HYPERNEPHROMA AND SPINDLE-CELL SARCOMA OF THE KIDNEY

M. M. BRACKEN, M.D.

(From the Department of Pathology, University of Toronto, and Toronto General Hospital, Toronto, Canada)

There has been continued interest in the nature of tumours arising in the kidney and suprarenal glands since Grawitz in 1883 described renal tumours arising from suprarenal rests, which he called hypernephroma. Others have described tumours varying from the hypernephroma type in cell structure, while yet maintaining in part the character of the true Grawitz tumour. The case which is presented here falls into this category. Because of its characters, it may be described as hypernephroma and spindle-cell sarcoma of the kidney, with sarcomatous and mesotheliomatous metastases.

CASE REPORT

The patient, a retired bank clerk, aged sixty-seven years, was admitted to the Toronto General Hospital in the service of Dr. Pearse on Oct. 11, 1935. His chief complaints were slight pain in the right flank, of three weeks' duration, and hematuria for one week. The pain in the flank did not radiate and did not increase in severity, but was fairly constant. The hematuria was not associated with dysuria nor frequency until two days before admission, when urination was accompanied by severe pain and partial retention. There was no previous history of similar symptoms except for a dull pain in the right flank one year before admission, which subsided after a few days. The patient had had uncomplicated gonorrhoea forty-seven years before admission and had suffered from severe asthma for twenty years, treated extensively at various clinics without much relief.

Physical examination showed an adult white male, cachectic and not acutely ill. The chest was hyperresonant throughout and there were a few râles just below the right scapula. The liver was palpated below the level of the umbilicus; it was smooth and not tender. The kidneys were not palpated.

The urine looked like pure blood and contained clots. The blood on admission showed haemoglobin 60 per cent, decreasing to 40 per cent during hospitalization, and red blood corpuscles 4,200,000; the non-protein nitrogen varied from 28 to 35 mg. The van den Bergh test (direct and indirect) was positive, 6 units. The Wassermann reaction was negative.

Severe hematuria continued until death, necessitating a blood transfusion. Cystoscopy revealed an obstructed right ureter, and x-rays showed the presence of a right kidney mass, diagnosed as hypernephroma. Roentgenograms suggested secondary growths in both lungs. The patient was considered too poor a surgical risk to justify operation. He gradually became weaker, due to loss of blood, and died two months after admission, Dec. 12, 1935.

Clinical diagnoses: Hypernephroma of the right kidney; secondary tumours in liver and lungs; anaemia.

Autopsy Findings: Autopsy was performed thirteen hours after death. The body was that of an elderly white male weighing 112 pounds. The skin of the entire body, the mucous membranes of the oral cavity, and the conjunctivae were jaundiced. There was a large, palpable mass in the right flank extending ventrally to within 8 cm. of the umbilicus.

The lungs were heavier than normal, voluminous, and somewhat emphysematous. Both showed old pleural adhesions at the apices and posterior surfaces. Scattered throughout all the lobes were nodular masses measuring up to 3.5 cm. in diameter. On section
these appeared as firm, fairly well circumscribed, yellowish-white masses showing areas of necrosis and haemorrhage. A haemorrhagic mass in either lower lobe had ulcerated through the visceral pleura and resulted in the leakage of 50 c.c. of blood into the pleural cavities. The lower lobe of the right lung also showed bronchopneumonic consolidation.

The heart was of normal size. A large area of fibrosis was present at the apex of the left ventricle along its anterior wall. An old thrombosis, with occlusion and canalization of the anterior descending branch of the left coronary artery, accounted for this myocardial fibrosis.

The peritoneal cavity contained about 400 c.c. of golden yellow, thin, flaky fluid. Numerous fibrinous adhesions joined the parietal peritoneum to the surfaces of liver, omentum, and intestines. There were also numerous firm, white tumour nodules on the parietal peritoneum and in the greater omentum. The perirenal tissues extended ventrally for about 2 cm. more on the right side than on the left. The kidneys, adrenals, retroperitoneal tissues, and aorta were removed en masse. There was a tumour, the size of a large grapefruit, occupying about five-sixths of the total substance of the right kidney, so that only the lower pole of the organ remained. The right perirenal tissues were much thickened due to invasion by tumour tissue. The mass in the kidney appeared as a large, poorly circumscribed, spreading tumour, the greater part of which was soft and yellowish-red, with large areas of necrosis and haemorrhage. The upper part was of a distinctly different appearance, firm and yellowish-white, enveloping the upper half of the softer mass. sending many strands of firm tissue deeply into it. The right adrenal gland could not be distinguished. The retroperitoneal tissues and lymph nodes were invaded by tumour tissue of the firm, white type, so that they formed a large, irregular mass compressing but not occluding the aorta. The inferior vena cava was also invaded by firm, white tumour tissue, but the renal veins and arteries were clear. The common bile duct was compressed but not completely occluded. As a result of this compression there was a moderate dilatation of the bile ducts and gallbladder with bile stasis in the liver. The latter organ contained many white, firm, fairly well circumscribed tumour nodules which were most prominent beneath the capsule. The left adrenal gland contained several firm, white nodules which compressed the cortex.

FIG. 1. HYPERNEPHROMA AND SPINDLE-CELL SARCOMA OF KIDNEY

The remaining portion of normal kidney is seen at the lower pole of the tumor. The central part of the mass is hypernephroma. The white, dense, peripheral portion, with extensions into the hypernephroma, is spindle-cell sarcoma.
FIG. 2. HYPERNEPHROMA OF RIGHT KIDNEY

This photomicrograph shows a section through the central tumor mass in the right kidney. The cells are typical of hypernephroma. × 200.

FIG. 3. SPINDLE-CELL SARCOMA OF RIGHT KIDNEY

The irregular growth of cells having a definite spindle shape, and showing frequent mitotic figures, is typical of the firm white mass in the kidney. × 200.
The left kidney, genital organs, ribs, and vertebrae showed no secondary growth. Permission for examination of the brain was not obtained.

**Microscopic Examination:** The microscopic appearance of the primary growth and metastases was extremely interesting. A section through the loosely constructed, haemorrhagic mass in the right kidney showed tumour tissue of the hypernephroma type. The cells were large and polyhedral, pale and somewhat transparent, with a finely granular and vacuolated cytoplasm and irregularly dense, rounded, and centrally placed nuclei. The cells were arranged singly, in irregular groups, and occasionally in fine strands, in the latter respect suggesting a renal epithelial structure. Mitotic figures and giant cells could be seen. The interstitial tissue was of loose structure and contained numerous small blood vessels and large, scattered areas of necrosis and haemorrhage. Sections taken through the firm, white mass at the apex and periphery of the hypernephroma showed cells of a distinctly sarcomatous character, mainly spindle-shaped and interspersed with some fibrous tissue and necrosis. This tissue was denser in appearance than that of the hypernephroma. The inferior vena cava showed invasion by hypernephromatous and spindle cells.

Careful examination of the secondary growths in all other organs, including the left adrenal, revealed no cells of the hypernephromatous variety. Indeed, these secondary growths were of the spindle-cell type with some variation in structure, so that in the lung many of the cells were ovoid or polyhedral with cytoplasm consistently pale and dense, chromatic round or oval nuclei occupying most of the cell; others were large and multinucleated, so that the cellular structure assumed a mesotheliomatous appearance.

**Discussion**

Following Grawitz' original description (1), many cases of hypernephroma or similar renal or suprarenal tumours have been reported, some authors agreeing and others disagreeing with Grawitz as to the origin of such tumours. De Paoli (2) in 1890 described similar tumours, but because of the seemingly close relationship of the cells to the capillaries, he thought that there was a true proliferation of the endothelial lining cells and called them angiosarcomas. Hansemann (3) supported this view. Beneke (4) in 1891 described two cases of renal tumours, both of which showed sarcomatous and adrenal cell tissue. He believed that the two cell types represented a differentiation of the one primary cell, rather than one type of tumour produced by the action of another. Berry (5) took the opposite view when he described three cases of primary renal tumours, one of them being "... a fibro-sarcoma and adrenal cell carcinoma," the second, "... fibro-sarcoma and papillary adenocarcinoma," and the third "adrenal cell carcinoma and leiomyosarcoma." He believed that these cases represented two distinct tumours in the one kidney, each of which was growing quite independently of the other.

Wilson (6), Stoerk (7), and Muir (8), among others, point out that some of the tumours classified as hypernephroma in reality arise from abnormal renal epithelial structures such as adenopapillary tissue and papilliferous cysts in which the epithelium may come to contain myelin and the cells appear large, clear, vacuolated, and rich in glycogen and fat. There is no doubt that tumours of this type have been reported. Indeed, such tumours may occur in which part of the tumour is carcinomatous and part hypernephromatous. Balch (9) reported a case of papillary carcinoma and hypernephroma occurring in the same kidney and the last two of Berry’s cases come into this classification.
FIG. 4. INFERIOR VENA CAVA, SHOWING THROMBOSIS DUE TO INVASION BY HYPERNEPHROMA AND SPINDLE-CELL SARCOMA

The two types of tumor cells are in close apposition without showing a variation of either cell type. × 200.

FIG. 5. MESOTHELIOMA AND SPINDLE-CELL SARCOMA OF LUNG

This secondary growth shows a few spindle cells, but the majority of the cells are undifferentiated, and giant cells are fairly numerous. The section also shows widespread acute inflammatory reaction of bronchopneumonia. × 120.
The majority opinion, however, tends to accept Grawitz' belief that hypernephroma arises from adrenal rests. These adrenal rests have been found in many and diverse locations; most commonly under the kidney capsule, at the upper pole, though some have been found in the kidney substance and even at the lower pole; others along the ureter, under the capsule of the liver, on the broad ligament and ovarian veins in women, and occasionally in the testis, pancreas, and transverse colon. The hypernephromas are most common in the kidney, but Ewing (10) states that their structure may be exactly reproduced by tumours of the adrenal gland. He believes that many so-called "renal" hypernephromas arise in the adrenal gland and invade the kidney, fusing the two organs.

Adami (11) was the first to emphasize the mesoblastic tendencies of hypernephroma. He pointed out that in some cases of hypernephroma large areas of spindle cells are seen and the appearance is distinctly sarcomatous. Woolley (12) in 1902 presented a case which he called "a primary carcinomatoid (mesothelioma) of the adrenals with sarcomatous metastases." The primary growths showed adenomatous and epithelial characters, and the metastases a somewhat alveolar type of round-cell sarcoma verging toward spindle-celled, and subendothelial in location.

Since then many others have reported cases of atypical hypernephroma of the kidney or adrenal or curious mixed tumours in adults, in which sarcomatous tissue predominated, but the mesoblastic tendencies were also pronounced. Thus Baroni (13) in 1925 reported a case of "Grawitz tumour with partial osseous metaplasia," and Haining and Poole (14) in 1936 described what they called an osetoblastoma of the kidney, histologically identical with osteogenic sarcoma and showing a tendency to form mesoblastic cells. Valdes (15) described a hypernephroma of the kidney having giant-cell metastases in the brain, and Ritter (16) reported a case of hypernephroma within a solitary cyst, in which the cells varied to the mesothelial type. It would be unreasonable to consider any of these cases showing varying cell structure as instances of multiple malignancy. Such cases as these are rare, it is true. In a total of 4,000 autopsies at the Toronto General Hospital since 1925 there are records of 18 cases of hypernephroma of the kidney and none of these showed the variation in cellular structure of the tumour and metastases presented in this case.

If these tumours are not examples of multiple malignancy, how are they to be explained? It would be of value in this connection to trace the origin of the adrenal cortex and the urogenital tract. After the development of the two primitive cell layers, ectoderm and entoderm, an intermediate cellular structure develops, the mesoderm. This latter tissue is gradually differentiated into two types. That nearest the medullary groove, the mesenchymal anlage, remains as a mass from which the connective tissue is derived. The rest of the primitive mesoderm separates into layers to form the mesoblastic cells of the splanchnopleuric and somatopleuric systems, later giving rise to the serous membranes, the urogenital tract (except the bladder), and striated muscle (17). If, then, the law of the specificity of the germ layers holds good in the reversion of tissue, the mesenchymal cells may more easily revert because of their comparatively single structure, but the mesothelial tissue, al-
though more highly differentiated, may ultimately in its reversion become in type that of mesoderm.

It is probable, therefore, that the case under discussion represents a reversion of the cell type through various stages from the highly differentiated cell of the normal adrenal tissue, through the hypernephroma cell stage as seen in the kidney, and the spindle-cell type in kidney and metastases, to the less differentiated mesothelial cells seen in the metastases in lung.

**Summary**

(1) A case is reported which may be described as a hypernephroma and spindle-cell sarcoma of the right kidney and adrenal with sarcomatous and mesotheliomatous metastases.

(2) This case is classified as hypernephroma and spindle-cell sarcoma of the kidney because of the gross site of the tumour. The absence of the right adrenal suggests that the cortical tissues of this organ had not been developed and that the tumour had arisen from the early anlage of this tissue.

(3) An examination of similar cases in the literature convinces us that this is an instance of single, not multiple, malignancy, and that the variety of tumour structure represents various stages in the process of metaplasia of the adrenal cells.

**Bibliography**