and the size of these capsular vessels and this loss of definition would prove to me that we are dealing with malignant neoplasm in the left kidney.

The history of numerous skin moles and cysts suggest two possibilities. One is that this is an angiomyolipoma, which would be unusual because of the hypo-vascularity in a patient who has tuberous sclerosis. The second possibility is that this is a metastatic malignant melanoma associated with a previously removed cutaneous melanoma. A third possibility is that this is a fibrosarcoma arising from the renal capsule. It is unlikely that this represents a tangentially attached relatively avascular renal cell carcinoma but that has to be included for completeness sake. Because of the blurring of the lower renal margin this should not represent a benign lesion such as a simple serous cyst.

Dr. Lalli's impression: 1)SARCOMA OF THE KIDNEY 2) METASTATIC MELANOMA.

Roentgenologic impressions submitted by mail:

Metastatic tumor	35
Peripheral cysts	17
Policystic disease	16
Lipomatosis	14
Hamartoma	10
Others	21

Dr. Lalli: Many radiologists thought that this was a metastatic tumor; I would venture a guess that probably most were thinking of metastatic melanoma. It is difficult to guess what is meant by peripheral cysts. Multilocular cysts occur but it is more likely in children than in adults. Policystic kidney disease is not the diagnosis that I would venture at all; that is a disease characterized by masses within the kidney displacing and distorting the internal architecture of the kidney. What we have here is something which is attached to the kidney like a poultice and, therefore, I do not think that this is a defensible diagnosis. Lipomatosis I find difficult to entertain because it will occur in the central portion of the kidney and will replace renal parenchyma as it is destroyed, for example, by

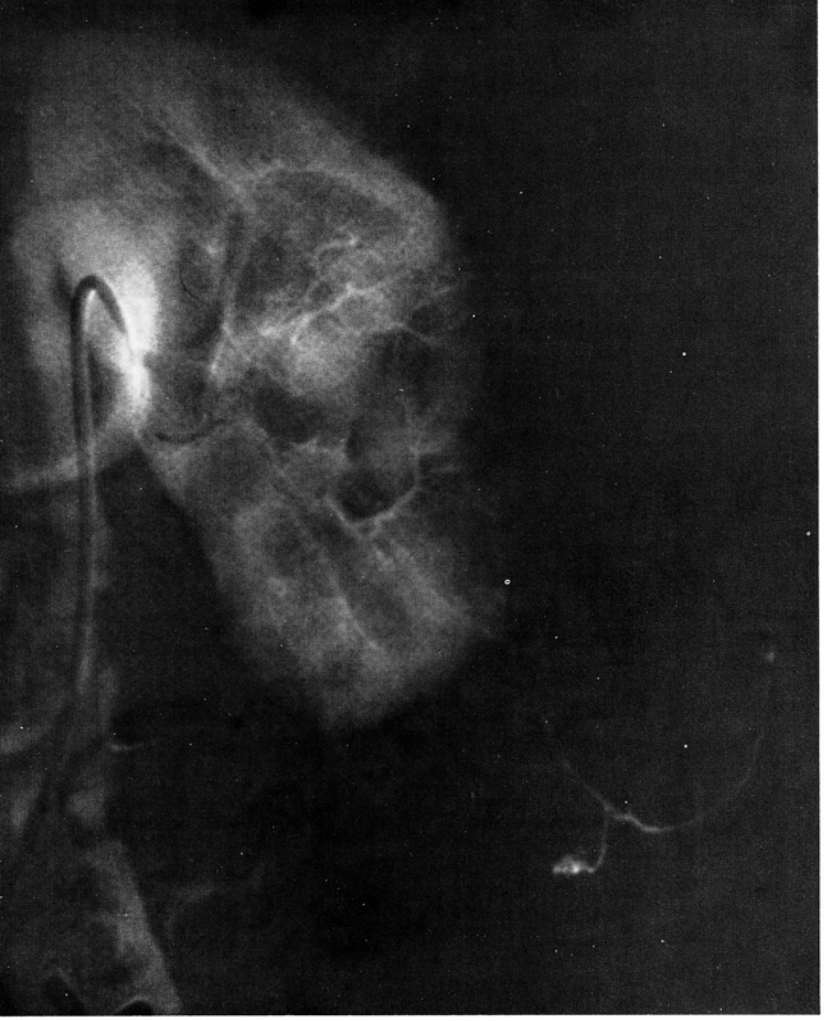

Fig. 1—Substraction roentgenogram of a left side angiogram showing large capsular vessels extending laterally.

chronic pyelonephritis; you can have lipomatosis occurring in aging patients as the renal parenchyma tends to diminish in thickness, but I would not consider this to be a likely diagnosis. Hamartoma is a good diagnosis; I think they are thinking somewhat in terms of an unusual angiomyolipoma.

Dr. Regato: Dr. John Pettigrew, of Colorado Springs, offered an impression of hamartoma. Drs. Wendell Stampfli, of Salida, Colorado, and J. Maxey Dell, of Gainesville, Florida, suggested hamartoma of tuberous sclerosis. Dr. Milton Elkin, of New York, also suggested metastatic melanoma. Dr. C. H. Meng, of New York, preferred polycystic kidney.

Operative findings: On June 4, 1970, the exploration of the left kidney uncovered a very large multicystic mass; frozen sections revealed no neoplasm. The mass was dissected from the kidney. The specimen measured 9.5x9x6.5 cm, was formed by numerous cysts containing fluid with abundant fat globules in some and crystals in others.

Dr. Bauer: This large well delimited cyst is subdivided into multiple large and small locules. There is no evidence from the slides that communication between locules exist. The component cysts are separated for the most part by thick and thin stromal septa that are relatively avascular, hypocellular, myxomatous and poorly collagenized. Thick and dense fibrous septae partition some of the larger cysts. The cyst lining is a very indistinct flattened epithelium. No residual of the fluid contents remains to be seen in sections.

Smaller cysts of microscopic size retain enough cytologic detail so that the structure of the epithelial lining may be described. The cells have a dense cytoplasm that is flattened against the cyst wall and which bulges into the lumen at the site of the nucleus. Sometimes the cells protrude into the lumen in a "hobnail" or "hanging drop" fashion. The nuclei are large, circular in outline and the nucleoli are also large and prominent. The outlines of such cysts are close to being circular but often show a flattened side or an indentation. Occasionally a few wisps of stringy proteinaceous material is seen in the lumen but often only several desquamated cells or nothing at all is seen.

At a microscopic level cysts of this kind resemble tubules, perhaps mesonephric. They are surrounded by a cellular stroma composed of immature mesenchymal cells with crowded elongated nuclei with rounded ends. Stromal cell cytoplasm is dense, eosinophilic and suggestively fibrillar. Mitoses among stromal cells are very rare. The areas of primitive stromal cells and "hobnail" tubules are tucked in the interstices of the larger cyst locules and so make up a minor proportion of the lesion.

A second type of tubule is seen scattered throughout the immature mesenchyme in small groups. These are closely grouped tubules with round outlines and narrow lumina. They are lined by a more cuboidal epithelium with vacuolated or clear cytoplasm. The nuclei are round, vesicular and with small indistinct nucleoli. Some tubules would appear to be just cords or clear cells, others are filled with a homogenous eosinophilic fluid. Associated with the clear-cell tubules are single or grouped foamy cells that resemble lipid-laden macrophages. However, several such clusters of lipoid cells have cytoplasm that appears transitional and raises the possibility that they are derived from the clear or vacuolated epithelial cells.

No areas of cartilage, skeletal muscle, or adipose tissue are found. Similarly no immature, or frustrate glomerular structures are observed. The cellular areas of stroma appear primitive or immature but not sarcomatous.

One last finding needs emphasis. In the thick fibrous capsule that separates the lesion from the rest of the unremarkable adult kidney, one may find well-differentiated bundles of smooth muscle. These are readily apparent on a Masson stain. Some of the cellular stromal areas also would appear to be smooth muscle with this stain.

Differential diagnosis: Multilocular cystic disease (nephroma); multilocular cystic disease with adenocarcinoma; multilocular nephroblastoma (Wilms' tumor); segmental dysplasia.

This is a very difficult and unusual case and one which has engendered certain feelings of insecurity on my part. Taking the gross and certain microscopic findings we certainly must consider this some sort of multilocular cystic kidney. The solitary nature, sharp demarcation from kidney and pelvis, epithelial-lined non-communicating multiloculation, and absence of developed nephra, or portions thereof, are sufficient to suggest this entity and also serve to differentiate this case from all other forms of cystic disease. The microscopic characterization of the larger cysts, the intervening septa, and the smooth muscle bundles in the capsule also fit the usual descriptions of the lesion. What is unusual is the primitive cellular stromal areas with the "hobnail" and clear cell tubules.

Fig. 2—Surgical specimen showing numerous apparently intercommunicating cystic spaces.

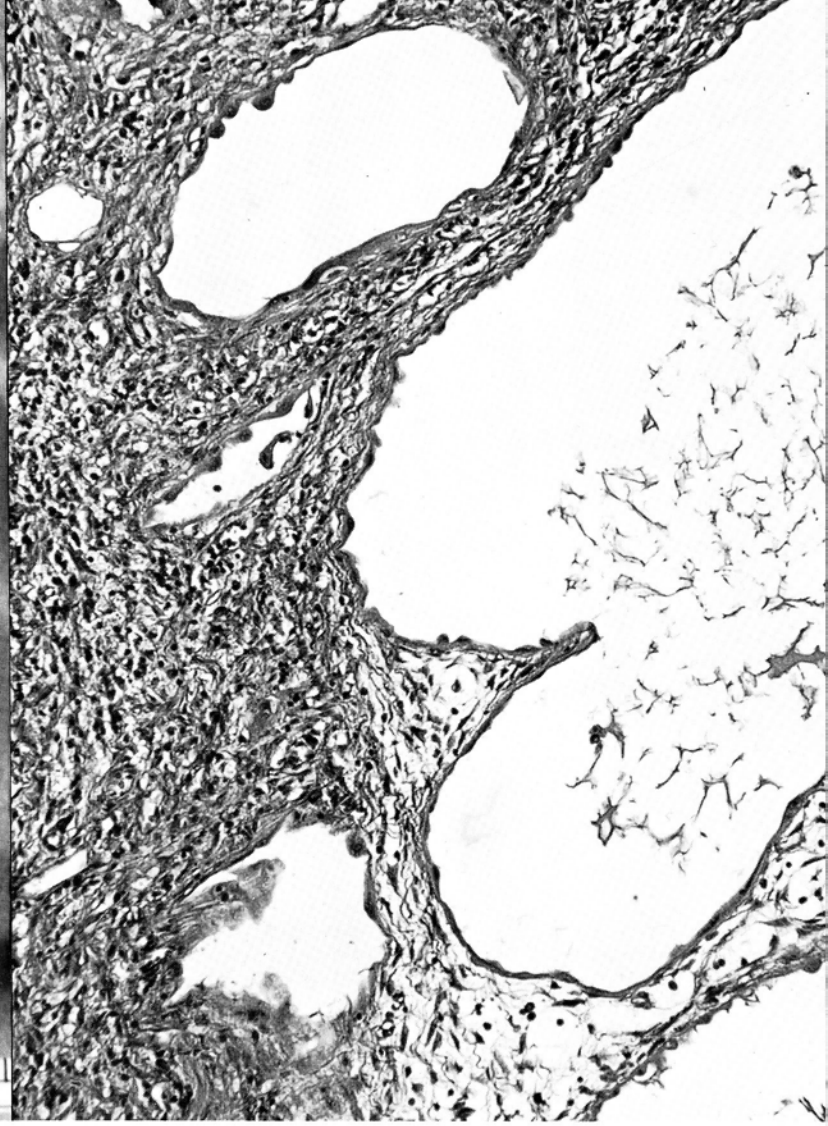

Fig. 3—Thin wall cyst with a flattened lining is seen adjacent to a cellular stromal area. Several dilated tubular spaces are seen with "hobnail" lining cells. X150 W.U. Ill. 72-5617.

However, multilocular renal cysts with these unusual features have been reported previously. A recent case with an identical description occurred in a child 10 months of age reported by Christ. Another case, also in an infant, was described by Boggs and Kimmelstiel. A third case, perhaps the first to be described, was published by Frazier in 1951. Two other cases, both in children, may possibly be similar; the first reported by Uson et al and the second, a 1958 Penrose CANCER SEMINAR case discussed by Dr. Landing. Some of these cases were thought to be well-differentiated nephroblastomas (Wilms' tumor) with or associated with cystic disease. Although the follow-up information on some of these cases is sketchy or of short duration none of these children are known to have died of metastatic malignancy. This type of case raises questions of the pathogenesis of multilocular cystic disease and suggests a neoplastic origin rather than a developmental abnormality. An excellent discussion of these possibilities are to be found in the papers by Christ and Boggs and Kimmelstiel.

My own opinion on this case is that this lesion does not have the primitive sarcomatous elements of a Wilms' tumor and I would expect it to behave in a benign fashion. I would favor the name suggested by Boggs and Kimmelstiel, "multilocular cystic nephroma," as indicating its possible neoplastic origin and its expected benign course. Although the reported cases all seem to involve children about half of all multilocular cystic kidneys occur in adults. All have been unilateral.

Adult forms of carcinoma have been reported with multilocular cysts but I do not believe this is a good diagnostic possibility here. The absence of immature or persistent mesonephric structures indicating failure of differentiation speaks against segmental dysplasia.

Dr. Bauer's diagnosis: MULTILOCULAR CYSTIC NEPHROMA.

Histopathologic diagnoses submitted by mail:

Polycystic kidney	41
Pyelonephritis (xanthogranulomatosis)	38
Angiomyolipoma	25
Renal carcinoma	14
Tuberous sclerosis	14
Benign, by any name!	1
Others	45

Dr. Bauer: This is not polycystic kidney as we ordinarily use that word. I can understand how some might have thought of this diagnosis because of those foam cells. This would be an unusual renal carcinoma; one would have to make some kind of explanation for the cystic component of the lesion.

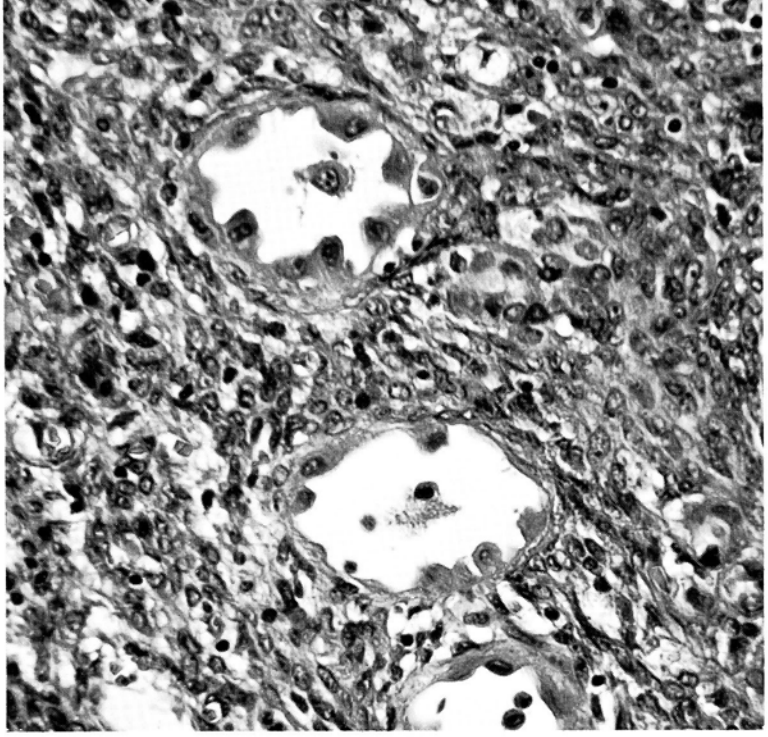

Fig. 4—High power photomicrograph of small tubules with "hobnail" cells. X300 W.U. Ill. 72-5619.

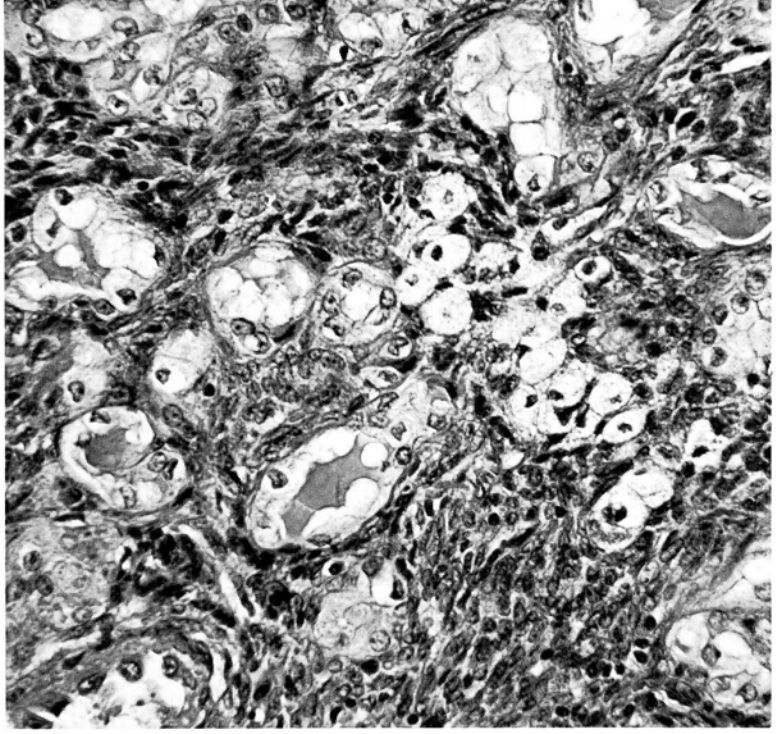

Fig. 5—Tubules with clear or vacuolated cells and adjacent "lipoid" cells in a plump cellular stroma. A dense homogenous material is present in the lumen. X300 W.U. Ill. 72-5618.

Dr. Regato: Dr. C. J. Farinacci, of San Antonio, made a diagnosis of renal adenocarcinoma resembling mesonephroma of the ovary with both solid clear cell and hobnail malignant tubular lining cells. Dr. Leo Lowbeer, of Tulsa, offered complex renal hamartoma in tuberous sclerosis. Drs. Y. LeGal, of Strasbourg, G. D. Toll, of Denver, and F. Cabanne, of Dijon, France, preferred angiomyolipoma. Dr. G. Blizard, of Denver, offered dysgenetic kidney. Dr. Carlo Sirtori, of Milan, offered dysontogenetic cyst and tubular mesenchymal structure.

The AFIP was consulted in reference to this case (Accession No. 1350323). The report rendered by Dr. Mostofi concluded to a diagnosis of mesonephric hamartoma in spite of the "disturbing" spindle-cell areas. The "staff" considered the possibility of a Wilms' tumor but was reluctant to make this diagnosis without demonstrating its origin from renal parenchyma.

Subsequent history: In August, 1971, the patient presented signs of recurrence and abstention was decided upon.

Dr. Glenn: The angiogram, was not very helpful; we were not able to see definitive tumor vessels; there is an irregularity on the lateral border of the kidney that does not look like a benign cyst, but this is not the way benign cysts of the kidney appear on an angiogram. Dr. Bauer's remarks I accept; I notice that there was almost a "unanimous disagreement" between the pathologists; this is rather disturbing. The gross pathology bothers me a great deal; this doesn't look like a benign cystic lesion; these are thick wall cysts with interpolated stroma. I have never seen a lesion exactly like this, but I think I would have to regard it as malignant from a clinical point of view. I would have been inclined to go back and do a radical nephrectomy.

H. Braunstein, M. D., San Bernardino, California: Was this a lesion demonstrably within the kidney? I gather, from Dr. Mostofi's discussion, that the Armed Forces Institute was not certain from the information given to them whether the lesion was actually in the kidney or not.

Dr. Regato: The exploration of the left kidney uncovered a very large multicystic mass and that is all the information that we have.

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9. *Leiomyosarcoma of the Kidney*

Contributed by **W. F. Doyle, Maj., M.C.,** and **G. E. Simon, Maj., M.C.** U. S. Army,
San Francisco, California

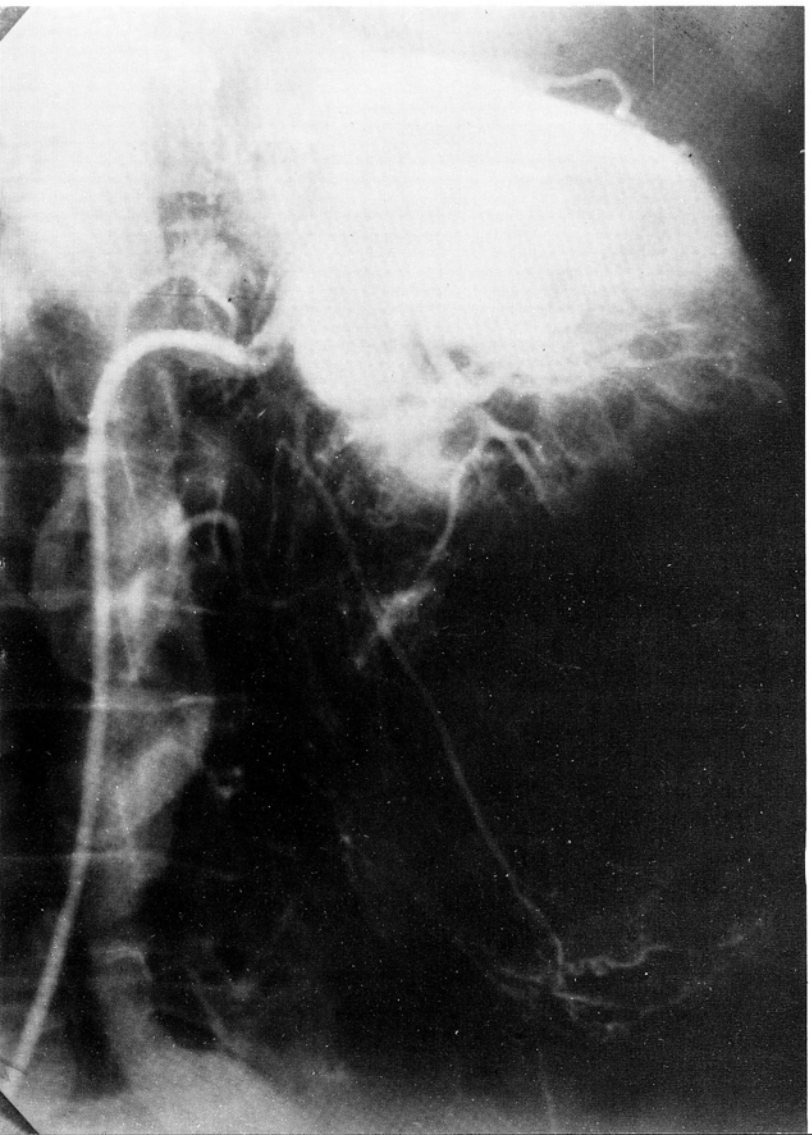
THE PATIENT was a 75-year old woman in January, 1971, when she gave a four months history of vaginal bleeding, forty pounds weight loss and pain in the left upper abdominal quadrant. The SMA-12 was normal.

Dr. Lalli: There is a large relatively avascular mass occupying the lower half of the left kidney with peculiarly fuzzy irregular margin of the nephrogram in the normal parenchyma of the upper half of the left kidney. There are also truncated vessels that can be identified in the midportion of the kidney. These are unusual for simple renal cell carcinoma.

Because of the truncated vessels, I am a little concerned as to the exact nature of this mass and believe that it may not fall into the usual category of renal cell carcinoma but could represent an unusual renal neoplasm such as a sarcoma or papillary adenocarcinoma. One must also consider the possibility of metastatic neoplasm to the kidney such as a bronchogenic carcinoma. The fact that the patient has vaginal bleeding raises the possibility of a metastatic malignancy such as a leiomyosarcoma or endometrial carcinoma arising in the pelvis and metastatic to the kidney. I have surveyed the literature looking for the possibility of estrogen elaboration by renal tumor and have not been able to identify a single instance which could be used to explain this patient's vaginal bleeding. Renal carcinomas have been known to produce erythropoietin and parathyroid hormone but none of the sex hormones. It is very unlikely that this mass should represent a benign simple serous cyst since the capsular vessels are larger than one would expect in such a circumstance and one could not explain the truncated vessels in the midportion of the kidney.

Dr. Lalli's impression: 1) PRIMARY RENAL SARCOMA 2) Atypical RENAL-CELL CARCINOMA

Fig. 1—Nephrogram showing relatively avascular mass of the lower half of the left kidney.



Roentgenologic impressions submitted by mail:

Renal-cell carcinoma	37
Necrotic carcinoma	18
Renal cyst	16
Renal sarcoma	10
Lipoma	9
Others	23

Dr. Lalli: The majority of the radiologists called this a renal cell carcinoma; I am sure that their reason for doing so is the fact that they know that five percent of renal cell carcinomas may be avascular. This is a very defensible diagnosis to make. The necrotic character enters into the explanation for the poor evidence of vascularity. Renal cyst is indefensible for the reasons that I have already given. Intrarenal lipoma is a lesion with which I have very little association; scouring the literature in preparation for this Seminar, I could not find any good evidence of angiography of renal lipomas. I am convinced that this lady has a malignant condition by virtue of the pattern of vascularity.

Dr. Regato: Dr. Harry Z. Mellins, of Boston, suggested a renal carcinoma with vaginal metastases. Dr. L. O. Martinez, of Miami, also suggested a primary necrotic carcinoma of the kidney. Dr. R. B. McMullen, of Denver, favored a cystic carcinoma. Dr. Milton Elkin, of New York, preferred a primary malignant tumor of the kidney without speculation as to histology.

Operative findings: On January 12, 1971, a left nephrectomy and splenectomy was carried out. The left kidney measured 14.5x9x7.5 cm and weighed 480 gm; it contained a tumor 9 cm in diameter occupying the major portion of the lower pole and having apparently broken out of the capsule anteriorly; it was hemorrhagic and necrotic in part.

Dr. Bauer: The low power topography of this case shows confluent nodules of tumor replacing the renal parenchyma with extension to the peripelvic soft tissue and through the renal capsule. Central areas of necrosis are easily seen as well as vessel invasion in the renal hilum.

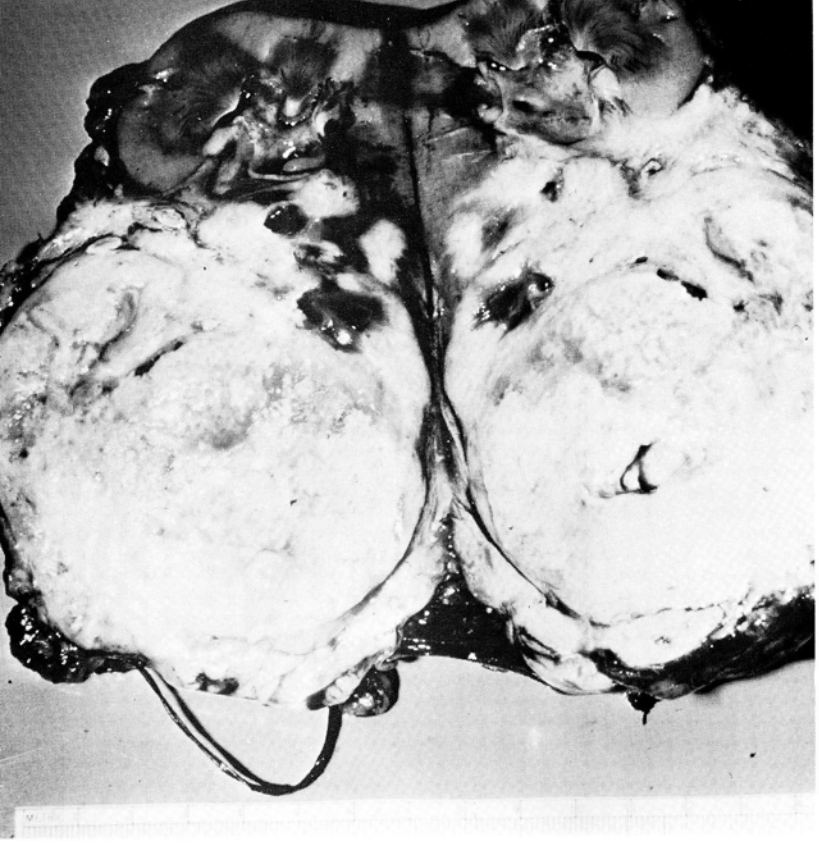


Fig. 2—Cut section of left kidney showing hemorrhagic and necrotic mass of lower pole.

The microscopic appearance is that of a disordered array of plump spindle shaped cells infiltrating and destroying renal tissue. The cellular features are those of a malignant tumor with considerable pleomorphism, frequent abnormal mitoses and an elongated sarcomatous appearance. Some areas are highly cellular with only a suggestion of nuclear alignment whereas other areas show quite definite interlacing fascicules. In the cellular areas malignant cells widely separate the surviving tubules and glomeruli and it is difficult to identify these structures. My impression is that all areas of the tumor show more or less the same histologic picture with some variation in the amount of collagenized stroma.

To me this is a sarcoma involving the kidney. The intra-renal growth of the tumor quite satisfactorily rules out a retroperintoneal sarcoma with extension to the kidney; so we are left with the problem of what kind of sarcoma and whether or not it is primary or metastatic.

Differential diagnosis: Leiomyosarcoma (primary or metastatic); rhabdomyosarcoma; liposarcoma; fibrosarcoma; neurifibrosarcoma; anaplastic renal carcinoma with sarcomatoid features.

In this case I would favor smooth muscle origin in that the outline of the nuclei with somewhat rounded ends, the moderately abundant amphophilic cytoplasm and the fascicular arrangement are in keeping with that idea. A pleomorphic rhabdomyosarcoma might be considered but I do not believe pleomorphism is severe enough; fused cells, strap cells and multinucleated tumor cells are not present. Liposarcomas are not frequent and usually are of the myxoid variety.

The impression of a leiomyosarcoma is supported by a Masson stain in which the reddish or amphophilic staining of the cytoplasm of malignant cells matches to a great extent the staining of the smooth muscle cells in the wall of arteries in the same section. A reticulin stain shows a fairly delicate reticulin pattern in most areas, a pattern of collagenization that is maintained in areas of intraluminal growth of tumor in veins of the kidney pelvis.

Although the last three possibilities were not considered seriously a word should be said about anaplastic renal carcinoma. In a study of 80 unusual tumors from the Mayo Clinic by Farrow, Harrison and Utz there were thirty-eight cases in which the renal carcinoma showed an additional sarcomatous element. In every case but one the adult portion of the renal carcinoma was of the clear cell variety and the sarcomatous portion was a pleomorphic or spindle-cell tumor resembling rhabdomyosarcoma or leiomyosarcoma. Areas of malignant osteoid or cartilage were found in a few of the spindle cell tumors. Although zones of transition from carcinoma to spindle cells could be illustrated in many of these anaplastic tumors, areas of typical adult renal carcinoma was seen in all. The apparent uniformity of histologic pattern in our seminar case without any areas of clear cell carcinoma, removes from consideration, in my opinion, the diagnosis of anaplastic renal carcinoma with sarcomatous pattern.

Referring to the same Mayo Clinic study leiomyosarcoma is the commonest of the mesenchymal sarcomas primary in the kidney and carry a poor prognosis. Only one of fifteen cases was alive and free of tumor six years after operation. The extensive vessel invasion found in our case foretells of a similar unhappy outcome. I suppose it is possible that this sarcoma could be metastatic, say from the uterus. The history of vaginal bleeding might be in keeping with that. But in the absence of further information I will stick with the primary in the kidney.

Dr. Bauer's diagnosis: LEIOMYOSARCOMA OF THE KIDNEY

Histopathologic diagnoses submitted by mail:

Renal-cell adenocarcinoma	41
Atypical carcinoma	16
Leiomyosarcoma	25
Fibrosarcoma	16
Sarcoma, unclassified	14
Fibroma	12
Others	48

Dr. Regato: Drs. D. R. Dickson, of Santa Barbara, California, and W. M. Russell, of Las Vegas, Nevada, also made a diagnosis of leiomyosarcoma. Drs. C. F. Farinacci, of San Antonio, and R. D. Schultz, of Sioux Falls, diagnosed renal-cell adenocarcinoma. Drs. L. B. Henly, of Fort Sam Houston, and K. R. Holloman, of Denver, preferred spindle-cell carcinoma. Drs. J. F. Fennessey, of Detroit, and E. M. Donowho, of Fort Sam Houston, offered fibrosarcoma.

The AFIP was consulted in reference to this case (Accession No. 1374524). A diagnosis of sarcoma was rendered in consideration of the absence of clear cell areas. However, Dr. Mostofi reported that Masson stains showed individual tumor cells surrounded by a collagenous frame work; no collagen production by cells was seen.

Subsequent history: On March 3, 1971, the patient expired. Autopsy revealed the presence of residual tumor in the left renal fossa and metastases to the opposite kidney, adrenal glands, liver, both lungs, pleura, pericardium and interatrial septum.

Major G. Simon, M. C., San Francisco, California: Our interpretation of the primary tumor was either of a renal cell carcinoma with spindle cell pattern or a fibrosarcoma. At autopsy the lung presented these firm gray

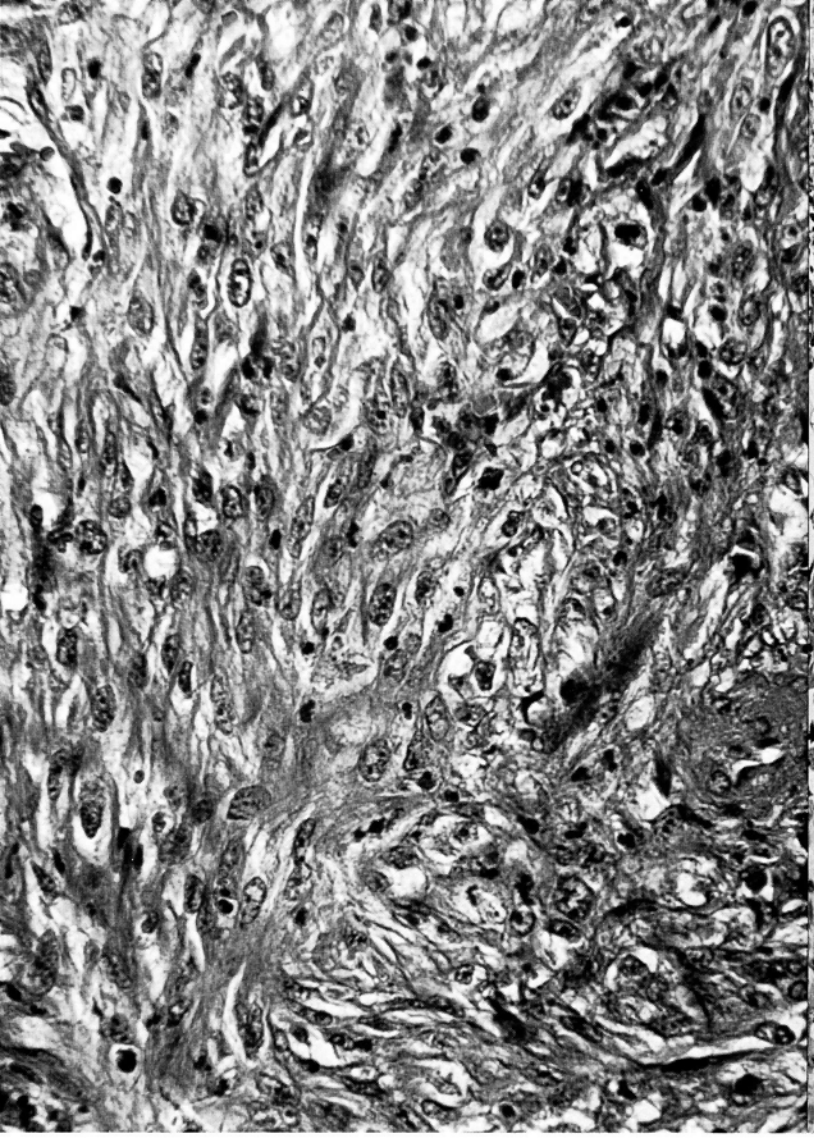


Fig. 3—Elongated malignant cells arranged in fascicles. In this area the tumor is quite cellular with little collagenization of the stroma. X350 W. U. Ill. 72-5220.

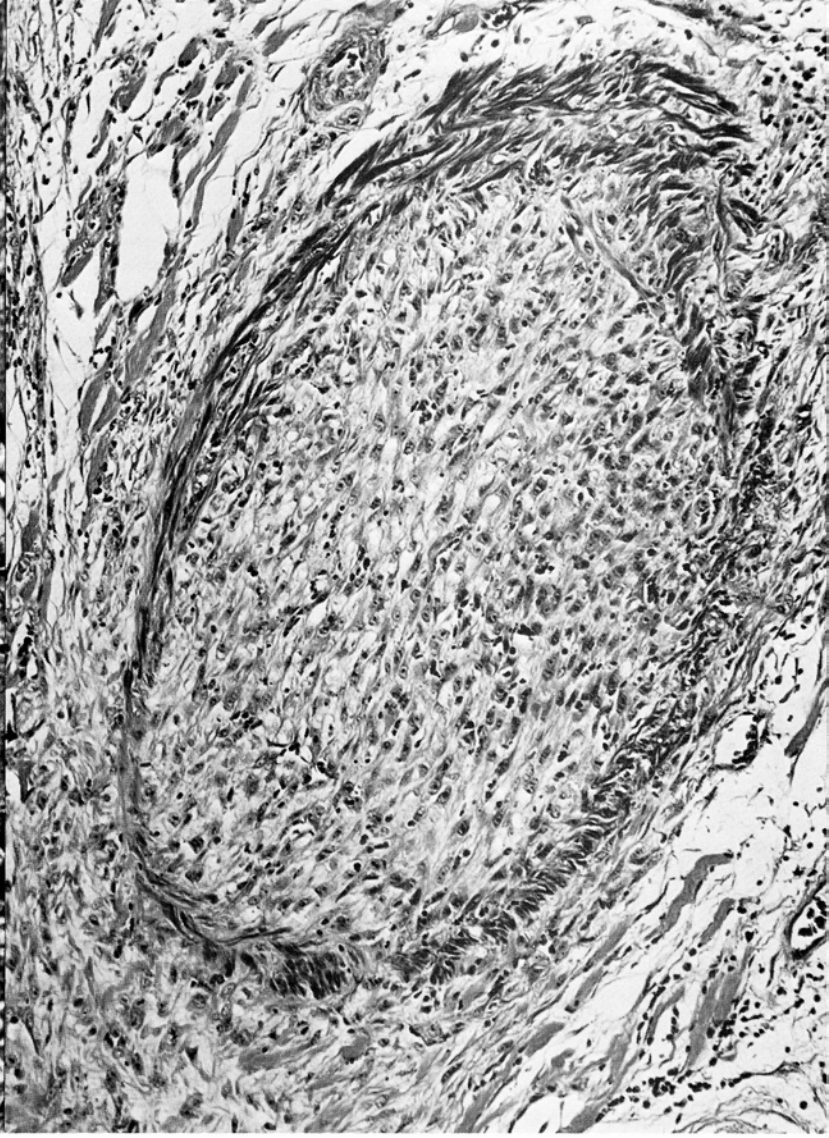


Fig. 4—This Masson stain shows the leiomyosarcoma completely filling the lumen of a vein. X150 W.U. Ill. 72-5224.

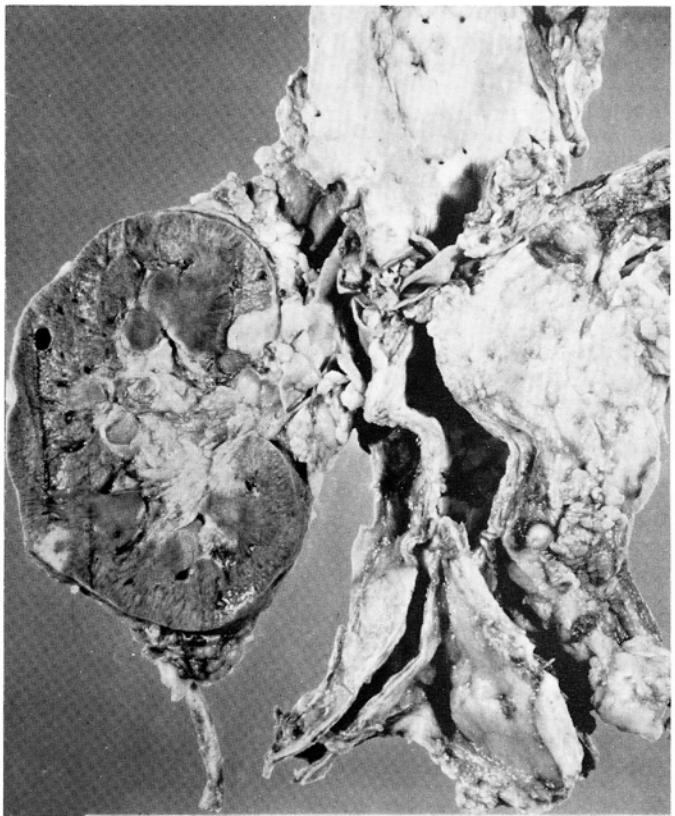
fibrous nodules which were metastatic; there was residual tumor in the left renal bed as well as metastatic tumor involving both adrenal glands and there were two foci of metastatic tumor in the right kidney and also metastasis to the calvaria. We have over 150 electronphotomicrographs. In no case could we see a change from a carcinoma type pattern to spindle cell pattern. We interpreted the connective tissue stains as showing tumor production of collagen; we felt that this was a sarcoma, probably a fibrosarcoma.

Dr. Regato: Dr. Simon, what happened to this patient's vaginal bleeding?

Dr. Simon: The vaginal bleeding, I believe, is a red herring. At autopsy her uterus was atrophic and the endometrium was atrophic.

Dr. Glenn: Certainly the nephrectomy was a palliative measure. If it was thought that the patient had an adenocarcinoma there is some slight justification for palliative nephrectomy, hoping that the secondary lesions will regress. There are about 35 documented cases of regression of secondary lesions upon removal of a primary adenocarcinoma. But, I would agree with Dr. Lalli that the angiographic findings strongly suggest sarcoma. The absence of the small vascular pattern of an adenocarcin-

Fig. 5—Autopsy specimen of right kidney showing metastatic foci.



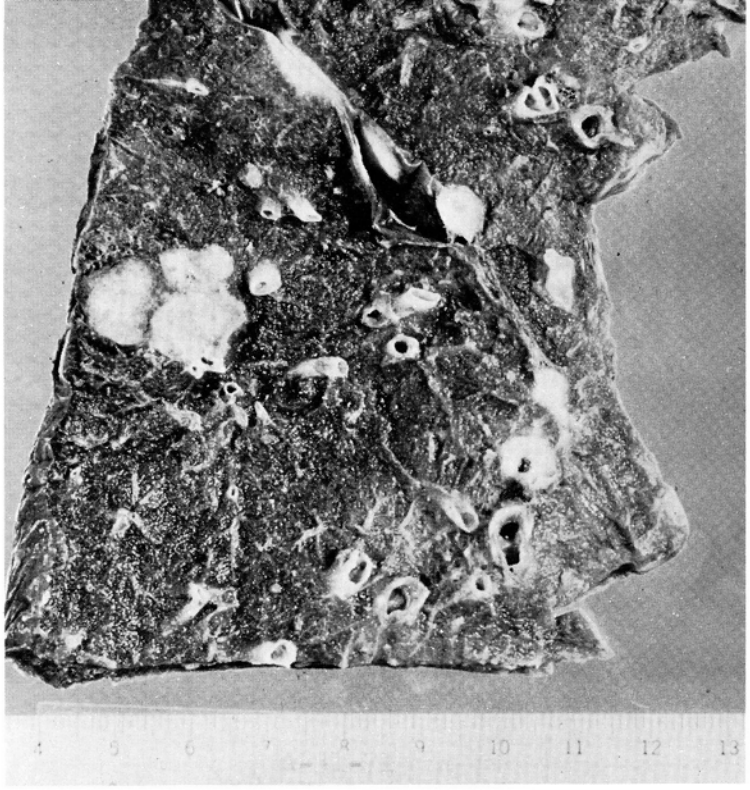


Fig. 6—Autopsy specimen of the lung showing metastases.

oma and yet very definite tumor vessels would lend great weight to this pre-operative diagnosis. From a clinical point of view it appears to make very little difference whether it is a fibrosarcoma, a liposarcoma, a rhabdomyosarcoma, a leiomyosarcoma; all of these tumors are relatively radio resistant and unfortunately they all are very insidious; the few patients with tumors of this sort sort that I know about have died rather rapidly.

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10. *Adenocarcinoma of the Kidney*

Contributed by **Edwin L. Bemis, M.D.,** Milwaukee, Wisconsin

THE PATIENT was a 63-year old man in March, 1971, when he gave a two year history of pollakiuria and intermittent pain in the left flank radiating to the lower extremity. Physical examination revealed no tenderness or masses in the abdomen, liver slightly enlarged. On palpation the prostate was large, but soft, the left lower extremity was painful when mobilized. The blood count and urine analysis were within normal limits.

Dr. Lalli: There is an enormous mass occupying the lower half of the left kidney with peculiarly widespread vascularity which is less in volume than the vascularity in the upper half of the kidney. Accompanying this is a loss of the left psoas muscle and the peculiar history of pain with motion of the left lower extremity. It would be my impression that we are dealing with a long-standing mass in the left kidney and I would question whether there is even some small area of calcification in the lower pole in an area approximately a centimeter in diameter. This is one of the few cases in this Cancer Seminar where I could consider an inflammatory lesion, such as a tuberculoma. The left psoas is not indentifiable and one could consider extension of the tuberculous process as explanation of the left leg pain. Another possibility is that this represents metastatic neoplasm, perhaps arising in lung and also involving the left femur. This pattern of vascularity and this constellation of radiographic appearances would not be one associated with renal-cell carcinoma, but extension of a renal-cell carcinoma to the psoas muscle and retroperitoneal space might explain all the symptoms. I doubt that it represents replacement of the lower half of the left kidney by an invading transitional-cell carcinoma but I shall not be surprised by such a diagnosis.

Dr. Lalli's impression: 1) RENAL-CELL CARCINOMA 2) CHRONIC ABSCESS.

Roentgenologic impressions submitted by mail:

Renal-cell carcinoma	31
Renal cyst	23
Metastatic tumor	12
Malignant tumor	10
Your guess is as good...!	1
Others	28

Dr. Lalli: I get sanguine as people agree with me. Renal cyst is a diagnosis which could be considered only because of the fact that the mass is relatively avascular; if it was a renal cyst we should not have seen even the vessels that we do have and we should have had a much sharper demarkation. Metastatic tumor is a useful thing to think about but this would represent the largest metastasis to the kidney that I have ever encountered. Malignant tumor is an indiscriminant diagnosis with which I will have to agree.

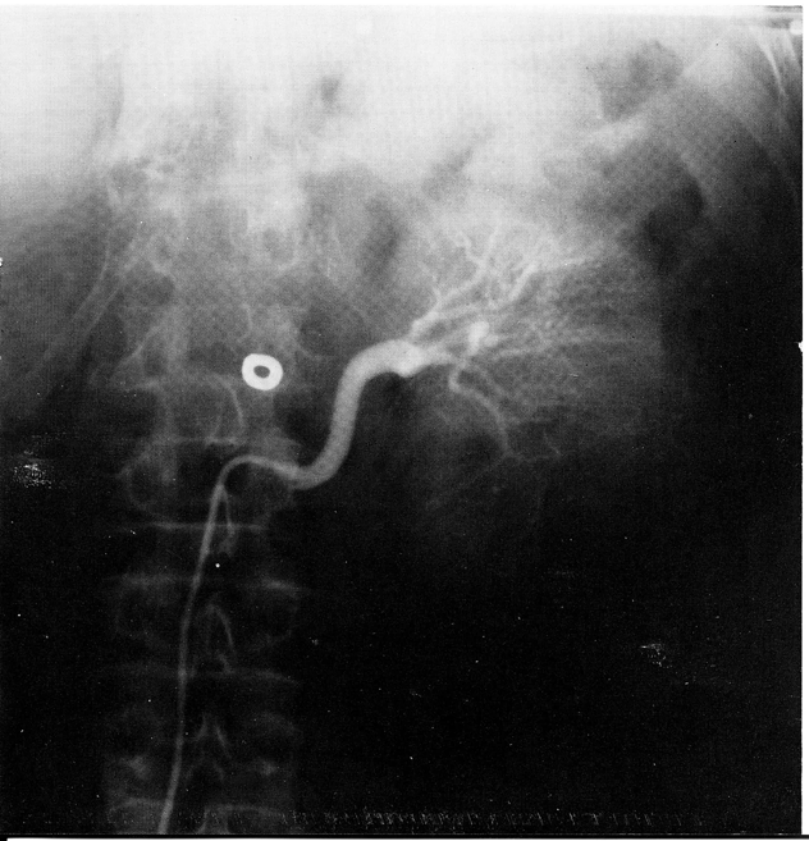
Dr. Regato: Dr. Harry Z. Mellins, of Boston, also suggested a chronic renal abscess of the tuberculous type. Dr. R. O. Martinez, of Miami, preferred necrotic carcinoma of the kidney. Dr. Milton Elkin, of New York, commented that a two-year history was difficult to tie with a chronic abscess and suggested a benign tumor such as adenoma. Dr. J. Maxey Dell, of Gainesville, Florida, also preferred a low-grade malignant tumor.

Operative findings: On April 14, 1971, a left nephrectomy was done; there were strong perinephric adhesions and profuse bleeding. The specimen measured 14.5x4x 3.5 cm and contained a large, well circumscribed, rubbery-mass, 11x8x6 cm.

Dr. Bauer: This large sharply delimited tumor is composed of pink granular cells growing in a predominately solid tubular pattern. The cells resembling those of renal tubules, have rather large regular nuclei, prominent nucleoli and abundant cytoplasm. Occasional cells with very large nuclei showing multiple nucleoli and a coarse chromatin distribution are observed. The intervening stroma is very vascular, sparsely cellular, and poorly collagenized. In some areas the solid tubular pattern gives way to a glandular pattern with a single layer of tall columnar cells outlining lumina of various sizes and complexities of shape. A papillary component is noted rarely. Interstitial and intratubular hemorrhages are frequent and erythrophagia by tumor cells is common. A few cells are seen with cytoplasmic changes giving a foam cell appearance; a change more extensively seen in Case 13 of this CANCER SEMINAR.

I believe this is fairly classical granular cell adenocarcinoma of the kidney with a tubular growth pattern. The cytological features are sufficient in my judgment to warrant a diagnosis of carcinoma; although, I am not always so sure I can distinguish adenomas from adenocarcinomas on histologic grounds alone. Variation in nuclear size and shape, coarseness of chromatin distribution, multiplicity of nucleoli, the presence of degeneration, necrosis, hemorrhage, and vascular invasion are all helpful in deciding the question of a malignant diagnosis; but, at best, together with the parameter of size, they give only an indication of the relative risk of metastases and poor prognosis.

Fig. 1—Large mass with abundant vascularity in the upper pole of the left kidney.



Dr. Bauer's diagnosis: ADENOCARCINOMA OF THE KIDNEY.

Histopathologic diagnoses submitted by mail:

Renal-cell adenocarcinoma (oxyphilic, alveolar, granular-cell, oncocytic)	125
Renal adenoma (oncocytic, tubular, acidophilic)	25
Others	28

Dr. Bauer: There are those that felt that this was an adenoma; I suppose that there are some well differentiated areas that led to that diagnosis.

Dr. Regato: Dr. John B. Frerichs, of El Paso, submitted a diagnosis of granular-cell adenocarcinoma; Dr. C. F. Farinacci, of San Antonio, called it oncocytic and Dr. Leo Lowbeer, of Tulsa, as pseudo-benign. Dr. A. O. Severance, of San Antonio, and Dr. F. Cabanne, of Dijon, France, designated it as adenoma or oncocytoma of the kidney and Dr. G. Gricouroff, of Paris, called it an adenomatous tumor. Dr. D. Venzon, of Colorado Springs, offered tubular adenocarcinoma.

The AFIP was consulted (Accession No. 1377695). Dr. Mostofi reported that the "staff" considered this tumor basically as an adenoma, probably malignant but, if so, certainly of low grade; he described the cells as pleomorphic with variation in size and staining of nuclei; the tumor was encapsulated and while some cells were seen within blood vessels, no unequivocal vascular invasion was seen.

Subsequent history: In August, 1971, the patient was reported in good health.

Dr. Glenn: This is an absolutely delightful case because we all think it is an adenocarcinoma of the kidney. This is not a highly vascular tumor and one could guess that this is probably a tumor of relatively benign characteristics. Dr. Bauer gives us help by pointing out that there are elements in this tumor that are very well differentiated and probably adenomatous in character. My inclination in a situation like this is not to advocate post-operative irradiation; I would appreciate hearing Dr. Regato's comments about this.

Dr. Regato: We really do not have any evidence of our own that would permit us to strongly advocate one thing or the other. Dr. Riches and others have reported that a systematic post-operative radiotherapy in cases in which there is evident tumor left behind or a strong suspicion of tumor left behind, results in a greater proportion of survivals; one can only add that it is not always grossly certain that tumor has been left behind. Actually, post-operative radiotherapy can be carried out in these adult patients with perfect safety. Since the kidney is no longer there, there is no question of damaging the kidney, it is only a matter of delivering within the renal fossa a sufficient amount of radiations to sterilize tumor. A great deal depends, of course, on the nature of the tumor and radiotherapy will do better in the cases that are a little more differentiated than in the highly anaplastic tumors; radiotherapy has to be carried out thoroughly and carefully because of the large area to be treated, but without important sequelae. I think that

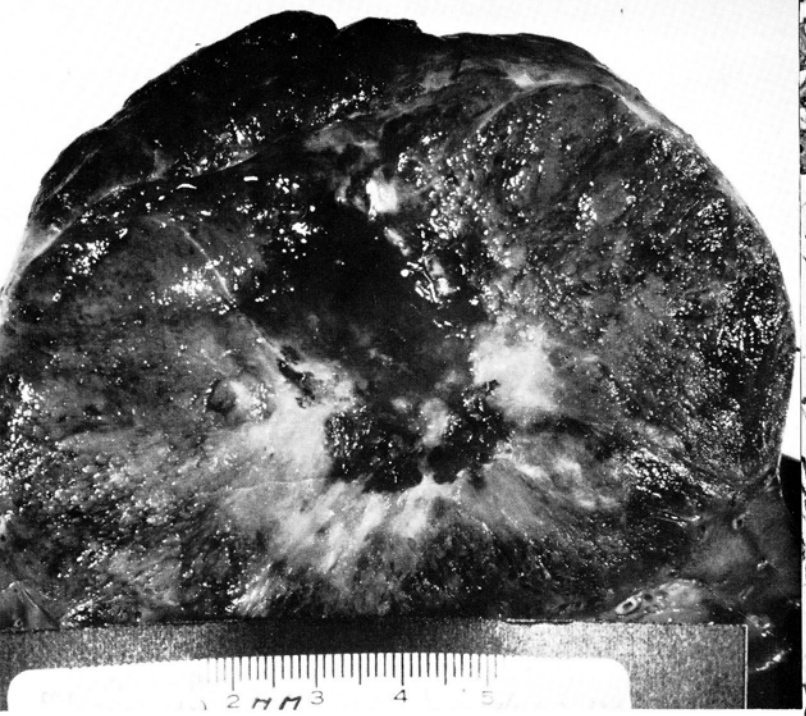


Fig. 2—Large mass with central necrosis in continuity with the kidney.

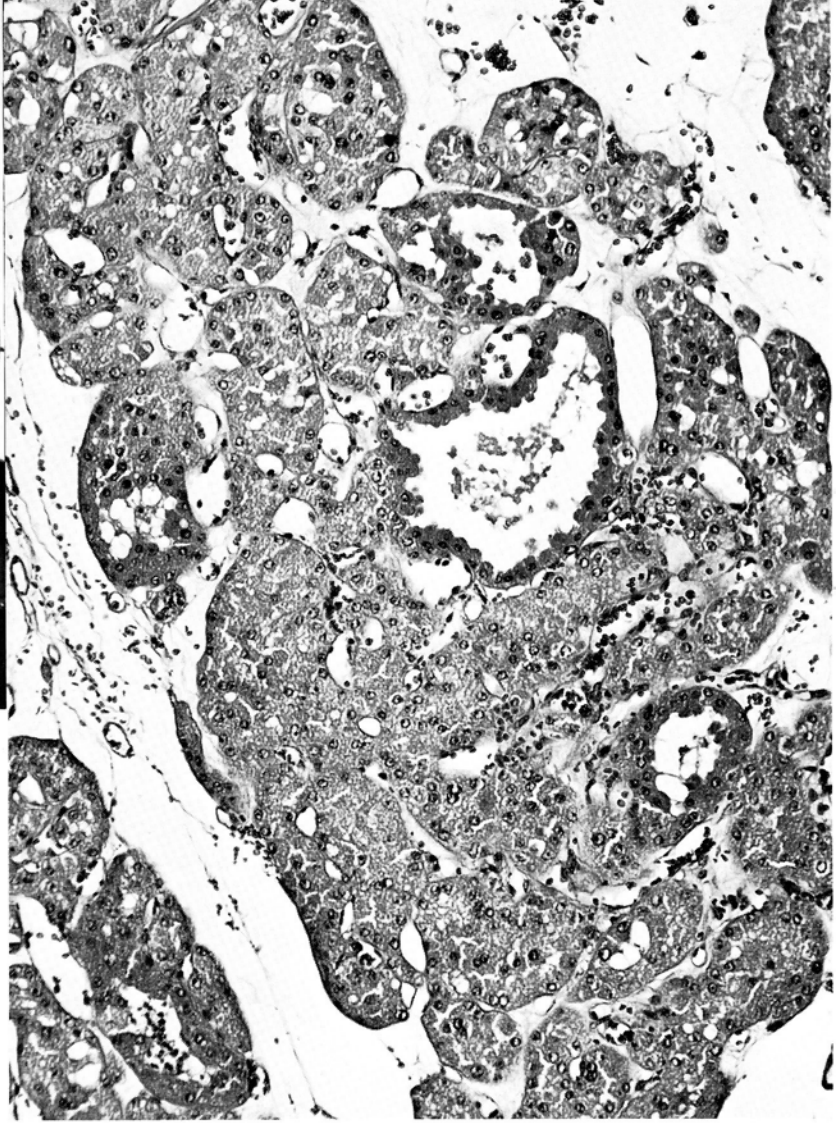


Fig. 3—A granular cell adenocarcinoma of the kidney in a predominantly solid tubular pattern. X150 W.U. Ill. 72-5605.

this is a proper course to follow awaiting the evidence of a well randomized study.

E. L. Bemis, M.D., Milwaukee, Wisconsin: At operation this tumor presented adhesions due to hemorrhage but the psoas muscle was not invaded. This patient was last seen on October 22 by his urologist and was found to be free of recurrent tumor or evidence of metastasis. I was a little disappointed that there was not more controversy among the pathologists as to accurate classifications of this tumor. We saw an identical tumor, a large brown tumor, in a 24-year-old woman who has survived since 1963 without recurrence or metastasis. I thought that we had discarded the theory propounded by Dr. Braunstein that all adenomas over 3 cm in size are malignant regardless of histologic appearance.

H. Braunstein, M.D., San Bernardino, California: I cannot claim credit for that theory. A number of years ago we had a medical student with a tumor identical with this. It was about 15 cm across; he had it resected and seemed to be doing well for about 10 years; then he reappeared presenting recurrence and ultimately metastasis.

H. Azar, M.D., Kansas City, Kansas: I would like to suggest that this is an unusual histologic type which has a striking resemblance to proximal convoluted tubules. We had the opportunity of studying a tumor which we incubated with tritiated thymidine: unlike most adenocarcinomas the uptake was nil in the nuclei, but formidable in the cytoplasm. This occurs very rarely and suggests that you have a very highly specialized cell where the uptake of thymidine is probably in mitochondria rather than in nuclei; I think this is perhaps a well differentiated adenocarcinoma, possibly of proximal convoluted tubular origin.

Dr. Glenn: I think Dr. Braunstein's point is very well taken. Adenocarcinoma of the kidney can manifest itself by delayed recurrence. I have operated one patient who had a recurrence 17 years after the primary; the pathologists tell me that the two tumors are histologically identical. Bronson Ray has reported several patients on whom he operated to remove metastatic brain lesions; one of them 23 years after the removal of his primary. Adenocarcinoma of the kidney is a peculiar tumor with which patients seem to have the ability to live in symbiosis for many, many years. Some urologic surgeons question whether a large adenocarcinoma of the kidney should be removed in an elderly and debilitated patient, since indeed they may have had it for a long time and they may live with it for a long time. I personally do not subscribe to that view, having been trained by Bard and Parker, but intellectually I am challenged by the idea.

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11. *Malignant Lymphoma (Reticulum-Cell Type) of the Kidney*

Contributed by **William R. Platt, M.D.,** Saint Louis, Missouri

THE PATIENT was a 29-year old man in January, 1971, when he gave a history of surgical intervention for a left-sided varicocele and umbilical hernia, three months previously; left-sided flank pain had persisted since operation. On examination there was tenderness and fullness below the left costal margin and in the left flank. The hemoglobin was 11 grams %, and the white cell count 15,900 per mm^3 with 87% polymorphonuclears; the urine was normal.

Dr. Lalli: We have an enormous left kidney with a loss of renal outline with apparent decreased function when compared to the right side. The calices also appear to be somewhat spread when compared to the right side. There is a peculiar appearance of the urinary bladder, which I hope is of no importance but could be produced by extrinsic effect upon the bladder by masses posterior to it. I believe I am identifying gas in the rectum behind the bladder and am hopeful that I can exclude this as being part of the problem.

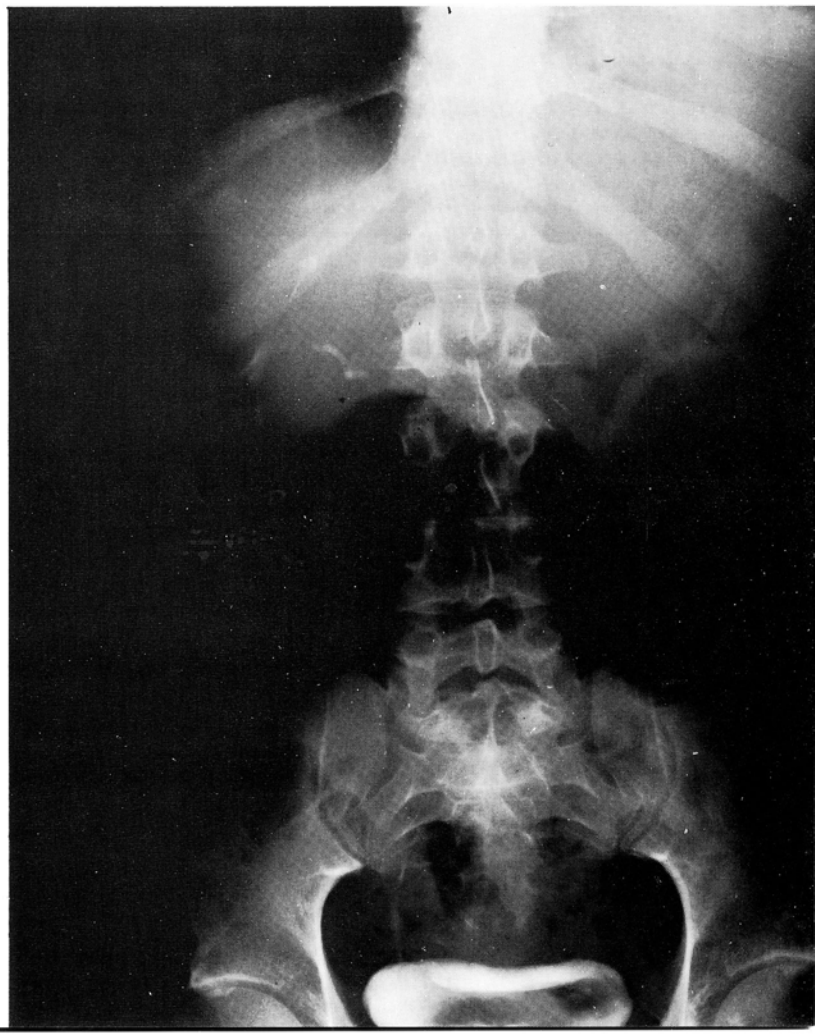
The cause for the enlargement of the left kidney and the decrease in function when compared to the right side may be attributable to compression of the kidney by a parapelvic mass, by arterial embarrassment, renal vein obstruction, or by parenchymal replacement by neoplasm. Considering the history of the patient, one is encouraged to think that this is related to renal vein obstruction and that in turn is associated with the surgical procedure three months previously, as we know that the left gonadal vein empties into the left renal vein. This young man may have a renal abscess, perinephritis and renal vein thrombosis as complications of the surgery. The varicocele may have been symptomatic, however, because of renal cell carcinoma invading the renal vein. Hopefully all of these things do not represent "red herrings;" I would favor a malignant condition rather than a benign infectious process; I think in terms of renal neoplasm probably complicated by hemorrhage into the neoplasm. The cell type would be either renal-cell or an older, unusual Wilms' tumor. I do not believe the first diagnosis should be the complications of or extension and metastases to the kidney from a testicular neoplasm such as seminoma.

Dr. Lalli's impression: 1) RENAL-CELL CARCINOMA 2) RENAL ABSCESS.

Roentgenologic impressions submitted by mail:

Renal-cell carcinoma	35
Renal vein thrombosis	23
Perirenal abscess	12
Leukemia	12
Retroperitoneal sacoma	7
Others	22

Fig. 1—Large left kidney with spread calices.



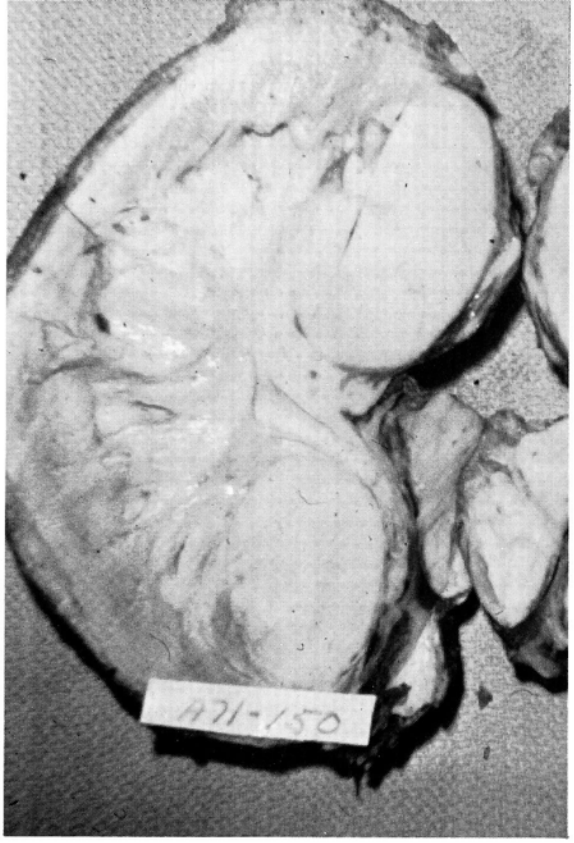


Fig. 2—Hemisection of the kidney with diffuse involvement.

Dr. Lalli: Renal vein thrombosis I have touched upon in terms of whether this is related to simple thrombosis or whether it is related to an abscess. Perirenal abscess is a very useful diagnosis and I think is made largely because of the history and the fact that the renal outline was so obscured; that can occur both with tumor and with inflammatory lesions. Leukemia is a difficult diagnosis for me to entertain; ordinarily when we do see this it is bilateral rather than unilateral. Lymphoma needs to be considered; I had not mentioned it because it is so unusual. This is an intrarenal lesion, I do not think it is a retroperitoneal sarcoma.

Dr. Regato: Drs. L. O. Martinez, of Miami, and Harry Z. Mellins, of Boston, suggested renal vein thrombosis. Dr. Mostafa Batata, of New York, preferred malignant lymphoma. Dr. John Marshall, of Colorado Springs, suggested a leukemic infiltrate.

Operative findings: On January 18, 1971, a left nephrectomy was done; there were numerous adhesions and an enlarged lymph node was removed. The specimen measured 21x14x5 cm and weighed 900 gm; the entire cortex and medulla of the kidney were replaced by a yellow, homogeneous neoplasm which obliterated the pelvis.

Dr. Bauer: Diffuse involvement of the entire kidney without recognizable landmarks characterizes the topographical view of this case. At low power one sees widely separated glomeruli floating as it were in a sea of infiltrated cortex. These glomeruli are virtually the only surviving landmarks of renal tissue. The infiltrate is composed of pleomorphic cells with oval, elongated or folded nuclei with prominent multiple nucleoli. Rather abundant cytoplasm is present. Occasional cells are multinucleated but I was unable to find Sternberg-Reed cells in my sections. The stroma around individual cells or groups of cells is desmoplastic and in some areas heavily collagenized.

Differential diagnosis: Malignant lymphoma, histiocytic type (reticulum cell sarcoma); Hodgkins; leukemia (myelocytic, monocytic).

I believe this is a malignant lymphoma of the histiocytic type (reticulum cell sarcoma). A long search of several sections failed to turn up a convincing Sternberg-Reed cell. In cases such as this the possibility of a diffuse leukemic infiltration should be considered as we have seen several masquerading as histiocytic lymphoma or Hodgkins. In our experience the infiltrate has been of the myelocytic series and we have found the Leder stain helpful. It was negative in our CANCER SEMINAR case and the clinical information gives no indication of the presence of leukemia.

I strongly suspect that the unilateral involvement of the kidney is merely the initial clinical presentation of disseminated disease. The papers of Dr. Lalli on "Lymphoma and the Urinary Tract" and of Dr. Kiely et al on "Renal Complications of Lymphoma" would bear that out. Histiocytic lymphoma was the most frequent type presenting with unilateral renal involvement in a Mayo Clinic study and nearly all died of disseminated disease.

Dr. Bauer's diagnoses: MALIGNANT LYMPHOMA, RETICULUM-CELL TYPE, OF THE KIDNEY.

Histopathologic diagnoses submitted by mail:

Malignant lymphoma	56
Hodgkin's disease	46
Leukemia	15
Undifferentiated carcinoma	24
Chronic nephritis	7
Others	32

Dr. Bauer: I see that a large number of pathologists agreed with me. Leukemia I have discussed as well as undifferentiated carcinoma.

Dr. Regato: Drs. D. F. Wiench, of Fort Sam Houston, and C. R. Vest, of San Antonio, also submitted a diagnosis of malignant lymphoma, histiocytic type. Dr. L. B. Henley, of Fort Sam Houston, and E. C. Farkas, of Sioux Falls, called it Hodgkin's disease. Dr. Margarette Hesselvik, of Tunis, and M. J. DeMeo, of Santa Rosa, California, preferred a leukemic infiltrate. Dr. D. L. Dawson, of Colorado Springs, called it an undifferentiated liposarcoma.

Subsequent history: Post-operative radiotherapy was administered to the region of the renal bed. In March, 1971, the patient developed pleural effusion and presented bilateral hilar adenopathy; he received Cobalt 60 teletherapy. In August, 1971, the mediastinal masses had regressed but he had residual right pleural effusion. He was given nitrogen mustards; ascites developed. In October, 1971, he was scheduled for re-examination.

Dr. Glenn: There are some features in this urogram which speak for infiltration of the kidney by a malignant process: this left kidney was larger, the calyces were not distorted but appeared to be blunted and enlarged, there is a relative degree of lesser concentration of contrast medium indicating that the parenchyma may be diffusely involved by an infiltrated process. This can be a malignant lymphoma, commonly Hodgkin's disease, and even bronchial carcinoma. I have seen three patients with carcinoma of the kidney metastasizing in diffuse pattern. It is very difficult to pin down, these are all speculations. Most varicoceles are asymptomatic; many patients do not even realize they have them until you, as the examining physician, point it out to them. A patient that comes in

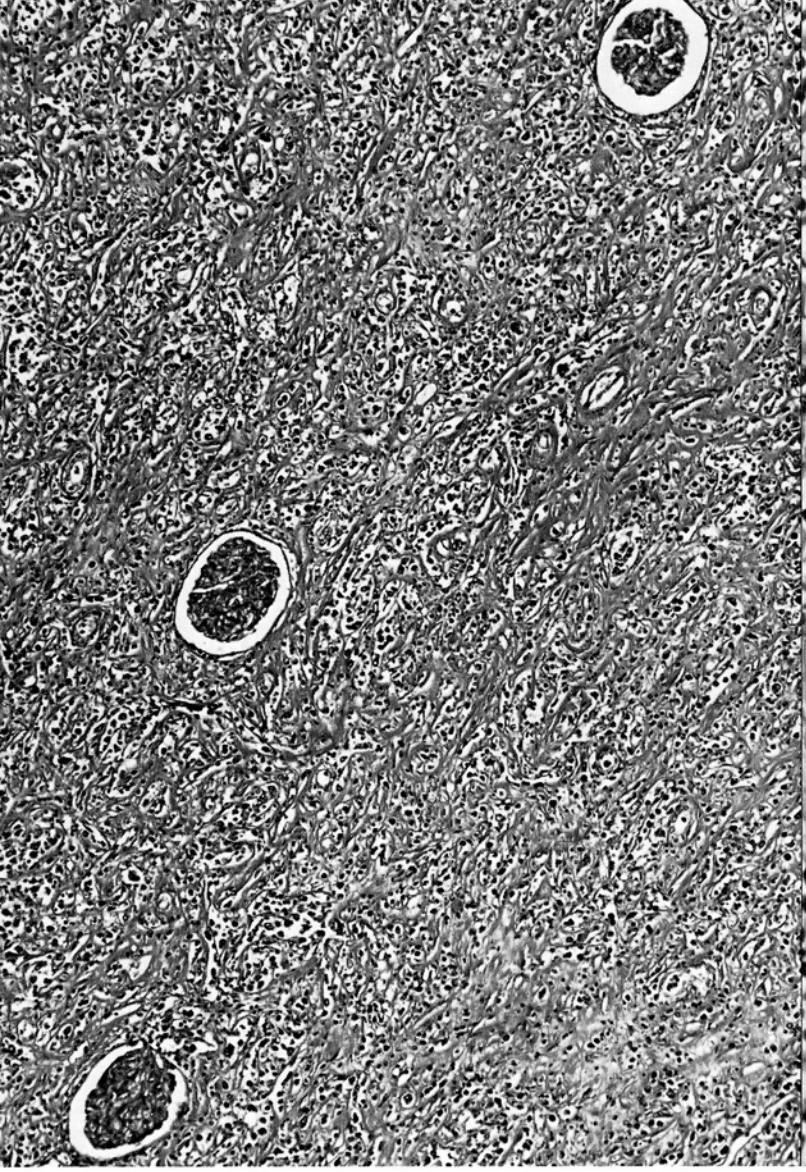


Fig. 3—A low power view showing three widely separated glomeruli. Complete replacement of other glomerular structures by tumor is seen. X90 W.U. Ill. 72-5223.

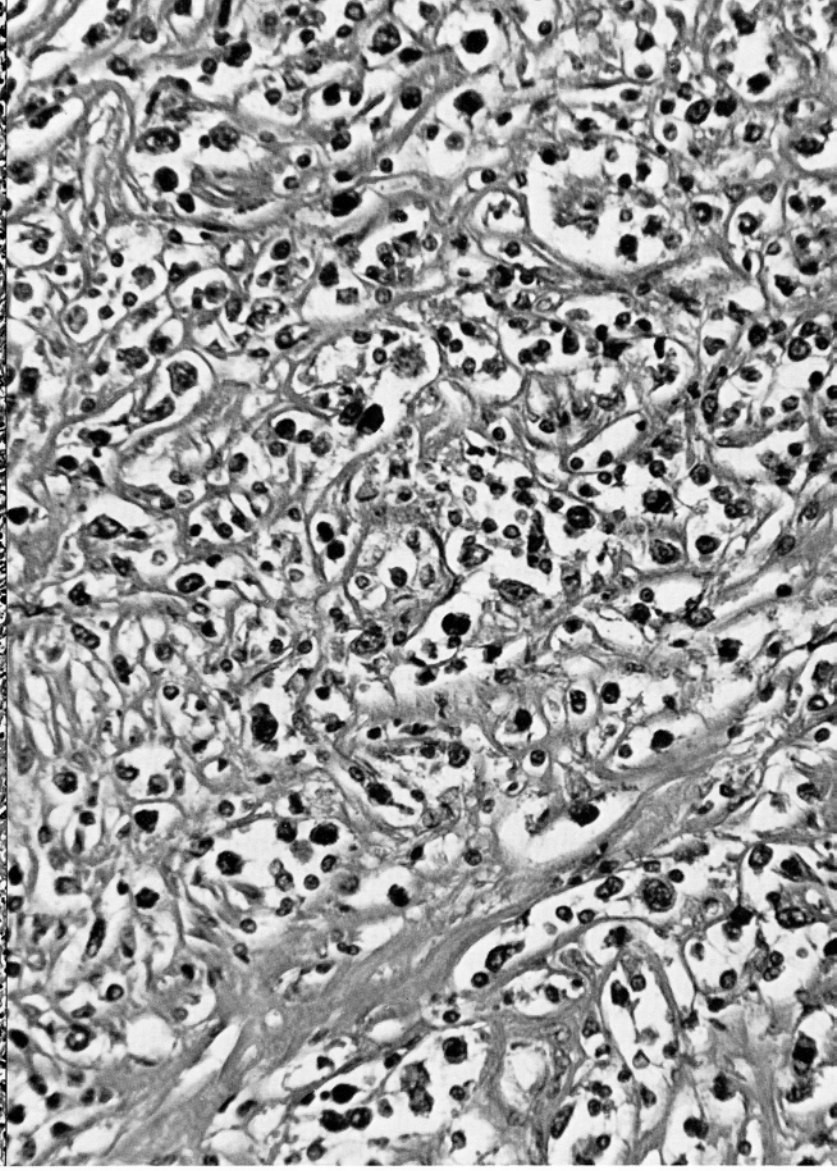


Fig. 4—Infiltrate of pleomorphic histiocytic cells. Sternberg-Reed cells were not seen. X350 W.U. Ill. 72-5222.

with a symptomatic varicocele should be suspect. Obviously you cannot do intravenous pyelography on everybody that has a varicocele, but certainly in those selected few who are symptomatic, it is a justifiable study.

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12. *Renal-Cell Adenocarcinoma and Transitional-Cell Carcinoma of the Kidney*

Contributed by **Walter C. Bauer, M.D.**, Saint Louis, Missouri

THE PATIENT was a 70-year old man in August, 1970, when he complained of hematuria and right flank pain. On examination there was a palpable mass in the right upper abdominal quadrant. Blood chemistries and hemogram were normal.

Dr. Lalli: There is an enormous mass in the lower pole of the right kidney with fairly sharp cut off of the parenchyma in the lower portion with several long capsular arteries and with an interesting extension of the renal margin laterally above the mass and with a loss in the same area of the corticomedullary junction. Several of these vessels also look a bit irregular in this area.

The primary diagnosis to consider in this case is a renal cell carcinoma which is relatively avascular, perhaps papillary adenocarcinoma, although these tend to occur in younger patients. This may be avascular because of the nature of the tumor but it also may be avascular because the main portion of the tumor is necrotic. There are some mild fibromuscular changes in the renal artery but these are of no clinical significance under these circumstances. Of great interest is the fact that the corticomedullary junction has been interrupted in the lateral aspect of the kidney immediately above the radiolucent portion. This would suggest to me that there is a neoplasm in this area although I do not identify tumor vessels. It is because of this interruption of the corticomedullary junction that I am quite certain that this represents a malignant tumor of the kidney and not a benign condition such as a simple serous cyst. Because of the symptomatology and the roentgen appearance, I would not recommend percutaneous puncture for diagnosis, although I do not believe the puncture would harm him or hinder his surgical curability. My best roentgen interpretation of this particular case is that we are dealing with a malignant tumor of the kidney and because of its size I would favor renal cell carcinoma.

Dr. Lalli's impression: RENAL-CELL CARCINOMA

Roentgenologic impressions submitted by mail:

Renal cyst	40
Renal carcinoma	19
Fibrosarcoma	18
Others malignant	17
Others benign	15

Dr. Lalli: They might have favored a benign diagnosis because having gone this far in the book they figured one of these cases had to turn out to be a benign simple renal cyst and this would be the best candidate. I would disagree with that psychological interpretation of the radiographic findings. Fibrosarcoma is a defensible diagnosis.

Dr. Regato: Dr. J. L. Eller, of Denver, also offered an impression of renal-cell carcinoma. Dr. L. O. Martinez, of Miami, suggested a necrotic carcinoma.

Operative findings: On August 14, 1970, after exploration of the kidney and needle aspiration brought no fluid, a right nephrectomy was done; an attempt was made to remove a large lymph node between the vena cava and aorta; silver clips were placed as markers of its site. The specimen measured 17x12x5 cm and weighed 300 gm; the small kidney presented areas of discoloration and contained a yellow-white nodular mass 3x3 cm in diameter apparently extending to the peripelvic fat and calyceal system; the mass was attached to a cystic lesion occupying the lower pole and which contained chocolate color fluid. The renal artery was abnormal in that it had four branches. Three large indurated perihylar lymph nodes, measuring from 1.5 to 3 cm were removed.

Dr. Bauer: The sections from the large cystic mass in the lower pole of the kidney showed a thick fibrous wall lined by necrotic cellular debris in most areas. In a few locations there were surviving cellular areas that showed a typical papillary granular-cell adenocarcinoma. Some solid areas of carcinoma were found infiltrating the capsule. Thus the large relatively avascular cyst is an adenocarcinoma which had undergone extensive hemorrhagic necrosis. All areas of surviving tumor had the same typical histology.

The kidney held an additional surprise. There was a second, solid, yellowish-white tumor, 3 cm in diameter, involving a calyx and adjacent pelvis with extension into the peripelvic fat. At one point this nodule of tumor came close to the capsule of the necrotic adenocarcinoma but it was definitely separate from it. The sections of this tumor showed a moderately differentiated transitional cell carcinoma. Several periaortic lymph nodes accompanying the nephrectomy specimen contained foci of metastatic transitional cell carcinoma. None of the nodes showed metastatic adenocarcinoma. Unfortunately it was not possible to obtain many blocks showing both tumors in the same section, so that I suspect that most of you received sections of either one cancer or the other.

Simultaneous adenocarcinoma of the renal parenchyma and transitional cell carcinoma of the renal pelvis are reported but rarely. Graham and Vynalek, in 1956, were able to find only ten cases including one of their own; Walker and Jordan reported a recent case in 1958. The association of the two is so infrequent that the presence of a second carcinoma is unsuspected clinically. So was it in this case where clinical attention was focused on the lower pole mass which our radiologists thought was a benign cyst. At operation the surgeon needled the mass prior to unroofing the cyst; when thick bloody fluid aspirated he decided upon a nephrectomy. In our experience benign cysts may occasionally be filled with old blood but in this instance the aspirate correctly identified the nature of the cyst and the correct surgical

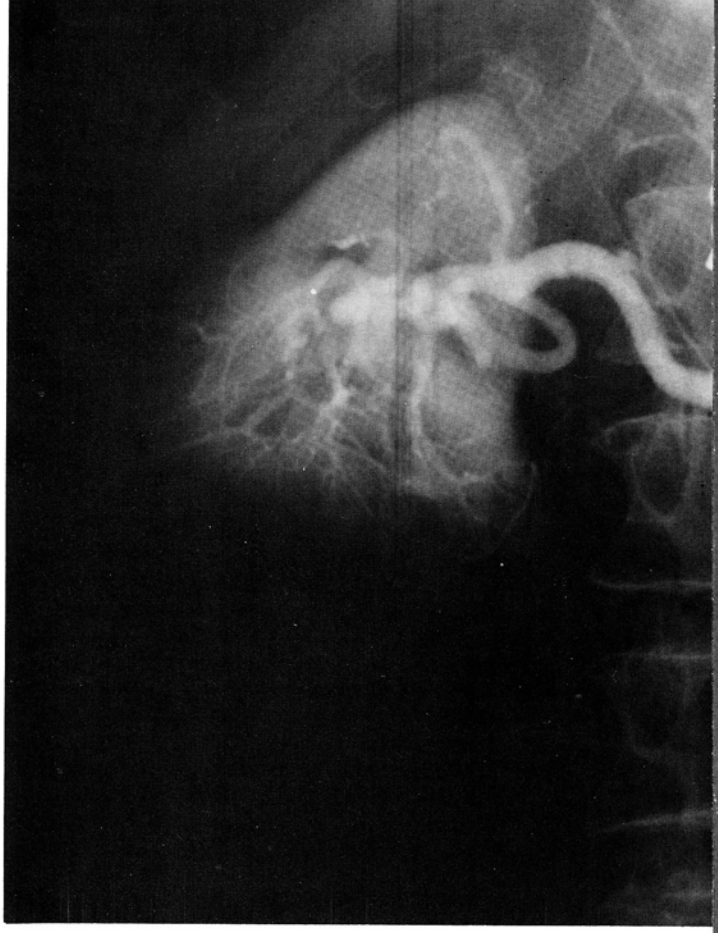

Fig. 1—Very large mass in the lower pole of the right kidney with large capsular vessels.

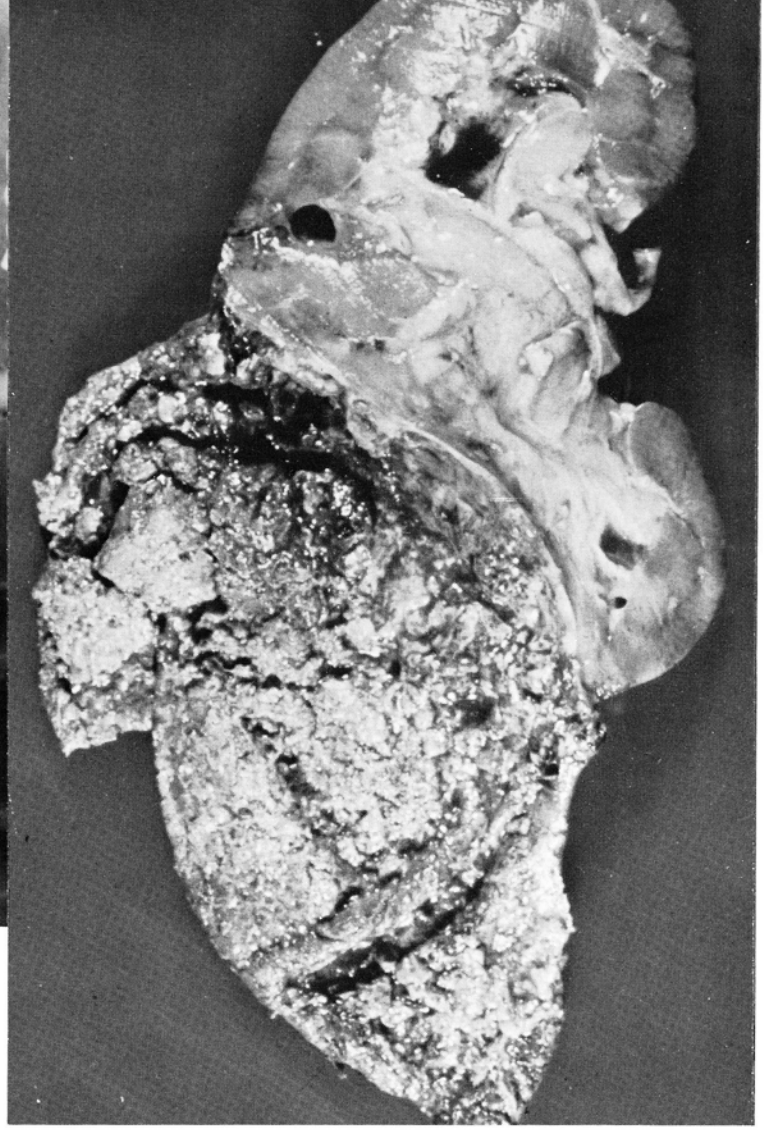

Fig. 2—Surgical specimen with necrotic tumor.

procedure was carried out. The presence of the second carcinoma was not discovered until the kidney was examined in the laboratory and, unfortunately for the patient, had already metastasized to periaortic lymph nodes.

Dr. Bauer's diagnosis: 1) ADENOCARCINOMA OF KIDNEY, necrotic 2) TRANSITIONAL-CELL CARCINOMA OF RENAL PELVIS.

Histopathologic diagnoses submitted by mail:

Renal-cell adenocarcinoma	82
Transitional-cell carcinoma	12
Malignant lymphoma	25
Myosarcoma (leio-, rhabdo-)	16
Poor slide, or something!	1
Others	22

Dr. Bauer: Some of the areas of the transitional-cell carcinoma were poorly differentiated and malignant lymphoma could be considered.

Dr. Regato: Dr. W. J. Holaday, of Columbus, Ohio, offered a diagnosis of renal carcinoma masquerading as sarcoma. Dr. Leo Lowbeer, of Tulsa, called it an outright leiomyosarcoma. Dr. J. B. Frerichs, of El Paso, favored reticulum-cell sarcoma. Dr. G. Vogt, of Tunis, called it a metastatic trophoblastic tumor; Dr. L. B. Henley, of Fort Sam Houston, a seminoma, Dr. D. B. Troxel, of Lafayette, California, a plasmacytoma, Dr. E. C. Farkas, of Sioux Falls, Hodgkin's disease, Dr. Keith Hallman, of Fort Sam Houston, lymphosarcoma and Dr. D. R. Dickson, of Santa Barbara, California, transitional-cell carcinoma.

Subsequent history: The patient started to receive post-operative radiotherapy when pulmonary metastases were discovered and the irradiation was discontinued. On November 19, 1970 he expired.

Dr. Glenn: I have never seen both lesions existant in the same kidney; it is certainly a "fascinoma." I don't believe that what we are seeing on the angiogram was the transitional tumor; I think it was the lateral extension of the papillary carcinoma. It looks abnormal on the angiogram. We have a great deal of trouble in seeing transitional-cell tumors with even the best angiogram.

F. P. Bornstein, M.D., El Paso, Texas: I would like to ask what was the histology of the metastases, which tumor metastasized, or both?

Dr. Bauer: The transitional-cell carcinoma.

J. Taubman, M.D., Denver, Colorado: In addition to the features of malignancy that Dr. Lalli pointed out, there is another feature in that relatively normal vessels of the outside of the kidney were descending vertically, perpendicularly into this lesion; this is a feature of malignancy; where you see vessels entering a lesion at right angles, I think this is a good sign of malignancy.

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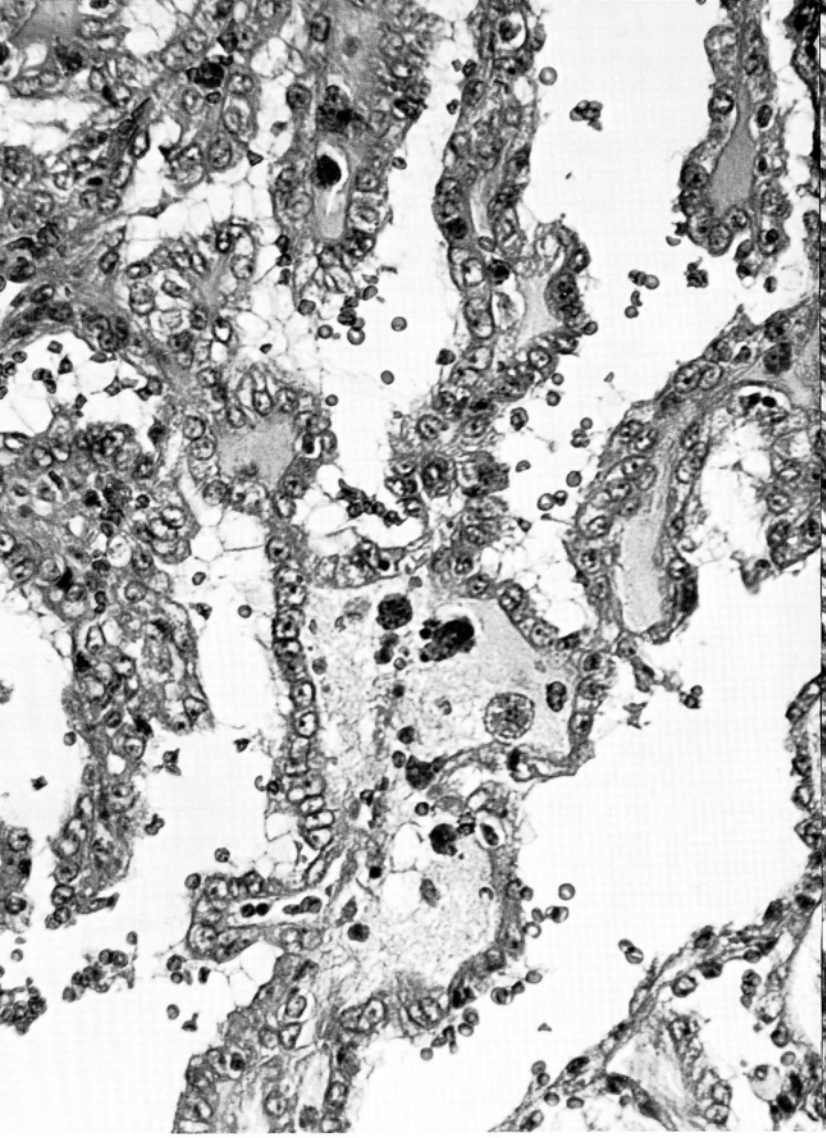

Fig. 3—A typical papillary adenocarcinoma in the largely necrotic lower pole mass in the kidney. X350 W.U. Ill. 72-5612.

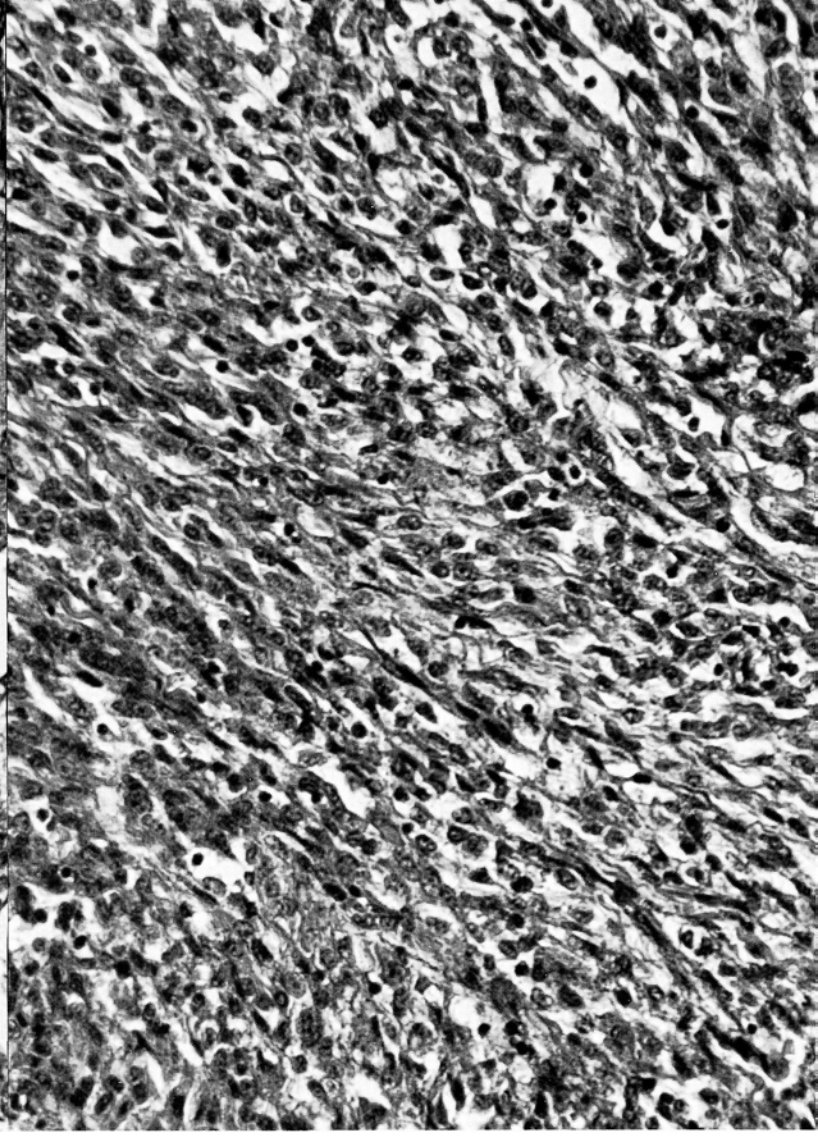

Fig. 4—A separate transitional cell carcinoma involving a calyx and adjacent pelvis. X350 W.U. Ill. 72-5613.

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13. *Papillary Adenocarcinoma of the Kidney*

Contributed by **Mark E. Williamson, M.D.,** Palm Desert, California

THE PATIENT was a 56-year old man in June, 1971, when he complained of rectal discomfort. Examination revealed only the presence of hemorrhoids; the barium enema showed no abnormality but a shadow was revealed in the region of the left kidney. The uric acid was 8 mg% ml; the hemoglobin, white cell count and urine analysis were all within normal limits.

Dr. Lalli: There is a large mass which appears to be below the hilum of the kidney not disturbing the left psoas muscle outline and containing a rim of calcification. The mass is approximately 6 cm by 8 cm and while it is displacing the renal pelvis cephalad, it is not causing obstructive uropathy; the calices appear normal and contrast medium is seen in the distal left ureter. It seems possible to separate this calcified rim from the medial left renal margin, lending greater evidence to the mass being extrarenal.

The differential diagnostic possibilities include a large aneurysm or A-V malformation of the left renal artery, although more commonly these present as intrarenal masses rather than extrarenal masses. The possibility of a tangentially attached renal cell carcinoma causing

displacement of the kidney must also be considered. It is most unlikely that this represents a renal cyst with peripheral calcification tangentially attached to the kidney. A calcified retroperitoneal hematoma as a previous injury might be considered but there is no good roentgen evidence, such as fractures of ribs or transverse processes. The possibility of a calcified dermoid cyst and calcified echinococcus cyst must also be considered but are believed to be very much less likely. It would be most unusual for a lymph node to grow this large and to have a peripheral calcification.

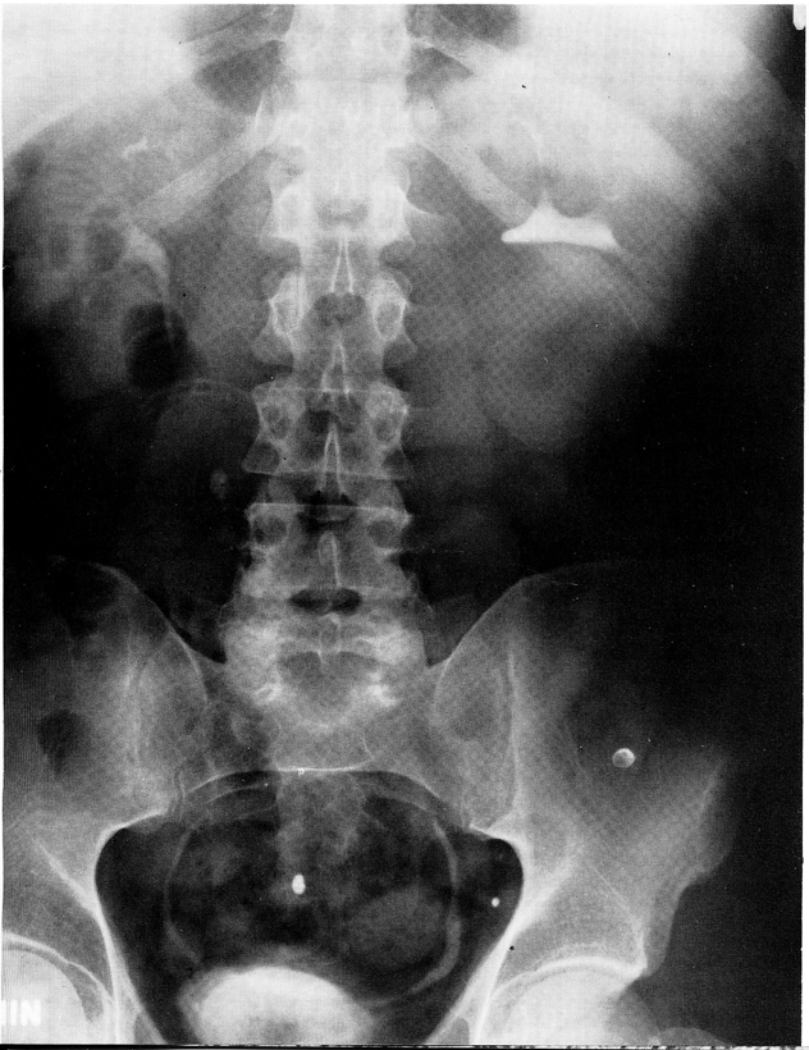
Dr. Lalli's impression: 1) ANEURYSM OF RENAL ARTERY. 2) RENAL-CELL CARCINOMA.

Roentgenologic impressions submitted by mail:

Renal carcinoma	43
Renal cyst	25
Malignant lymphoma	14
Abscess	9
Others	24

Dr. Lalli: I have had occasion to study lymphomas, I have never seen calcification in one of them; you might consider something like an old abscess which is calcified, I do not think that is worthwhile. There are a couple of other things that could be mentioned: this patient might have had a leakage of urine, a urinoma might have formed and this well might have become calcified after a long period of time; he could have had a hematoma, which became calcified. However, I am persuaded by virtue of the location of this lesion and what it does in terms of displacing the kidney, that it should be a renal-cell carcinoma.

Fig. 1—Large mass apparently situated below the left renal pelvis with a rim of calcification.



Dr. Regato: Dr. Wendell Stampfli, of Salida, Colorado, and Dr. J. L. Eller, of Denver, also suggested renal-cell carcinoma. Dr. Frank Wilson, of Colorado Springs, preferred a carcinoma of the renal pelvis. After considering the hemorrhoids, the elevated uric acid, the nontranslucent renal mass and linear calcifications and lamenting the lack of an angiogram, Dr. Milton Elkin reached the conclusion that carcinoma of the kidney was the best bet.

Operative findings: On July 10, 1971, an exploration of the left kidney was done through a retroperitoneal approach; the lower pole of the kidney was freed and a cyst dissected and removed from the kidney. The specimen measured 7.8x6.7x5.4 cm and weighed 113 gm; an 8 cm cyst contained yellow-brown necrotic material and an irregularly nodular growth.

Dr. Bauer: Microscopically this case presents a striking papillary arrangement of tall columnar cells with large round to oval nuclei and abundant pink granular cytoplasm. Cellular variation is considerable and prominent nucleoli, sometime multiple, are not infrequent. An unforgettable sight is the presence of many large foamy cells filling up the stromal projections of the papillary fronds. Their cytoplasm resembles that of lipid-filled macrophages or histiocytes and their nuclei are usually smaller, rounder and eccentrically placed in the cell. The interstitial location and bland visage of these "lipoid cells" is not without exception because they also may be found on the surface of the epithelial fronds, mixed with the granular cells and occasionally free in lumen. A gradual transition of cellular characteristics from granular cells to "lipoid cells" may be seen in some of these areas.

The tumor cells are remarkably phagocytic; their cytoplasm is often stuffed with dark reddish-brown granules of various sizes. This material is PAS positive and contains iron. The cells in "transition" from granular to lipoid cytoplasm also show such cytoplasmic granules; but most of the "stromal" cells show a paucity of such material.

I believe this is a papillary adenocarcinoma in which one finds many so-called "foam cells." Small foci of such cells can be found in both adenomas and adenocarcinomas and occasionally they may form a significant part of the tumor.

Several authors (Murphy and Mostofi; Evans and Sanerkin) believe that such cells originate from tumor cells that have undergone lipoid degeneration. That view is supported in part by finding areas with the appearance of transition from one to the other. Others including Willis regard such cells as lipid macrophages. Although electron-microscopy has been done on renal adenocarcinomas no one has as yet described the ultrastructure of such cells.

Dr. Bauer's diagnosis: PAPILLARY ADENOCARCINOMA OF THE KIDNEY.

Histopathologic diagnoses submitted by mail:

Renal adenocarcinoma	67
Papillary adenocarcinoma	60
Papillary cystadenoma	34
Adenoma plus carcinoma	10
Others	17

Dr. Bauer: The phony component of these neoplasms does not indicate their benignity or their malignancy. I have seen patients with these tumors survive after surgery without recurrence or metastases and I have also seen cases in which the tumor metastasized and the patient died.

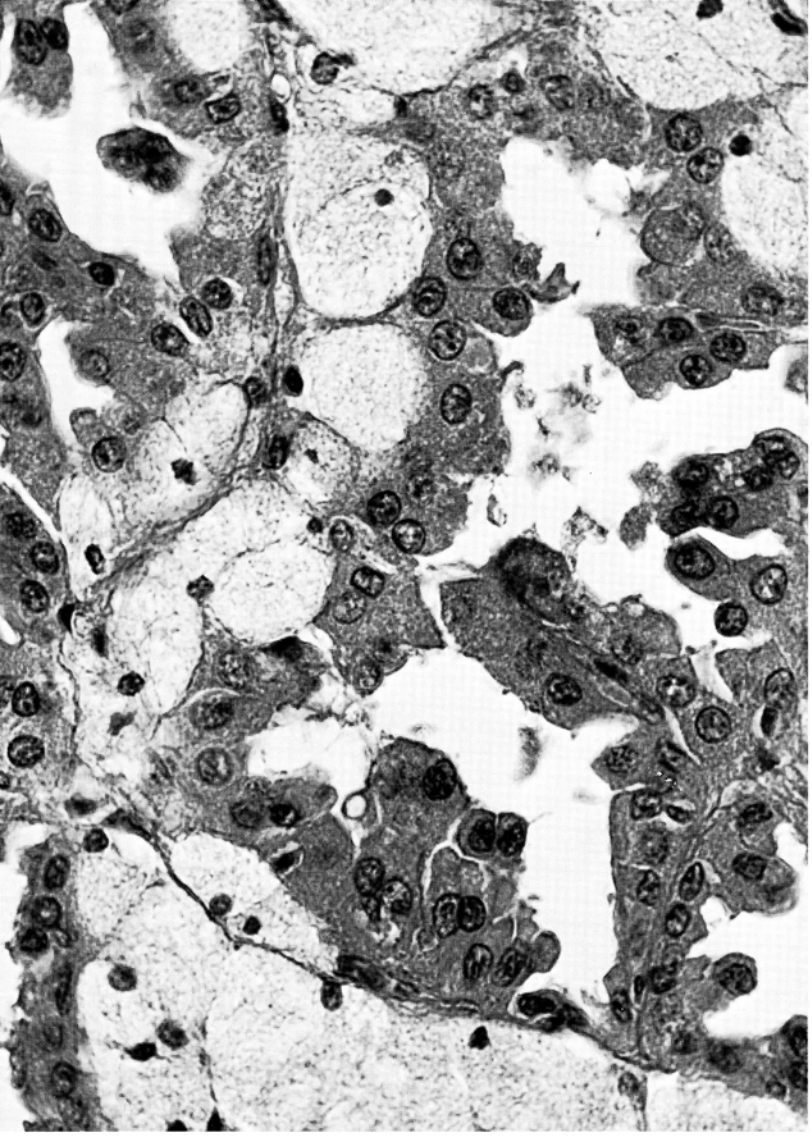


Fig. 2—A papillary granular cell adenocarcinoma associated with large numbers of "lipoid" cells presumably of tumor cell origin. X600 W.U. Ill. 72-5616.

Dr. Regato: Dr. E. B. Price, of Denver, and Dr. A. O. Severance, of San Antonio, submitted a diagnosis of papillary cystadenoma. P. W. Gikas, of Ann Arbor, preferred renal-cell adenocarcinoma.

Subsequent history: On October 12, 1971 the patient was operated for hemorrhoids; there was then no evidence of regional recurrence or distant metastases.

Dr. Glenn: The man should have had a radical nephrectomy. When one is dealing with carcinoma of the kidney one does not do limited excisional surgery. We would feel that perhaps the wrong operation has been done. With an angiogram, we would have made the proper diagnosis, because I suspect this was a fairly vascular tumor.

J. Kepes, M.D., Kansas City, Kansas: In xanthogranulomas of the choroid plexus there are benign findings at autopsy showing foamy cells just like the ones we have in this lesion and on the outside they are covered by plexus epithelium. Traditionally they have been considered as mesenchymal cells picking up some debris, fat and other things. However, Shuangshoti and Netsky were able to show the transitions between surface epithelium and the inside xanthoma cells; they found some foamy cells on the surface and by a series of sections were able to see some of them turning inward and making their appearance inside the stroma. At the University of Kansas we were able to find a papilloma of the choroid plexus in a one year old child, who also showed the same phenomenon: some of the surface epithelium turning foamy and then migrating into the stroma and becoming like one of the stroma cells. Apparently this does exist in the kidney and other areas also.

H. Braunstein, M.D., San Bernardino, California: If I am not mistaken there have been electromicrographic studies on kidneys from the congenital nephritis which have a similar interstitial foam cell reaction and have been thought to be epitheleal in origin. Perhaps Dr. Bauer would comment on that.

Dr. Bauer: I am not familiar with it.

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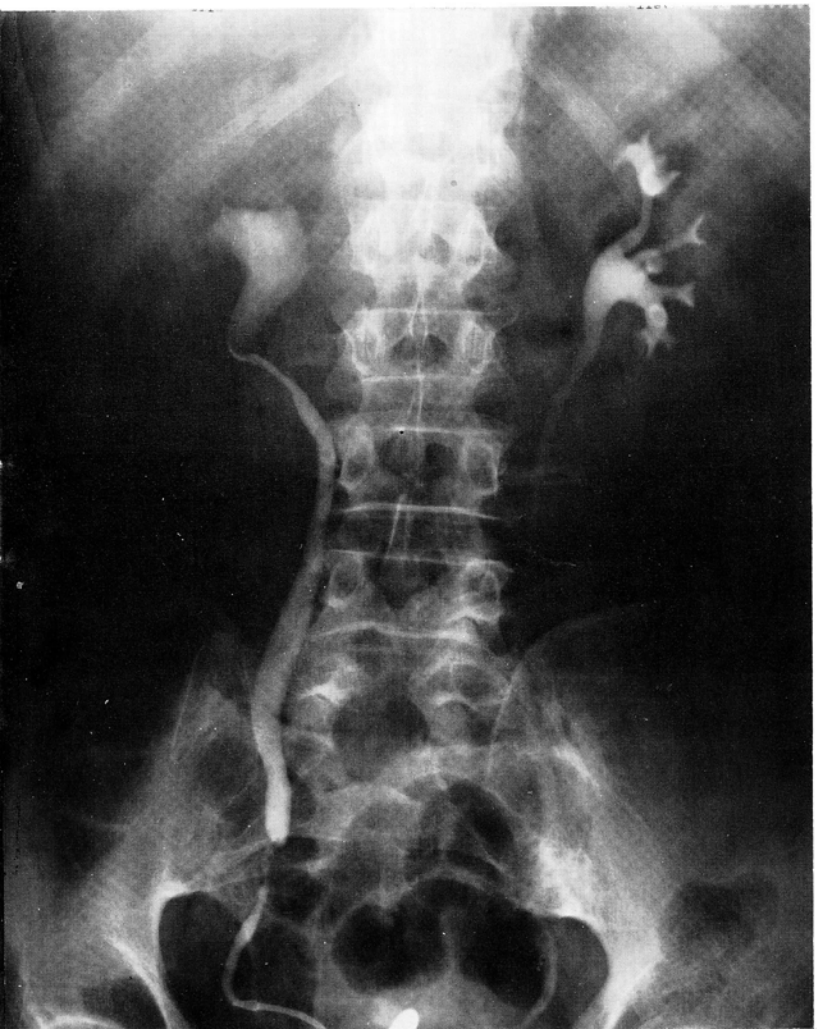
14. *Amyloid Tumor of the Ureter*

Contributed by **B. L. Pear, M.D., R. Urwiller, M.D.,** and **J. Boline, M.D.,**
Denver, Colorado

THE PATIENT was a 73-year old man in November, 1968, when he complained of pollakiuria and nycturia. Examination revealed the presence of an enlarged prostate and on further evaluation, the right kidney showed no function. The BUN was 28 mgm%.

Dr. Lalli: This is a bilateral retrograde pyelogram showing normal renal architecture of the left and thus giving us no explanation for the patient's BUN; it may be due to the prostate gland and obstructive uropathy. We are told that the right kidney did not function on urography and the retrograde pyelogram made with acorn tip catheter shows an area of marked narrowing at the level of the right iliac artery with irregularity of the mucosa. There is no post-stenotic dilatation of the ureter as is sometimes seen with primary ureteral carcinomas. Of note is the fact that the distal ureter is not dilated despite the injection which dilates the ureter above the point of constriction. This would suggest that there is a long area of potential involvement of the distal ureter. The right renal pelvis is not adequately filled with contrast medium to be able to make any intelligent observations. The entire appearance suggests disease of long duration.

Fig. 1—Retrograde pyelogram showing marked narrowing at level of right iliac artery.



The diagnostic possibilities include primarily transitional cell carcinoma, involving a long segment of the right ureter in an unusual fashion, and metastatic carcinoma which would be more likely in a female with carcinoma of the cervix. Ureteral carcinomas almost always produce hematuria. Retroperitoneal fibrosis, perhaps as a result of previous urine spill, would be considered but it is unusual in location; narrowing of the ureter due to urinary tract tuberculosis is also to be considered. There are no calcifications in the kidney as might be the case if we had an autonephrectomized right kidney due to tuberculosis. The possibility, although rare, of renal-cell carcinoma metastasizing to the ureter must be remembered. An analysis cannot be made of the colon under these circumstances but the possibility of retroperitoneal involvement from a carcinoma of the colon should be given serious consideration. Lymphoma is unlikely to involve the ureter. I note that the sacroiliac joints are largely obliterated, presumably as the result of ankylosing spondylitis but I cannot associate that with the ureteral changes. Involvement of the ureter by Crohn's disease is also to be considered. The frequency and nocturia suggest reduced bladder capacity which could occur with tuberculosis, but he does have an enlarged prostate gland.

Dr. Lalli's impression: 1) METASTATIC TUMOR 2) URETERAL CARCINOMA.

Roentgenologic impressions submitted by mail:

Ureteral carcinoma	45
Metastatic tumor	18
Carcinoma of bladder	15
Carcinoma of renal pelvis	10
Pear's amyloidotic neoplasm	1
Others	18

Dr. Lalli: Most of the radiologists, with great justification, suggested ureteral carcinoma. Some suggested that there was a metastasis to the ureter from a primary lesion of the bladder and there was a story of pollakiuria and nycturia; but the fact that he had prostate gland disease was the cause of his difficulty with urination, in our opinion, and not the carcinoma of the bladder. Carcinoma of the renal pelvis is a possibility in terms of the fact that the ureteral lesion would represent the metastasis. However, I do not see that patient's renal pelvis well enough. The contrast medium is simply being diluted by the contents in that renal pelvis and is not being disfigured by the presence of neoplasm in that site. Dr. Pear has published cases of amyloidosis of the urinary tract and I think that we will find out that this is the diagnosis.

Dr. Regato: Dr. R. B. McMullen, of Denver, suggested malakoplakia. Dr. J. Maxey Dell, of Gainesville, Florida, preferred a primary carcinoma of the ureter.

Operative findings: On December 9, 1968, a right nephro-ureterectomy and partial bladder resection were done. The specimen contained a markedly hydronephrotic kidney and an indurated lesion obstructing the ureter.

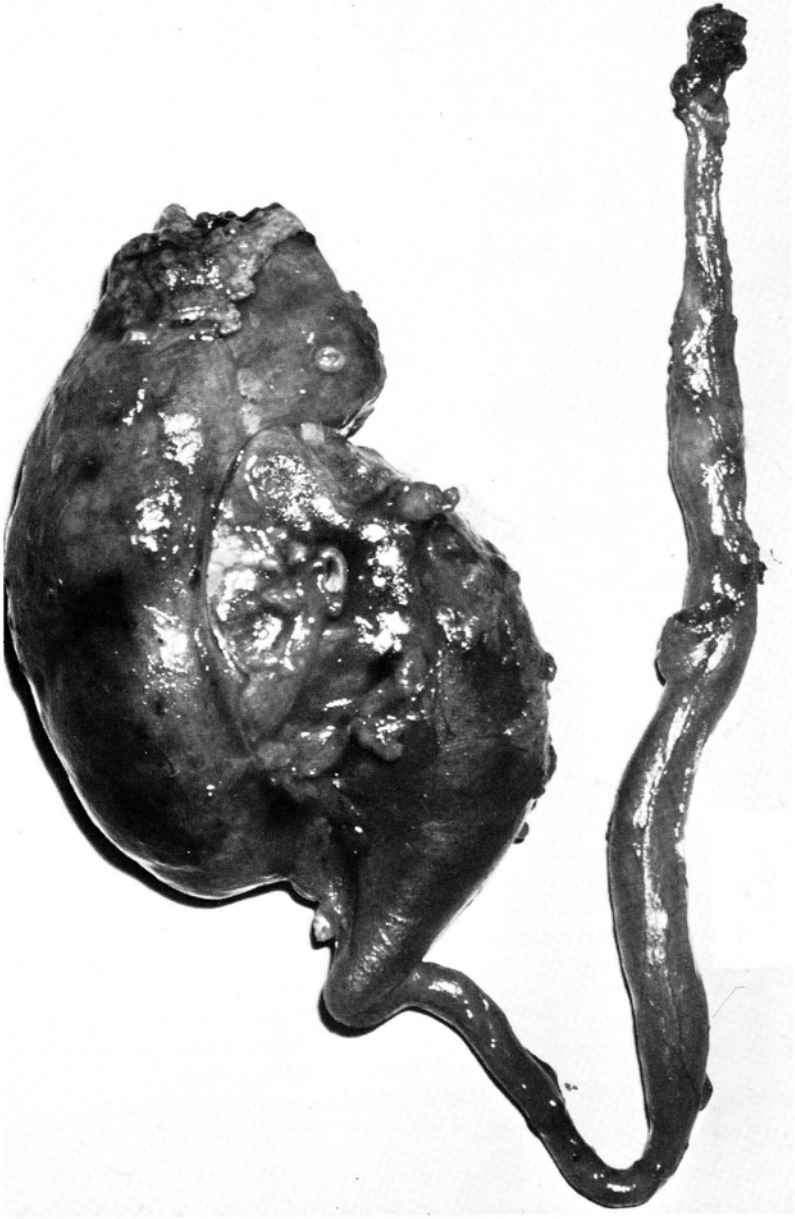


Fig. 2—Resected kidney and ureter showing dilatation of the pelvis.

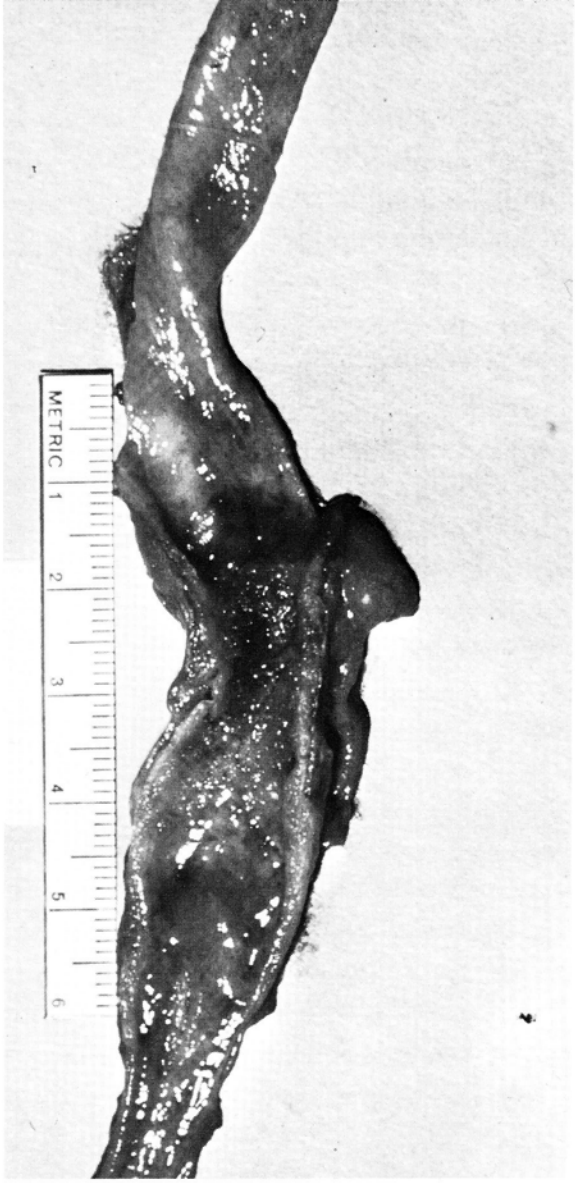
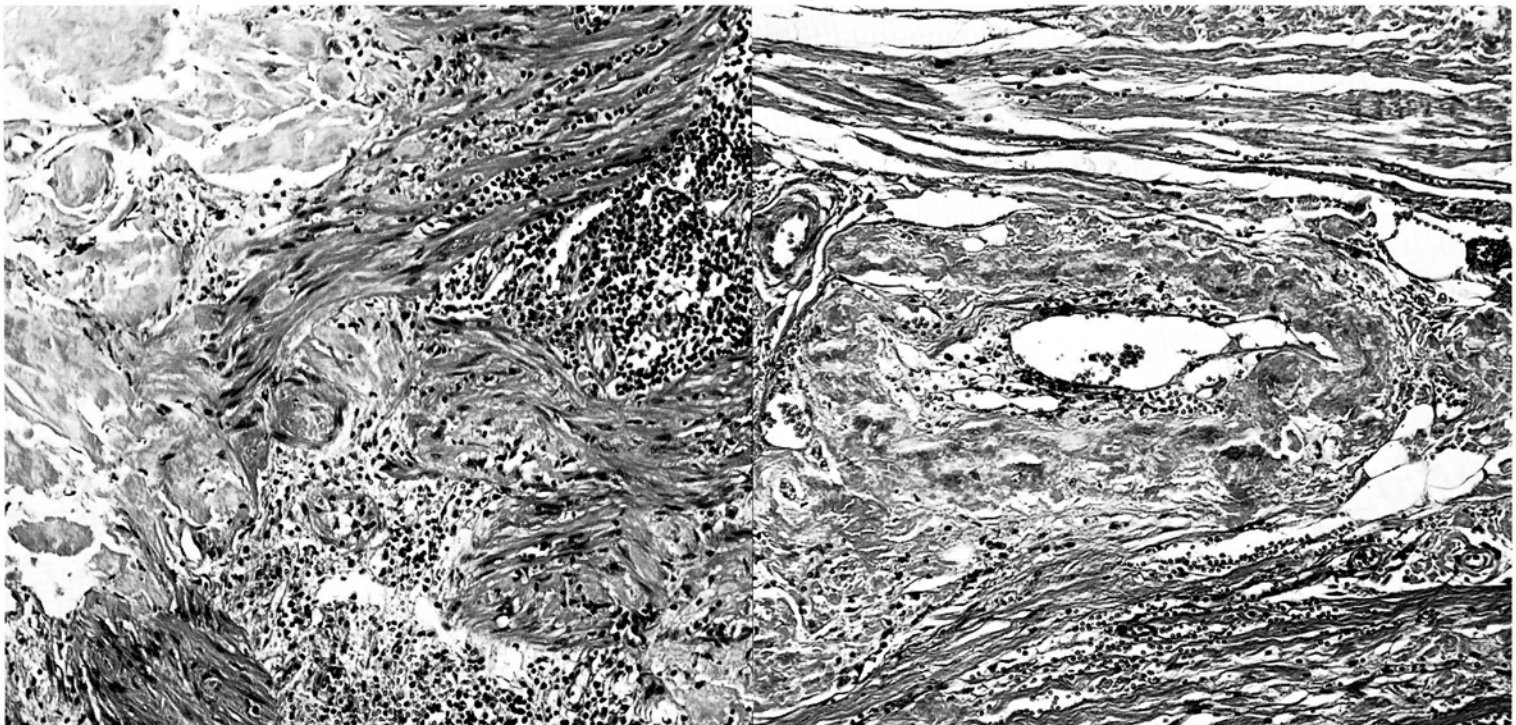


Fig. 3—Close up of the ureteral lesion showing thickened walls and pebbly surface.

Fig. 4—Masses of amyloid infiltrating smooth muscle bundles of the ureter and associated lymphocytic infiltrate. X150 W. U. Ill. 72-5608.

Fig. 5—Fluffy masses of amyloid surrounding a delicate vascular channel. X150 W. U. Ill. 72-5609.



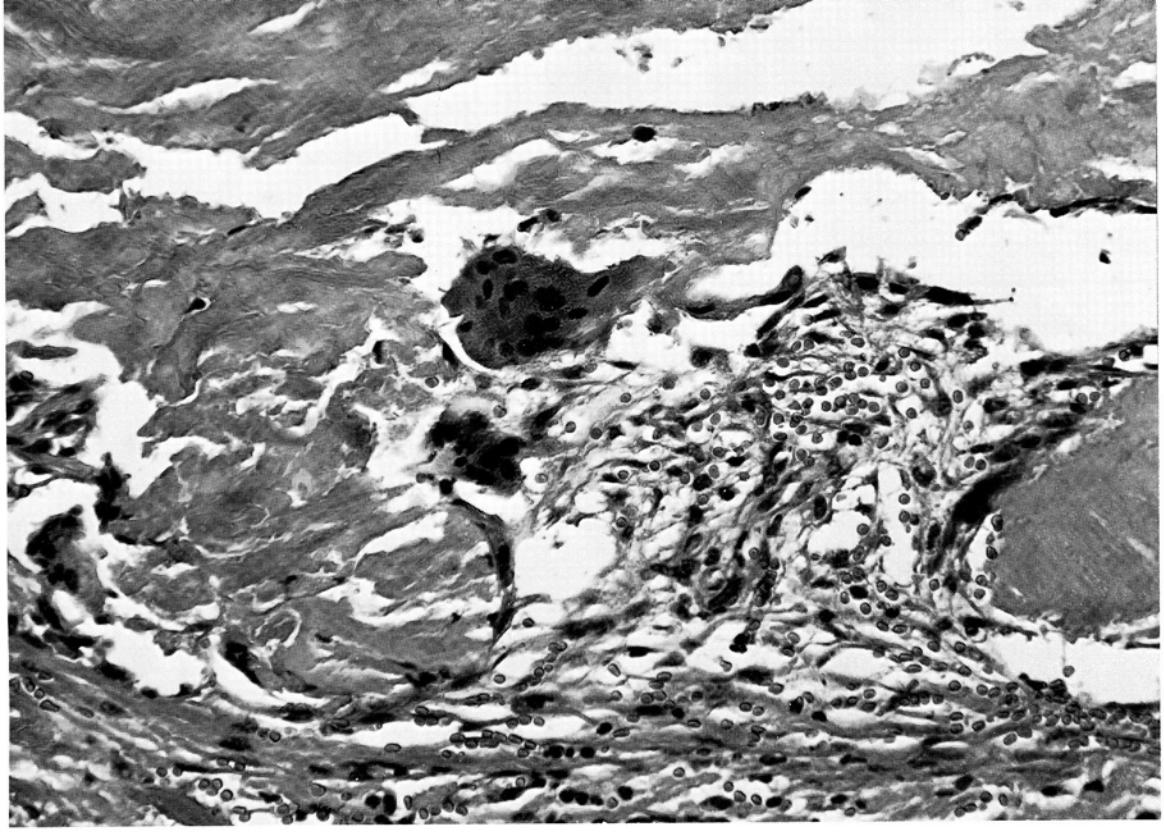


Fig. 6—Coarse, compact, masses of amyloid in the wall of the ureter with foreign body giant cell reaction. X300 W. U. Ill. 72-5610.

Dr. Bauer: The slides on this case show a diffuse replacement of the entire wall of the ureter by large and small confluent masses of an acellular proteinaceous material. Solid compact linear masses and nodular nondiscrete clumps of a pink-staining nonhomogeneous fluffy material replaces the mucosa and submucosa, infiltrates the muscularis and resides in the periureteral soft tissue. Some areas show a cellular inflammatory response with collection of lymphocytes, few plasma cells and focally, histiocytes. Fusion of histiocytes to form foreign body giant cells and granulomas can be found. Near the granulomatous reaction proliferating capillaries and fibroblasts are seen, along with some resolving interstitial hemorrhage. Homogeneous bands of the proteinaceous material form around sinusoidal vascular channels.

The interstitial and perivascular deposition of fluffy, wispy clouds of acellular material gives an impression of amyloid material that is confirmed with several special examinations. My sections were positive for Congo red and exhibited red-green dichroism when examined with crossed, plane-polarized light. The material also gave an apple-green fluorescence when thioflavin-T stained sections were viewed with ultraviolet light.

I believe this material is amyloid. This interesting case, so easily confused clinically with cancer of the ureter, represents one of about 29 or 30 cases of localized amyloid tumor involving the ureter (Johnson and Ankenman). There was a similar case (Stampfli) in the 1955 Penrose CANCER SEMINAR discussed by Dr. Mostofi. Amyloidosis may involve the kidney, renal pelvis, bladder, urethra, prostate, seminal vesicle and testis as well as the ureter (Tripathi and Desautels). Unilateral ureteral involvement is nearly always thought to be cancer clinically. Both ureters were involved in a case reported by Johnson and Ankenman.

A peculiar and striking finding was reported in a case of pelvocalyceal involvement by Gardner et al. A linear submucosal calcification was seen outlining the pelvis and calyces on roentgenograms of both kidneys. Amyloid and bone was seen in the sections from these areas. This unusual radiographic sign may be helpful in making the clinical diagnosis of amyloidosis of the upper urinary tract. I mention this because one of the striking features of the 1955 Penrose CANCER SEMINAR case was a circumferential deposit of bone beneath the intramural amyloid deposits. Perhaps bone deposition in amyloidosis is more common than we realize and pathologists should be looking for it with specimen roentgenograms.

Dr. Bauer's diagnosis: AMYLOID TUMOR OF THE URETER

Histopathologic diagnoses submitted by mail:

Amyloidosis	140
Others	35

Dr. Regato: There was a surprising almost unanimity of opinion among the experts. This case was not submitted to the AFIP.

Subsequent history: Dr. Bolin and Dr. Pear report that this patient is at present well and without abnormalities in his gamma globulins.

J. E. Boline, M.D., Denver, Colorado: We did a bone marrow examination and it did show 10 per cent plasma cells of mature type in a reactive perivascular rather than a neoplastic nodule or arrangement; we signed it out as a reactive plasmacytosis. He did have proteinuria which has cleared. A regional lymph node was full of amyloid. There was a slight amount of amyloid in the vessels in the kidney, which was markedly pyelonephritic as well as hydronephrotic. I don't think we have the last word on the follow-up. The patient had a BUN of 28 prior to surgery, a BUN of 49 two days after the kidney had been removed and it is now returned to a BUN of 25.

Dr. Glenn: This is not characteristic of a primary ureteral tumor; most ureteral tumors will exhibit a meniscus, which is usually convex in character; this is an extrinsic lesion to the lumen of the ureter, presumably something that infiltrates the ureteral wall as indeed we have seen that it does. I have never operated on a patient for amyloid disease of the ureter, nor have I ever seen one before. I am fascinated by this case.

H. Azar, M.D., Kansas City, Kansas: All amyloidosis are secondary to something, although we may not know precisely in a given situation what they are secondary to. It is obvious that we are not dealing with a localized amyloidosis; short of an autopsy we would never find out exactly the spread of this process. We know that a lymph node is involved and scattered arteries are involved in the kidney. In my experience, there are very rare localized amyloidosis as in medullary carcinoma of the thyroid, basal cell carcinoma of the skin, etc. In this instance, I think it is too premature to call this situation localized amyloidosis. I would not be surprised if this individual develops a dysproteinemia; you are probably all aware of the significance of extra production of heavy chain polypeptides in relationship to the pathogenesis of amyloidosis.

B. Pear, M.D., Denver, Colorado: I was worried that Dr. Lalli might recognize this case from a previous publication: but the truth is, I did not recognize the case either because my patient had dysuria, nocturia, urgency and frequency and this patient had something called pollakiuria and nycturia.

Dr. Regato: These are the proper professional designations for frequent micturation in general and for frequent micturation during the night.

Dr. Bauer: There are cases which may be recognized radiologically; some may present bone formation. In one of these CANCER SEMINARS, a case very much like this one, with bone formation, was seen in the ureter.

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15. *Embryonal Rhabdomyosarcoma of the Bladder*

Contributed by **J. A. Carney, M.D.,** Rochester, Minnesota

THE PATIENT was a 3-year old boy in May, 1971, when he presented hematuria. Cystoscopy revealed a polypoid mass arising from the base of the bladder. The hemoglobin was 12 gm%.

Dr. Lalli: Multiple varying-sized masses protrude into the lumen at the base of the urinary bladder. The kidneys and ureters and skeleton appear to be normal.

The differential diagnosis includes rhabdomyosarcoma arising in the bladder or prostate gland, which is not unusual in a three year old boy. Differentiation of the site of origin is often difficult or impossible. Sarcoma botryoides is a term commonly used in females since the lesion may occur in the vagina and protrude from the entroitus. This is definitely a malignant condition involving this bladder and differential diagnosis would be inappropriate. This refers to the "grape-like" appearance of these masses which is produced by the fact that the tumor has a chance to grow freely in a hollow viscus.

Dr. Lalli's impression: SARCOMA BOTRYOIDES

Roentgenologic impressions submitted by mail:

Sarcoma botryoides	63
Carcinoma of bladder	14
Sarcoma of prostate	12
Others	25

Dr. Lalli: This case was so characteristic in its appearance that of all the cases that we have seen this one shows the greatest degree of unity among the radiologists. Carcinoma of the bladder is very unusual in this age group and it would be unusual to produce these multiple rather smoothly contoured masses. Sarcoma of the prostate is a very respectable diagnosis because when some of these children get operated upon it is difficult to identify whether the sarcoma arose in the bladder or whether it arose in the prostate.

Dr. Regato: Drs. J. Maxey Dell, of Gainesville and L. O. Martinez, of Miami, Florida, suggested a sarcoma of the prostate. Drs. J. Mira, of Colorado Springs, and Mostafa Batata, of New York, preferred sarcoma botryoides of the bladder.

Operative findings: On May 12, 1971, a total cystectomy, prostatectomy and urinary diversion were done. The specimen contained a growth 2.5x1.5x1 cm surrounded by a submucosal plaque 7x4 cm.

Dr. Bauer: The slides in this last case present a classical picture of botryoid sarcoma. In many areas the mucosa is intact and thrown up into large bulbous folds by an edematous appearing submucosa populated by interlacing

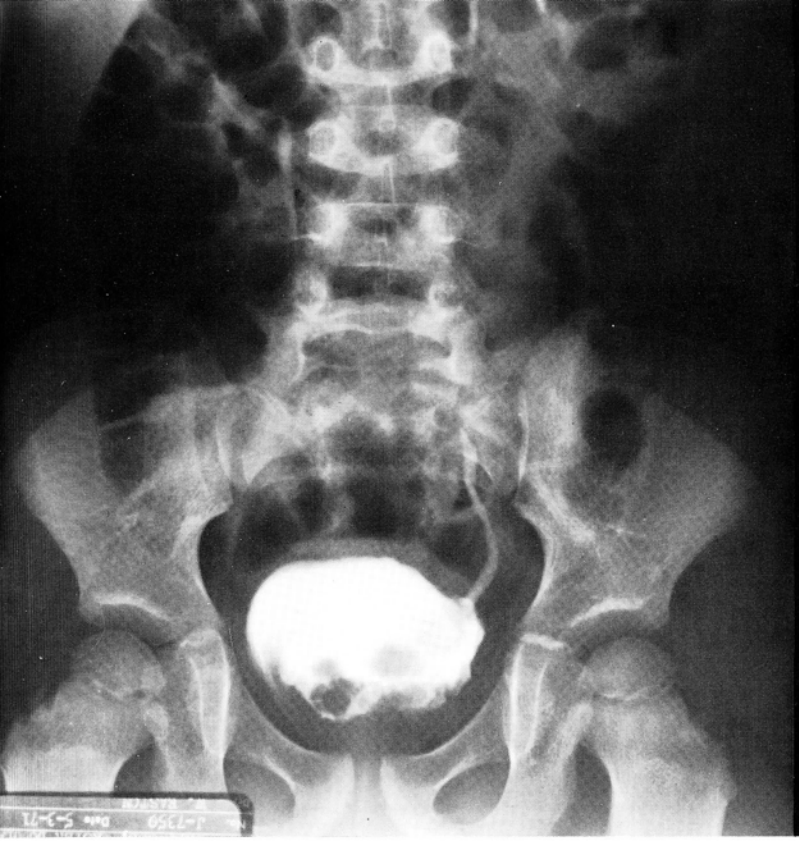


Fig. 1—Cystogram showing filling defects of the bladder.

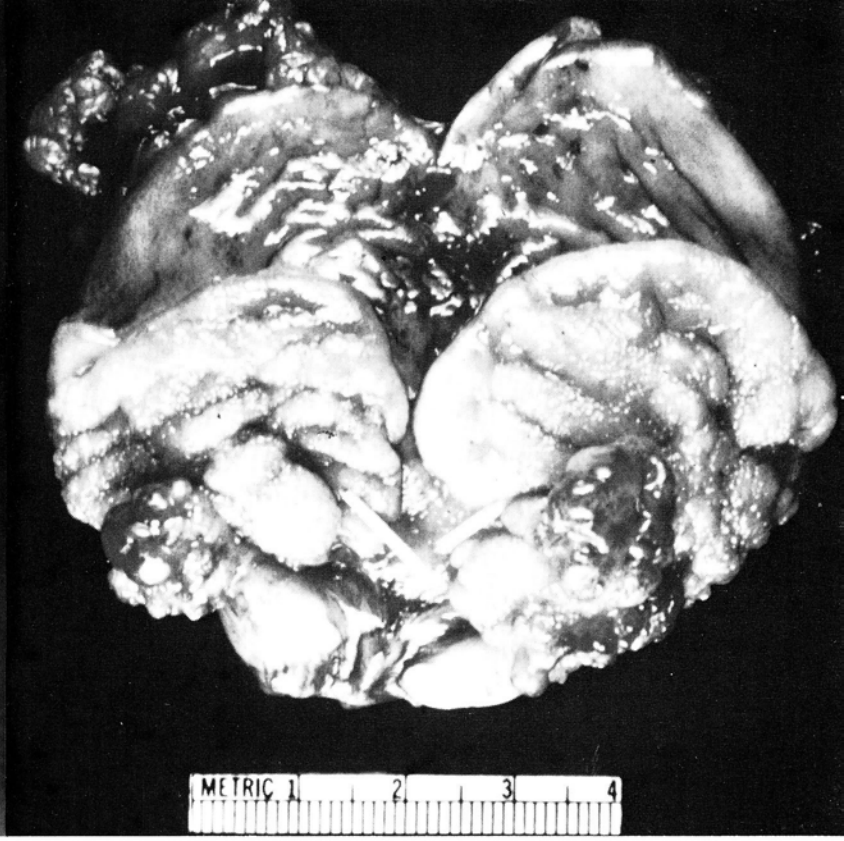


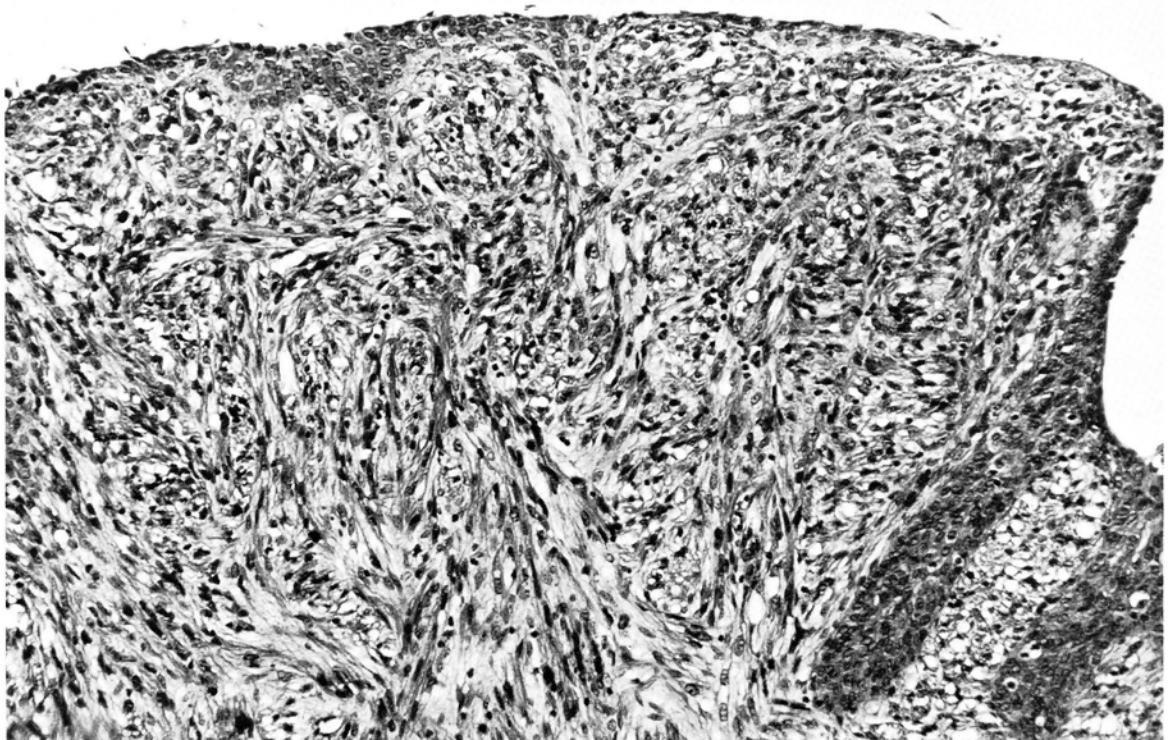
Fig. 2—Gross appearance of the resected bladder with polypoid tumor.

bundles of elongated cells. Characteristically the cells have square-ended nuclei and abundant cytoplasm. In the subepithelial zone the cells are more compact and primitive appearing while in depths of the submucosa multi-nucleated strap cells and racquet cells are seen. Cross striations are seen in such cells in PTAH stained sections.

Differential diagnosis: Embryonal rhabdomyosarcoma (botryoid sarcoma); inflammatory mucosal polyps.

The key to the diagnosis is the recognition of rhabdomyoblasts. In the material offered this is accomplished easily but in biopsy material taken with the transurethral resectoscope it may be difficult. Any polypoid material taken from the urogenital tract of infants and young children should be carefully examined before dismissing it as inflammatory in nature.

Fig. 3—Botryoid sarcoma. A bulbous fold of bladder mucosa showing interlacing bundles of elongated cells replacing the submucosa. X150 W. U. Ill. 72-5225.



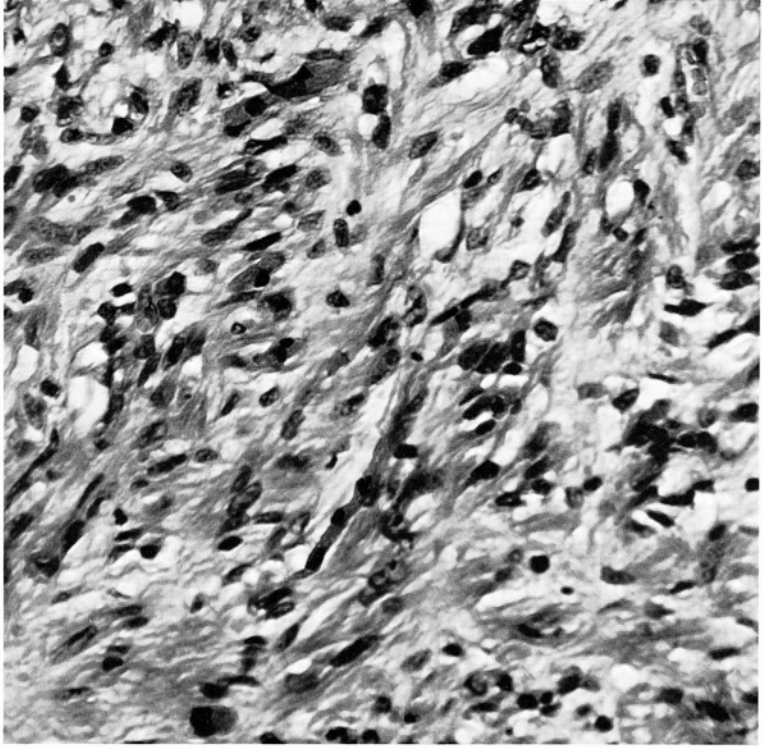


Fig. 4—High power showing long strap cells with multiple nuclei and dark cytoplasm. X350 W. U. Ill. 72-5395.

Dr. Bauer's diagnosis: EMBRYONAL RHABDOMYOSARCOMA (Botryoid sarcoma).

Histopathologic diagnoses submitted by mail:

Rhabdomyosarcoma (botryoides)	155
Others	32

Dr. Regato: Dr. Louis Dehner, of St. Louis, agreed with Dr. Bauer and with practically all other pathologists in the diagnosis of rhabdomyosarcoma.

Subsequent history: The patient has also been treated with cytoxan and Dactinomycin. In September, 1971, he was reported well.

Dr. Glenn: Rhabdomyosarcoma of the bladder in the child is a different entity from rhabdomyosarcoma of the prostate. This picture, both histologically and radiographically is characteristic of sarcoma botryoides or rhabdomyosarcoma of the bladder. You can be reasonably confident on the basis of the cystographic appearance alone; cystoscopic examination is absolutely characteristic. These are mucinous looking tumors, grape-like in character, arising on the base of the bladder over the trigone, they frequently fill the bladder. Fortunately, because of the location, they produce obstructive symptoms and they produce hematuria, so these children present to you at a relatively early stage. On the contrary, the children with rhabdomyosarcoma of the prostate, have a large lesion which grows like an iceberg. It does not impinge on the lumen, it does not erode the mucosa, at an early date and usually the horse is out of the barn by the time they reach you. David Innes Williams of the Great Ormond Street Hospital, in London, has had experience with 24 rhabdomyosarcomas of the bladder, 11 of which are surviving at the present time: a 50 per cent cure rate surgically. In our experience, out of 9 patients, we have 2 survivors of 4 and 5 years after surgery. Unfortunately, many are tempted to open the bladder and to biopsy these things; this is the wrong thing to do. Discourage your surgical and urologic colleagues from messing with these. Send these children to a center where they are accustomed to doing radical pelvic eviscerations and urinary diversion; this is what they need. The rhabdomyosarcoma of the prostate is, unfortunately, much more dismal. At the Great Ormond Street there are no long term survivors nor do we have any. I think this is probably pretty universally true.

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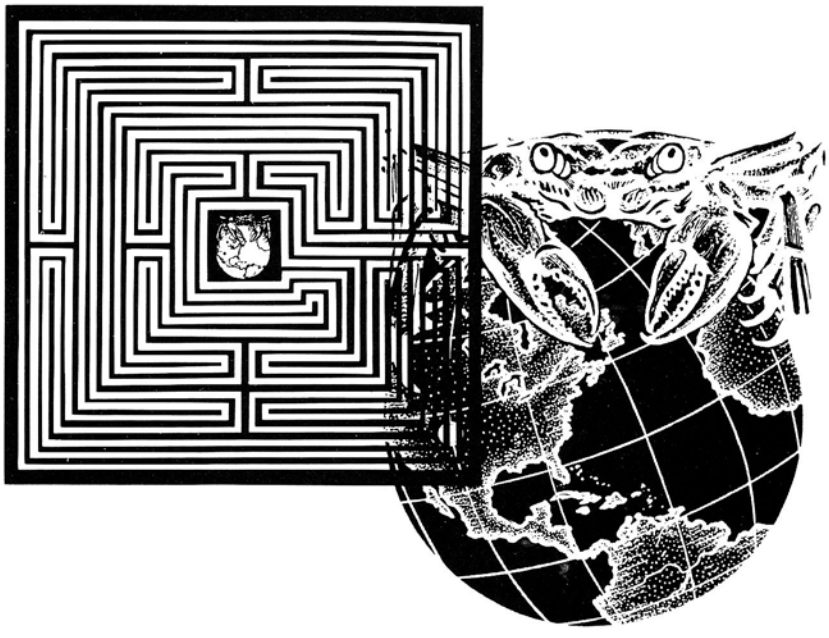
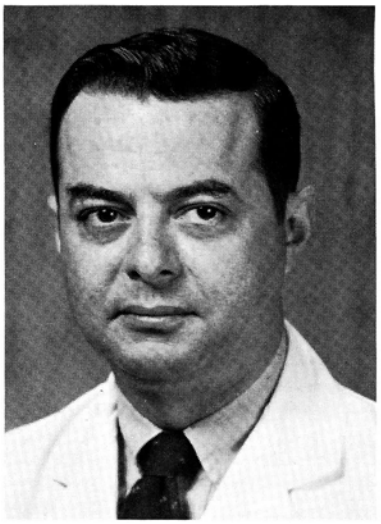


OUR GUEST SPEAKERS



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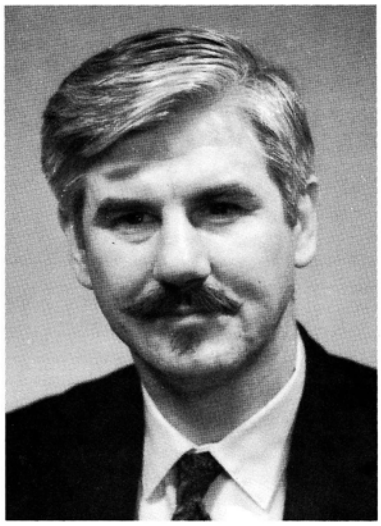

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