MALIGNANT TUMOURS OF THE KIDNEYS.

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The subject of malignant tumours of the kidney presents many features of great interest—interest to the pathologist, clinician and surgeon alike. Pathologists have for many years expressed varied and contrary views upon the genesis and true nature of these tumours and even at the present time no concensus of opinion has been reached. The clinician has improved his methods of examination in so marked a degree that he is able to demonstrate with a great degree of certainty whether a renal growth is present.

Malignant disease in the kidney may exist as a tumour of the renal tissue as either a carcinoma or a sarcoma, or may commence in the lining membrane of the renal pelvis as a papillomatous covered carcinoma or as a squamous epithelioma.

Tumours of the Renal Tissue.

Carcinoma of the kidney occurs most frequently between the ages of forty-five and sixty-five years. It may exist in any part though it is most commonly found in the upper or lower pole of the organ. It is at first rounded or globular in shape, gradually compressing the renal tissues as it increases in size, so that in some cases it appears to be encapsuled, whilst in others the renal tissues are directly invaded by the tumour and no clear demarcation exists between them. The mass may form a localised rounded bulging of the surface of the kidney and by its gradual extension towards the hilum may infiltrate into the calices or into the renal pelvis. The growth tends to spread into the veins, reaching the renal vein and giving rise to metastases which are most commonly seen in the lungs or in the bones of the skeleton. Extension of growth may also pass into the lymphatic nodes—nodes about the renal vessels and the abdominal aorta. In its further progress the growth may infiltrate through the renal capsule to the perirenal fat and become adherent to the diaphragm, liver or colon.

On section the growth presents a fairly characteristic macroscopic appearance. It is often surrounded by an apparent capsule of condensed renal tissue from which fibrous septa of a greyish colour spread into the tumour. The surface shows zones of a yellow colour in which both hæmorrhagic and necrotic areas are present. Occasionally semi-transparent areas of mucoid degeneration are seen. In other cases of more rapidly growing tumours, no capsule is seen and the tumour directly infiltrates the surrounding renal tissue.

On microscopic examination the tumour cells appear as large, clear polyhedral or cubical cells with a small nucleus which stains deeply. The cytoplasm is vacuolated from the presence of glycogen and lipid. The arrangement of the cells may vary considerably, sometimes as solid trabeculæ or alveoli, whilst sometimes in acinous or in papilliferous formation. These various types may be found in different parts of one tumour.

Much discussion has arisen upon the true genesis of these tumours. Interest was first aroused when von Grawitz¹ published his paper in 1883, describing these tumours as arising in "adrenal rests." These latter are minute subcapsular islets of suprarenal tissue left in immediate conjunction with the renal cortex in the process of development. Grawitz based his opinion upon the similarity, of the cells of the growth to those of the suprarenal cortex, quite unlike those of the renal tubule, and that they occurred beneath the renal capsule where adrenal rests were found. In 1893 Sudeck² contested this opinion and stated that these Grawitzian tumours arose from the renal tubules. Lubarsch³ (1894) first showed the presence of glycogen in the cells of the tumours and of the suprarenal and gave strong support to the Grawitz theory. In 1908 Stoerk⁴ showed that the tumours had a papillary structure which is absent in the adrenal and emphasised the marked difference between renal hypernephromata and adrenal carcinomata. Wright⁵ in 1922 supported the papillary formation in renal tumours and insisted that papillæ were a constant and essential feature of growth arising in the renal cortex.

Doubt has been expressed as to whether aberrant suprarenal rests do actually occur under the renal capsule, but Shaw Dunn⁶ and Ewing⁷ definitely state that they do exist. Arguments have also been put forward from the embryological side that these rests may originate from the remains of the Wolffian ridge from which the testes and ovaries are developed and in which organs somewhat similar tumours have been rarely recorded. Robertson Ogilvie⁸ states that in his opinion these tumours are of renal origin and not derived from adrenal rests. Shaw Dunn suggests that they may arise in the small cysts lined with lipoid-laden cells which are found most frequently in kidneys the subject of chronic interstitial nephritis, whilst MacCallum⁹ is inclined to favour the Grawitz view of origin from adrenal rests.

In the museum of the Royal Cancer Hospital there is a specimen which may throw some light upon the origin of these tumours. It was found in the kidney of a man who died from advanced epithelioma of the tongue with no symptom referable to the urinary organs. Embedded in the substance of the kidney is a rounded yellowish tumour $1\frac{1}{2}$ cm. in diameter and separated from the renal capsule by normal renal tissue fully 1 cm. in thickness. The tumour is lobulated, necrotic in the centre and shows small areas of hæmorrhage. Histologically it is composed of large vacuolated cells with small nuclei with tubular formation.

An important contribution on the subject of the genesis of hypernephromata was made by Nicholson¹⁰ in 1923 to which the reader is referred for a full historical record of the opinions expressed by pathologists up to that time. From a critical study of these papers and from his own observations, Nicholson came to the conclusion that hypernephromata arise in the renal epithelium and that no instance had been described whose origin in suprarenal tissue, assumed by Grawitz, is assured.

Ewing states that these tumours arise in the renal epithelium and divides them into papillary and alveolar carcinomata, reserving the term hypernephroma for the rare tumours arising from adrenal rests. Hawksley and Newcomb however have shown that both the papillary and alveolar types described by Ewing are both frequently present in parts of the same tumour.

Newcomb¹¹ in 1936 showed that small adenomata were frequently found in minute post-mortem examination of the kidney, and in 1,172 consecutive postmortems found 147 of these tumours, mostly being papillary cystadenomata, but which contain large clear cells containing much fat and closely resembling the vacuolated cells of the Grawitz tumour. Newcomb states that in his opinion the renal malignant tumours arise from these adenomata and are renal in origin and that there is no proof that they arise from displaced adrenal tissue.

Whilst so much confusion exists in the minds of pathologists as to the true origin of these tumours, it is perhaps advisable to include them under the generic term of carcinoma. It must be admitted from the clinical aspect that they differ widely in their virulence and metastatic spread, some remaining localised to the kidney and semi-encapsuled for months or years, whilst others rapidly infiltrate the substance of the kidney and give rise to early metastases.

A form of solid infiltrating adenocarcinoma is occasionally found in the kidney which does not show the yellow areas and clear vacuolated cells of the hypernephroid tumours. These show ill-defined edges and infiltrate and renal tissue irregularly and give rise to early glandular metastases.

There remains another group of malignant tumour of the kidney classified as sarcomata. These form a small group in comparison with carcinoma, and microscopically show round, spindle or mixed celled elements, sometimes including striped or unstriped muscle fibres or other forms of developed tissue. In one particular form, described by Wilms as embryonic adeno-sarcoma, there may be, in addition to muscle fibres, cartilage or fat, masses of tubules lined by cuboidal epithelial cells. These tumours usually occur in infants or children in early years, but may, like other sarcomata, be found in adults. The Wilms' tumour rarely gives rise to bleeding, but first attracts attention by the appearance of a tumour in the loin which rapidly increases in size and is exceedingly malignant.

Mode of Spread.

Hypernephromata are prone to spread along the veins to the renal vein from which small embolic masses of cells may reach the inferior vena cava and thence to the lungs. Malignant

renal growths may spread through the capsule into the perirenal fatty tissue and directly invade the peritoneum; they spread also *via* the lymphatics to the nodes about the renal vessels, aorta and vena cava. Metastases from renal growths are common in the skeleton, particularly in the long bones and in the bones of the skull. Metastases from hypernephromata may occur before there is any symptom referable to the kidney; thus a pathological fracture in a bone or a lymph node swelling be present in the neck of axilla due to metastases whilst the renal growth is small.

Symptoms.

The cardinal symptoms of renal growths are hæmaturia, tumour and pain.

Hæmaturia is the most common symptom and in the majority of cases is the first to attract the attention of the patient. It is present in 90 per cent. of all cases and occurs as the initial symptom in 70 per cent. Occasionally the blood may be slight in amount, but more frequently occurs as a profuse hæmaturia, sometimes following exertion or injury. Thus in one case it occurred after a fall and in another after mountain climbing. It is sudden in onset, may last a few days and then clear away to recur after an interval of weeks to even months. In one case under my care, attacks of profuse hæmaturia had been present for four years before nephrectomy was performed at the age of sixty-three and the patient survived for thirteen years. More often the patient comes under observation within a few months of the initial hæmorrhage. Hæmaturia occurs in all forms of renal growth, but is infrequent with sarcomata or in the embryonic adenocarcinoma of children.

The severity of the bleeding bears no relation to the type nor the size of the growth, for I have seen quite small hypernephromata give rise to profuse hæmaturia and large tumours which at no time have produced any macroscopic blood in the urine.

Pain in some form is present in the majority of cases. It may be severe, due to true ureteric colic from the passage of clots along the ureter. These clots are thin, rounded and wormlike in shape and if found in the urine are indicative of severe renal bleeding. Dysuria and increased desire to micturate may be caused by the retention of blood clot in the bladder. Pain may be present in the lumbar region from the increased tension in the tumour from small hæmorrhages which frequently occur in the substance of a hypernephroma or there may be more or less continuous aching in the loin due to extension of the growth into the perinephric tissues. In advanced cases pain may be present from pressure or direct involvement of a nerve root from metastases in the vertebræ.

A *tumour* may be palpable and in children may be the first symptom of a renal growth. The tumour causes a rounded mass which can be grasped bimanually and felt to descend on inspiration. The colon is usually placed in front of the swelling and may be rolled on the surface of the tumour and give a resonant note on percussion. The mass is usually smooth, but in some cases in thin subjects rounded bosses may be felt on the surface. A tumour of the upper pole of the kidney may not be palpable, but in such a case the lower pole of the organ may be felt to descend to more than the usual extent on deep inspiration. In two cases under my care a tumour of the upper pole of the right kidney displaced the liver in a transverse axis, so that the anterior hepatic margin descended well below the costal margin. A renal tumour that does not move freely with forced respiration implies that perirenal infiltration has already taken place and is a bad prognostic indication.

The Urine. Apart from the presence of blood, albumen may be present from the area of nephritis in the renal tissue immediately surrounding the growth. Pyuria is rarely present unless the kidney is also the seat of calculous disease. This occurred only in two cases under my care, in one of which the carcinoma was associated with calculous pyonephrosis and the second in which, in addition to the calculus, there was an epithelioma of the renal pelvis.

Varicocele has been stated to be frequently present, but I can only find a note of it in two out of fifty-one cases. If it is present and does not disappear upon lying down, it may be due to pressure by the growth or by secondary lymph nodes on the spermatic vein or possibly to extension of the growth into the renal vein.

Pyrexia was present in two cases in the absence of infection. It is stated by Israel¹² to be fairly frequent.

Diagnosis.

The combination of hæmaturia, localised lumbar pain and the palpation of a tumour in the renal area should form fairly conclusive evidence of a new growth in the kidney. In calculous disease pyuria will be present, whilst in polycystic disease both kidneys will nearly always be palpable, although one may be much larger than the other. In tuberculous disease the kidney is rarely much enlarged, pus and traces of blood are constant in the urine and tubercle bacilli may be found in it. Renal tuberculosis is most frequent under thirty years of age and increased frequency of micturition is a prominent symptom. Hæmaturia and renal enlargement may be present in a hydronephrosis.

It is not uncommon for a case to be presented in which hæmaturia is the only symptom. Intermittent attacks of fairly profuse hæmaturia without pain may be due to some form of growth either in the bladder or in the kidney. In either case the bleeding comes on suddenly and may as suddenly cease and the patient may be lulled into a sense of false security and valuable time lost in which the growth is spreading and metastases occur. It cannot be too strongly urged, therefore, that every case of hæmaturia should undergo a complete examination to determine the source of the bleeding. Cystoscopic examination should be carried out without loss of time, even whilst the hæmaturia is present. Should the bleeding be renal in origin, vesical irrigation will soon produce a clear medium, blood will be seen emitted from one ureteric orifice and the source of the bleeding immediately localised to that kidney. On the other hand, should the bleeding be due to a growth in the bladder or to an enlarged prostate, careful irrigation with a solution of silver nitrate 1 : 4000 or with adrenalin will usually produce a medium clear enough for diagnostic purposes. In a few cases in which hæmaturia has been accompanied by pain or by a swelling in the loin, cystoscopic examination has proved the presence of a vesical growth causing obstruction to one ureteric orifice enough to cause the pain from renal distension.

In those cases in which renal growth is suspected, but in which hæmaturia is absent or has ceased, cystoscopic examination may give no information as the vesical wall is normal and clear urine may be seen from each ureteric orifice. In such a case chromo-cystoscopy may be used. An intravenous injection of 4 c.c. of a .4 per cent. solution of indigo-carmin is given and the time of the appearance of a blue coloration of the urine from the ureteric orifices noted. In a normal functional kidney this coloration will be seen within six or seven minutes, at first as a faint coloration rapidly deepening in intensity to a dark blue. Delay in the time of appearance of the dye or failure to deepen in colour is evidence of renal dysfunction. Segregation of the urine from each kidney by ureteric catheterisation may show a diminished urea content on the affected side, especially if a urea meal (i.e., 15 grams of urea in 100 c.c. of water) be given one and a half hours before the examination. These tests should be carried out not only as diagnostic points of a kidney under suspicion, but also to prove the functional capacity of the other organ. No reliance should be placed upon the presence of blood in the urine collected by ureteric catheter, as it may be due to traumatism in the passage of the instrument.

A plain radiograph may show that the outline of the kidney is enlarged, but much greater value is obtained by pyelography. Films may be obtained after intravenous injection of uroselectan or pyelectan or by direct injection of the renal pelvis with sodium iodide or bromide after ureteric catheterisation, and it is frequently necessary to confirm the shadow obtained by the intravenous method by one obtained after catheterisation. There is no definite outline which can be said to be distinctive of renal growth owing to the very considerable variations that may occur, but elongation of one calyx, deformity of a calyx or of the renal pelvis with a concavity on one aspect would suggest the pressure of the rounded periphery of a growth. A growth in a pole of the kidney may obliterate the calices, but a more centrally placed growth would produce marked deformity of the pelvis. Difficulty is sometimes met with in the interpretation of a film in which a calyx may not be apparent but which is filled with blood clot. In such a case the examination should be repeated after an interval of a few days.

The elongated, spider-like calices of a polycystic kidney may resemble the deformities of a tumour, but usually all the calices will be affected and a similar condition will be present in the other kidney. In one case I diagnosed a tumour of the lower pole of the kidney in which the lower calices were pushed upwards and formed a concavity, but found at operation that

the lower pole of the kidney was occupied by a unilocular cyst. In cases in which a tumour is present in the upper lateral abdomen and in which other symptoms are indefinite, difficulty may be found in forming a diagnosis between a renal tumour or one of the liver, gall-bladder, spleen or colon. A pyelogram will probably show a deformity if the tumour is renal, but a normal kidney picture where the mass is extra-renal. In such cases the renal shadow may be displaced laterally or rotated.

In every case in which a carcinoma is suspected an X-ray examination should be made of the chest and of the skeleton to search for any metastatic deposit of growth.

Growths of the Renal Pelvis.

New growths arising in the renal pelvis are distinctly uncommon and are very similar to the epithelial tumours found in the bladder. A papilloma of the renal pelvis may give rise to intermittent profuse hæmaturia, and from its position may block the pelvic outlet and cause renal distension with pain and a tumour of varying size in the loin. A significant feature of these growths is their tendency to multiplicity from direct implantation. Thus small papillomata may be present in the ureter or in the bladder and small tufts of papillomatous growth may be seen to be extruded from a ureteric orifice on cystoscopic examination. As in the bladder, it is more common to find these transitional-celled papillomatous growths to be infiltrating the pelvic wall and to be in fact carcinomatous. Squamous epithelioma also occurs in the renal pelvis, probably in cases of old standing infection and, in one of the only two cases under my observation, a calculus was present in the pelvis.

In these forms of growth hydro- or hæmato- nephrosis from obstruction to the pelvic outlet is common and metastatic spread to the lymphatic nodes about the renal vessels appears to commence fairly early. They all cause hæmaturia and a pyelographic examination may show a filling defect in the pelvis or even complete absence of a pelvic shadow.

Treatment.

Nephrectomy, with removal of the perirenal fatty tissue and the lymphatic nodes along the aorta and vena cava, is the only procedure which holds any prospect of success. Before any operation is contemplated a careful search must be made by X-ray examination for metastatic spread in the lungs and in the bones and also an estimation of the functional activity of the other kidney. Immobility of a kidney the seat of a growth implies that perirenal infiltration has already commenced. The removal of a renal tumour may be a difficult operation, trouble being frequently encountered from profuse bleeding from the dilated, thin-walled veins covering these growths. The operation often commences as an exploration of the kidney for unilateral hæmaturia, when the fatty capsule is necessarily opened, but if a localised swelling is felt in the kidney it is better to proceed at once to the removal of the fatty tissue and lymph nodes with the kidney than to risk local recurrence by exposing the renal cortex. The choice between the lumbar and transperitoneal approach for nephrectomy will depend upon the individual surgeon. The transperitoneal operation may show the extent of lymph node invasion or of direct infiltration of the peritoneum and it has been stated that hæmorrhage is better controlled by early ligature of the renal vessels; by this method separation of the upper pole of the kidney is easier, as by the lumbar route troublesome bleeding may arise in this area. Gregoire has described an anterior extraperitoneal operation which gives good access and allows complete removal of the perirenal tissues. The danger of any operation for renal growth is hæmorrhage from the dilated veins, whilst the renal vein may be easily lacerated if it contains growth. The inferior vena cava has been injured, requiring lateral suture or even ligature.

In those cases in which a papillomatous growth is suspected in the renal pelvis, it is advisable to combine nephrectomy with removal of the ureter well down in the pelvis.

Results.

Owing to the exigencies of war service and the separation from my clinical notes of private and hospital patients who have been under my care, I have been unable to bring my records up to date. In a communication published in 1933¹³ I was able to collect the following figures. Of fifty-one cases of carcinoma of the kidney, operation was not advised in six cases owing

to the extent of the disease or the presence of metastases. Thirty-nine were operated upon, but in seven the growth was found to be too extensive for removal. The remaining thirty-two had nephrectomy performed. Of these five died as the result of the operation—two from shock, one from pneumonia and two within a month from the operation, one death being due to nephritis. Ten have subsequently succumbed from recurrence of the disease at intervals varying from four months to over two years, the most common seat of recurrence being in the abdominal lymph nodes, lungs, liver and bones. The fate of four is unknown. Thirteen patients recovered from the operation, but two of these have subsequently died from intercurrent disease—one from post-influenza pneumonia after seven years and one from cerebral hæmorrhage after five and a half years. Including these two cases, the interval since the operation has been: 12 years 1 case, 10 years 1 case, 9 years 2 cases, 7 years 2 cases, 6 years 1 case, $5\frac{1}{2}$ years 1 case, $2\frac{1}{2}$ years 1 case, under 2 years 4 cases.

Of five cases of Wilms' embryonic adeno-sarcoma in children three underwent nephrectomy; one was alive and well two and a half years later, one died from intrathoracic recurrence after six months and the fate of the remaining one is not known. Of sarcomata in adults, one showed recurrence in the lungs after eight months, one was alive and well after twelve months and one was irremovable.

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