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MALIGNANT PAPILLARY ADENOMA OF THE KIDNEY[1]

With Discussion of a Case

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THE definition of malignant adenoma has in itself occasioned quite a difference of opinion among pathological anatomists and clinicians. There are generally speaking two distinct appreciations of the term, one, that expressed for instance, by C. Ruge, Winter, and Gebhardt, is very restrictive. They limit the term to a tumor of adenomatous structure, malignant in character, showing throughout a single row of epithelium lining the alveoli and in no way microscopically differing from a simple adenoma. On the other hand, Kaufmann, von Hansemann, and Lubarsch understand by the expression, a tumor of malignant type, glandular in character, showing usually transitional or polymorphous epithelium, sometimes also solid cell aggregations. Their standards of malignancy are the same.

Borst, in regard to malignant adenoma, cites the various organs involved by this variety of neoplasm in the order of frequency.

Intestine and stomach, reported by Selberg.

Liver, von Hansemann.

Gall-bladder, Selberg.

Uterus, cases reported by Livius, Furst, Veit, Kaufmann, C. Eckhardt, Kuckenberg, Eberth, Olshausen, Schröder, Selberg.

Lung (bronchial mucous glands), von Hansemann.

[1] From the Pathological Institute of the City Hospital, Friedrichshain, Berlin, Germany. Professor Ludwig Pick, Director.

Sweat and salivary glands, von Hansemann.

Borst does *not* report its occurrence in the kidney, *nor* do any of the following authors in their writings on kidney tumors: Krönlein, Mönkeberg, James Israel, Franz Nürnberg, Albarran, and Imbert.

On a careful search of the literature, but one absolutely proven and undoubted case is to be found, namely, that reported by Sudeck in 1892. The cases of renal tumor reported as malignant adenoma have partly been confused with hypernephromata. Von Hansemann says that he has seen examples of this type of new growth in the kidney and cites James Israel's case, as the first one observed. Israel, however, reported this case in 1892 as a hypernephroma. Baumgarten's case reported as "congenital malignant adenoma of the kidney" belongs to that now well studied group of tumors, the congenital adenosarcoma, in which the adenomatous structure was very marked.

On account of the extreme rarity of this variety of neoplasm in the kidney and of the distinct characteristics of the case observed, I have thought it worthy of being placed in the literature. The primary tumor is far more typical in microscopical appearance than Sudeck's case, and by virtue of its widespread metastases much more malignant in type.

CASE REPORT

By courtesy of Dr. Braun, directing surgeon. History: Patient entered Hospital Friedrichshain, Berlin, March 14, 1910. F. R., male, aged 56 years, railroad pensioner. Since September, 1909, complained of frequent hematuria, dragging pain in right renal region without the occurrence of any colic or colicky pains. For three weeks before entrance to the hospital, he had been confined to his bed. The presence of a growing tumor in right renal region was determined by his house physician and he was sent to the hospital for surgical treatment.

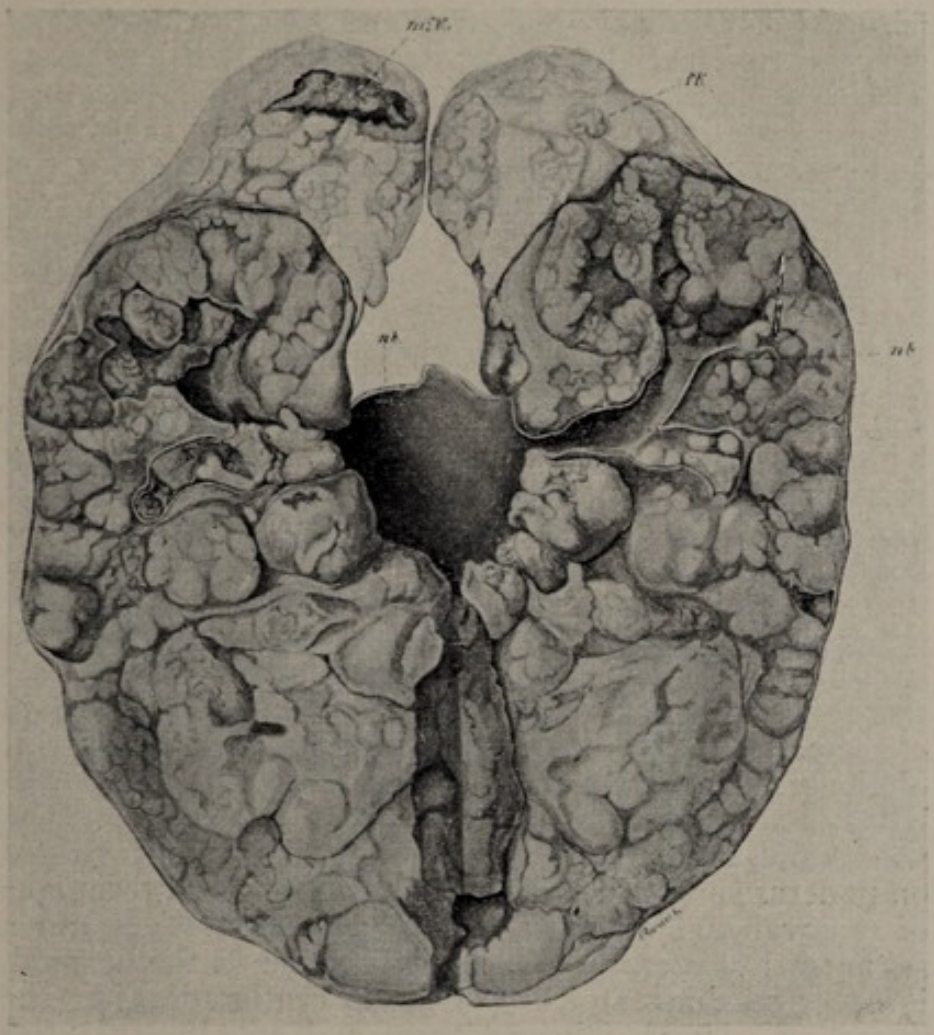

Fig. 1. Right kidney; mfk, show metastasis in fat capsule; fk, involved fat capsule torn away with kidney; nb, dilated renal pelvis.

Past illnesses. Acute rheumatic fever, gout. Venereal disease denied. No history of alcohol abuse.

Present condition. Examination. Middle sized man, of average muscular development in poor state of nutrition. Skin pale and of cachetic appearance. Supra and infra clavicular as well as intercostal spaces sunken. Mentality, patient dejected.

Thorax. Heart negative to inspection, percussion, and palpation. Systolic murmur at apex, not transmitted. General arteriosclerosis. Lungs give increased breath sounds over entire area, but nowhere true bronchial breathing.

Abdomen. Normal in contour and somewhat rigid. Skin transparent, veins prominent. In right kidney region, a tumor mass is noted, which is slightly movable,

hard in consistency and with nodular surface. This mass is not especially tender on pressure and reaches to within a finger's breadth of the umbilicus. The liver dullness can readily be distinguished from the tumor dullness, the two areas being separated by about 2 cm. of modified tympany. Inguinal glands enlarged.

Urine. Albumin in large quantity. Sediment shows few hyalin casts, and a few red and white blood corpuscles. No tumor cells found.

Clinical diagnosis. Tumor of right kidney.

Operation, March 16, 1910. Morphine, chloroform and ether narcosis. Incision in right lumbar region. Kidney exposed and found to be wholly involved by large hard tumor mass, and about three times as large as a man's fist.

The kidney was freed with great difficulty and in order to do so a portion of the twelfth rib was resected. The upper part of the tumor mass projected under the liver and here also involved the parietal peritoneum. This was necessarily removed with the kidney. The removal of the entire tumor mass was found impossible on account of the great involvement of surrounding structures. The kidney and part of fat capsule only were removed. The pelvis and ureter were enormously dilated and yielded on puncture a turbid urine. The usual surgical technique of removal of kidney was followed. The patient ran a subnormal temperature during entire time in the hospital, it never reaching above 36 degrees centigrade after the operation. Death followed three and a half days after operation.

Autopsy, March 20, 1910. Medium sized emaciated male cadaver, rigor mortis present. Slight postmortem lividity on posterior surface. In right lumbar region is a recent operative wound 20 centimeters long; partly closed by suture, in the upper and open part there are six blood stained gauze strips leading to a cavity, the size of newly born child's head. Right kidney wanting.

Thorax. Heart normal in size, myocardium flabby and of pale yellowish brown color. Epicardium contains somewhat less than the normal amount of fat. Valves intact, and competent to water test. Aorta and coronary arteries show slight arteriosclerosis.

Lungs. Bilateral pleural adhesions. Lungs contain much bloody fluid. Both show several white soft nodules, varying in size from a pinhead to a large pea. Bronchial glands anthracotic, but show no tumor nodules. Bronchial and tracheal mucosa, injected.

Diaphragm. In right half of diaphragm are several flat lentil sized tumor metastases of same appearance as those noted in the lungs.

Abdomen. Spleen showed well marked perisplenic adhesions, but no tumor metastases. Urinary bladder, mucosa injected. Prostate, negative. Rectum, mucosa injected.

Stomach and intestines. Mucosa slightly hypertrophic and of yellowish green color, partly covered with tenacious mucous.

Liver. Small in size, capsule adherent in places to parietal peritoneum. The organ contains many spherical tumor nodules, varying in size from a pinhead to a cherry; similar in appearance to the lung metastases, they are *not* umbilicated.

Gall-bladder. Negative.

Pancreas. The pancreas itself showed no changes, but the glands about its head are very large and show tumor metastases of the same appearance as those observed in the lungs and diaphragm.

Mesenteric glands. Greatly enlarged and markedly softened. On section most are of the same color as the tumor nodules.

The left kidney. The left kidney is enlarged and somewhat harder than normal. Capsule removed with slight difficulty. The cortex is reduced in diameter, but markings are distinct. No tumor nodules grossly recognizable.

Left ureter. Negative.

The abdominal aorta. Shows slight degree of arteriosclerosis. The exit of right renal artery is almost wholly obliterated, but does not contain tumor mass. Left renal artery, normal.

Vena cava inferior. This vessel is almost entirely surrounded by tumor growth and from its origin to within two centimeters of diaphragm contains a necrotic tumor thrombus mass. Cross section through this adherent conglomeration of tissue shows the tumor involvement affecting the region chiefly to the right of the vena cava, and the greatly thickened vessel walls partly destroyed by tumor invasion. The tissues to the left of the vena cava are not so markedly involved and the individual periaortic glands can be distinguished. These on section show tumor nodules of the same appearance as those noted in lung, diaphragm, and glands about head of pancreas.

Right renal vein. Shows the same changes as described for vena cava. The entrance of the left renal vein is thrombosed by tumor invasion, the remainder is free.

Right iliopsoas muscle. Shows several tumor nodules.

Brain. Section forbidden.

Bony system. Section forbidden.

Anatomical diagnosis. Malignant tumor of kidney (right) with metastases in following organs: Liver, lung, diaphragm, right iliopsoas muscle, periaortic glands,

mesenteric glands and lymphatics about head of pancreas, tumor thrombi of both renal veins, tumor thrombosis of inferior vena cava.

Arteriosclerosis of aorta and coronary arteries, bilateral pleural adhesions, hyperemia and edema of lungs, perisplenic adhesions, chronic interstitial nephritis, cystitis, chronic gastritis, and enteritis.

Gross pathology of right kidney. The entire organ is involved by new growth and no trace of renal tissue is grossly recognizable. It measures 18 cm. in length, from 6 cm. to 9.5 cm. in breadth and from 4 cm. to 5.5 cm. in thickness.

The color varies from yellowish gray to yellowish brown and here and there hæmorrhagic areas are noted. These measure from about 1 to 4 cm. in diameter and are irregular in contour, and are not confined to the boundaries of the individual nodules involved.

The whole kidney is made up of numerous tumor nodules, varying in size from a pea to an English walnut, and the surface is extremely irregular. The different nodules are separated by a firm, but very scant connective tissue. The true fibrous capsule is in places wanting, but when one tries to remove the remainder, tumor mass is torn away with it. A large area of necrosis, about the size of small hen's egg, is noted in lower pole. No suggestion of cyst formation is present.

Section through kidney. Cut section of kidney shows but few additional points of interest, the total involvement of tumor; the nodular structure and hæmorrhagic areas are all more distinctly seen than on surface.

Microscopic examination of tumor. Preparations made from diverse parts of primary tumor and of all tissues involved were hardened in formalin and alcohol, embedded in paraffin and cut in thicknesses from 5 to 10 microns and stained by hæmalaun-eosin. Fresh frozen sections were also made and stained for elastic fibers after Weigert and for fat with Nile blue and Sudan III.

Low power. No. 3 obj., No. 2 eyepiece (Leitz). All sections of primary tumor examined show identical structure, namely, a papillary new growth of distinct adenomatous type. Each microscopic nodule is seen to be made up of numerous cavities, surrounded by a small amount of fine connective tissue, poor in nuclei. These cavities contain numerous papillary proliferations of various sizes. Many of the larger ones show branching and secondary papillary excrescences. Some are long and narrow, others short and broad. They are made up of a fine fibrous stroma which supports an abundant blood supply and are clothed with a single layer of epithelium.

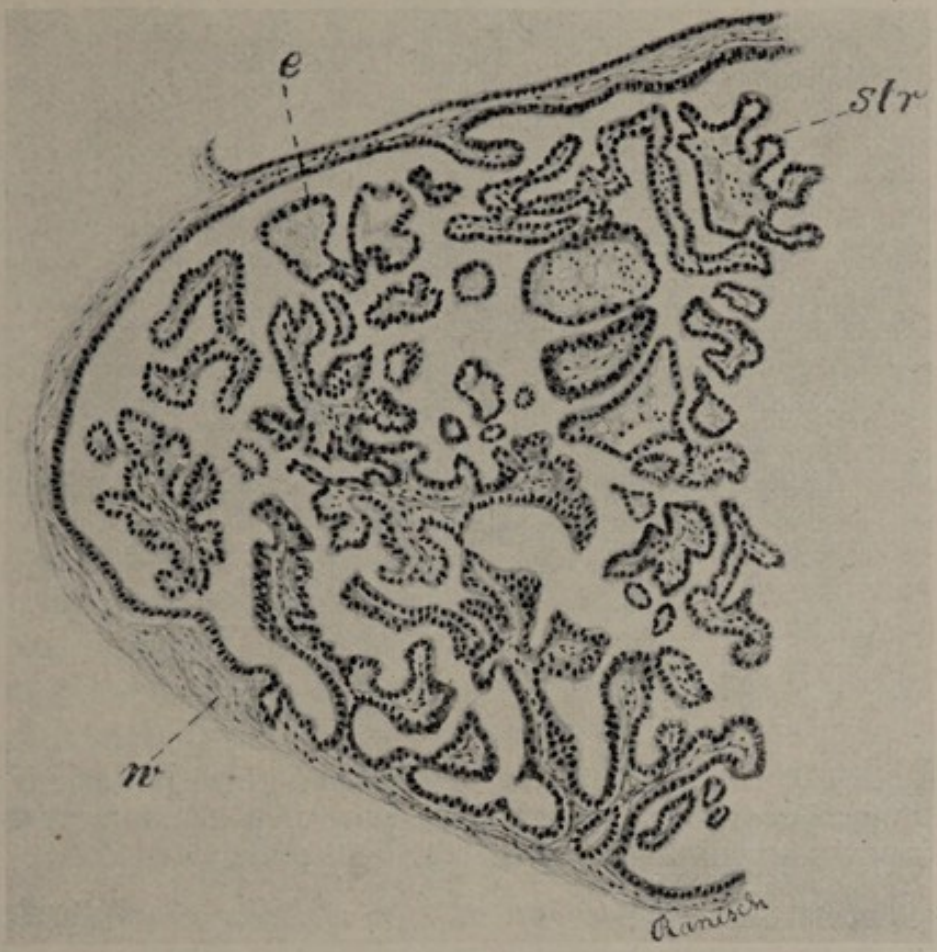

Fig. 2. Section of primary tumor (high power); e, single layer of columnar epithelium; str, connective tissue stroma of papilla; w, internodular septum.

Bleeding into the stroma of some of the papillæ can be noted, others are edematous.

No renal tissue is to be found in sections made from various parts of the organ.

High power. $\frac{1}{7}$ obj., No. 2 eyepiece. More minute study of the various preparations shows the papillæ to be made up of a fine connective tissue stroma, small in amount, the nuclei of which stain well with hæmalaun, and are somewhat shorter and broader than is the rule. Many capillaries are to be seen, some of which are greatly dilated. The other blood-vessels show no peculiarities. An almost regular epithelium, chiefly of the tall cylindrical type in single layer covers the papillæ.

The epithelial cells present a well staining (eosin) homogeneous protoplasm and relatively large oval nuclei which stain well with hæmalaun.

The nuclei are *vacuolar* and present nucleoli, sometimes

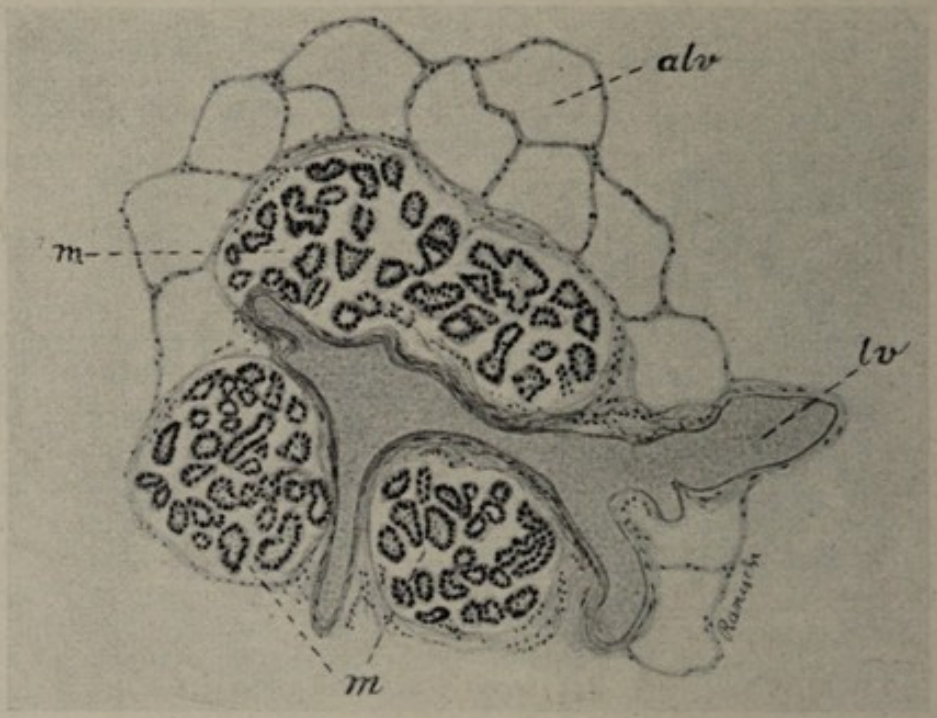

Fig. 3. Section of lung metastasis (low power); lv, branch of pulmonary vein; alv, lung alveolus; mm, metastases occluding lymph spaces about pulmonary vein.

as many as three in one nucleus. They are usually located near the base of the cell, but not infrequently quite near the middle.

In one or two sections the epithelium appears to be in two or three rows, but this was later shown by cutting very thin paraffin sections not to be the case, but *that throughout the epithelium is in single layer.*

Hyalin degeneration is found in various areas; and many of the alveoli are filled with necrotic epithelial and blood cell detritus.

Both Sudan III and Nile blue in frozen sections were used to determine the presence of fatty change in the epithelium, but such is absent.

Small round cell infiltration is found in various areas.

Microscopic examination of the various metastases. Preparations of all metastases examined show the same general picture as described for the primary neoplasm. The papillary structure in the larger and older metastases is exquisitely marked, while in some of the smallest and youngest nodules, one notes merely the tendency thereto, and finds some alevoli lined with two and three layers of epithelium and even solid cell aggregations. The papillary structure is *always* well marked in those metastases, which have advanced far enough in their development to demon-

strate the mutual growth and relation of connective tissue and epithelial elements. For example, nearly all the nodules in the lung show absolutely the same structure as the primary tumor, with the cylindrical epithelium in a single layer clothing the papillæ, while some of the metastases in the diaphragm, for example, being but microscopic and very young show the presence of a double or triple epithelial layer lining the alveoli. The capillaries in these minute nodules are very abundant and often greatly dilated. The blood-vessels in general, are not involved by tumor thrombi, but the lymphatics are frequently distended and obstructed by tumor growth. The metastases in the liver are chiefly necrotic, as are the same noted in the mass about the inferior vena cava.

This tumor then presents certain characteristics of interest. Especially the pure papillary structure of the primary tumor and older metastases with their single layer of epithelium throughout, a picture which we have been taught to regard as typical of certain benign epithelial growths. This neoplasm later giving rise to numerous and widely spread metastases, all showing the papillary tendency and being similar to the primary neoplasm. The variability observed between the smallest and largest metastases seems to depend wholly upon the stage of development.

A small metastatic nodule shows in its incipiency microscopically a minute solid cell aggregation, through which very early newly formed capillaries find their way, making a network throughout the nodule. As the blood gains entrance to the capillaries causing their distension, the appearance of alveoli is given, with certain of the epithelial cells applied directly to the thin capillary walls. Now if even the most minute resistance opposed to the blood by the capillary walls is overcome, as Sabourin says "a veritable cataclysm" occurs, the blood gaining entrance to the adenomatous tissue causes minute hæmorrhagic cysts with coincidental tearing of some of the epithelial cells from their insertion and destruction of others. Somewhat later

when the connective tissue grows in about the capillaries and the interdependent or mutual growth of the two elements occurs, we note the appearance of well marked papillæ projecting into the various alveoli.

Benign papillary adenomata of the kidney are by no means common in the literature. Franz Nürnberg, for example, in 287 cases of renal tumors examined, found adenomata in 66 cases, only 37 which showed papillary structure. Von Hansemann calls attention to the fact, that in papillary tumors, if the papillæ have a broad stroma and are clothed with a single layer of a cubical epithelium, a diagnosis of benignancy can be made; but if the reverse be noted an absolute diagnosis of malignancy *can not* be made.

Sudeck, however, found polymorphous epithelium with rather indefinite papillary structure in four cases of small and absolutely benign renal adenomata; and a similar picture in his case of malignant papillary adenoma of the kidney with lung metastases, which microscopically he could not distinguish from the benign adenomata.

This case however, presents well marked and definite papillæ, some short and broad, others long and graceful, all covered with a *single* layer of cylindrical epithelium. It differs markedly from the rule expressed by von Hansemann that in malignant papillary adenomata, the long narrow papillæ greatly predominate, in as much as we note a very large proportion of short thick papillæ.

Nota.—A small nodule of papillary adenomatous type was found on microscopic examination of left kidney, showing a chronic interstitial nephritis. The pure papillary structure in so *small* a nodule suggests that this adenoma is coincidental rather than a metastases of the above described tumor; as it showed in no place but a single layer of *cubical* epithelium.

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