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METASTATIC GROWTHS IN THE URETER*

A REPORT OF THREE CASES AND A BRIEF REVIEW OF THE LITERATURE

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PATHOLOGICAL lesions that are of rare occurrence, and that are usually diagnosed at the autopsy table or in the operating room, always stimulate considerable interest and discussion. Metastatic growths of the ureter belong to this class and lately we have encountered such a condition. The subject has inspired us to review the literature and collect other similar cases that have been met with at the Royal Victoria Hospital.

New growths of the ureter, whether primary or metastatic, are extremely rare occurrences; the former appears to be the commoner of the two. Although only 59 cases of primary growths of the ureter are reported, yet an appreciable amount of literature has been written on the subject. On the other hand, very little has been published on metastatic growths of that organ. Up to December, 1930, only 8 authentic cases could be found in the current literature.

It is of extreme importance to emphasize at the start that under the heading of metastatic growths of the ureter are included those lesions only that have been proved definitely to be the result of metastases conveyed to the ureter by lymphatics or blood vessels. Secondary growths of the ureter, due to direct extension of tumours of adjacent organs such as the uterus, bladder, kidney, etc., are not true metastases, and are not included, therefore, in this class. Moreover, in order to prove that a secondary growth is a true metastatic one, malignant cells must be

demonstrated in the perivascular lymphatic spaces or blood vessels of the ureter.

There is an abundant communication between the lymphatics of the pelvic organs and the ureters. This relationship is particularly striking in the cases of lymph vessels of the bladder and ureters. Despite these facts, metastatic growths of the ureter from tumours of the uterus, bladder or prostate are very uncommon findings. On the other hand metastases from growths of these pelvic organs are frequently met with in the lungs, liver, kidneys, bones, and other organs and tissues. Why this rather specific peculiarity of the ureters exists is difficult to understand. Robinson⁵ claims that the lymph-drainage of the lower portion of the ureters is downwards. That may help to explain the rarity of ureteral metastases.

The first authentic case of a metastatic growth of the ureter was reported by Giordano and Bumpus³ in 1922. The patient had a carcinoma of the prostate which metastasized to the left ureter, left renal pelvis, lungs and left kidney. They were able to demonstrate cancer cells in the blood vessels of the lungs and kidney, and were of the opinion that the metastases to the ureter were conveyed by the blood stream. Thomas and Regnier⁶ reported another case in 1924. The metastatic growth was secondary to a primary neoplasm of the bladder. Metastases were also demonstrated in the lymph glands, liver and psoas muscle.

In 1925 Carson¹ added 3 more cases to the literature. The first case was that of a man with

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a carcinoma of the bladder which metastasized to both ureters, prostate, mesenteric lymph nodes, lumbar vertebræ and liver. Patient No. 2 had an adenocarcinoma of the prostate with metastases to the right ureter, bladder, seminal vesicles, vasa, right kidney, lungs, fifth lumbar vertebra and lymph nodes. The third patient was a female who had a squamous-cell carcinoma of the cervix which metastasized to the right ureter, liver, and mesenteric lymph glands. In each of the above cases microscopic examination revealed cancer cells in the perivascular lymphatic spaces, thus proving beyond doubt that the growths in the ureters were true metastatic ones. In 1927 Carson² reported 2 additional cases. Patient No. 1 was a male with a carcinoma of the prostate which metastasized to the right ureter, bladder, seminal vesicles, lumbar vertebræ and mesenteric lymph nodes. The second case was also that of a carcinoma of the prostate with metastases in the right ureter, bladder, seminal vesicles, right kidney, pelvis, lungs and lymph nodes. The author was able to demonstrate very readily cancer cells in the perivascular lymphatic spaces of the affected ureters.

Rathbun,⁴ in 1929, described a single case. The patient, a male, had had a radical operation for a scirrhus carcinoma of the left breast in 1924. He remained well until 1927 when he began to pass blood in the urine. He was cystoscoped and provisional diagnosis of a left renal tumour was made. A nephrectomy and partial ureterectomy was then performed. The pathological report was metastatic carcinoma of the ureter, secondary to the carcinoma of the breast. The author unfortunately did not mention in his report the manner in which the growth of the ureter occurred. The tumour undoubtedly is a true metastatic one, but whether the metastases were conveyed by the lymphatics or blood vessels is a question.

We have carefully reviewed all the cases with lesions of the ureter that have been met with in the Departments of Urology and Pathology at the Royal Victoria Hospital, Montreal. Amongst them we have been able to find 3 cases of metastatic growths, thus making a total of 11 authentic cases. We venture to state that the condition is more common than the literature leads one to suppose. Furthermore, we are of the opinion that a number of the so-called pri-

mary carcinomas of the ureter are probably true metastatic growths.

Of the 3 cases that we are reporting 1 is in a female and 2 are in males. The female was 34 years of age and the males 45 and 61 years of age, respectively. Both the male patients came to autopsy, and the diagnosis was made on the post-mortem table. The female patient is still alive. The diagnosis in her case was made at operation.

CASE 1

J. E., a coloured male, aged 45 years, was admitted to the medical service of the Royal Victoria Hospital on December 19, 1922, complaining of shortness of breath, palpitation, swelling of the legs, cough, bloody expectoration and slight nocturnal frequency.

History of present illness.—The history dated back one year, when he first noticed shortness of breath on exertion. This symptom gradually increased in severity and was soon accompanied by palpitation and swelling of the legs. Cough started six months prior to admission and was associated with expectoration which at times was blood tinged. For about one year the patient had noticed a slight nocturnal frequency of two to three times—no day frequency or any other urinary symptoms.

Personal history.—He had had gonorrhœa and syphilis in 1902: had had treatment for both conditions, and was told that he was cured.

Family history.—His wife had had one pregnancy which ended in a miscarriage at the fifth month. No other pregnancies.

Examination.—On admission the patient was dyspnoic, drowsy and looked very ill. There was definite evidence of recent loss of weight. There was puffiness of both eyes and pitting œdema of ankles and feet.

The heart was enlarged to the left and a loud apical systolic murmur was present which was transmitted to the axilla. The aortic arch seemed wider than normal to percussion. The blood pressure was 190/96. The lungs showed dullness over both bases with increased vocal fremitus, and the presence of many moist râles. The liver was enlarged and the lower edge was felt two finger-breadths below the costal margin. The epitrochlear glands on both sides were readily palpated.

The findings in the genito-urinary tract were negative, except for a small smooth but rather firm prostate.

Laboratory findings.—Urine: hazy straw, acid, 1015; albumin +; sugar 0; acetone 0; diacetic acid 0; white blood cells scattered; red blood cells scattered; amorphous urates and epithelial cells; no casts seen.

Blood count.—Red blood cells, 3,010,000; white blood cells, 14,200; hæmoglobin (Sahli), 70 per cent; neutrophiles, 82.0 per cent; eosinophiles, 3.0 per cent; basophiles, 0.5 per cent. lymphocytes, 10.0 per cent; large mononuclears, 3.5 per cent; transitionals, 1.0 per cent.

Blood chemistry.—Urea, 2.67 grams per litre; urea nitrogen, 134.0 mg. per 100 c.c.; creatinine, 2.34 mg. per 100 c.c.; uric acid, 15.3 mg. per 100 c.c.

Blood Wassermann test.—Negative.

Clinical diagnosis.—Chronic myocarditis with decompensation; chronic nephritis; aortitis.

The patient was in the hospital about forty-eight hours and then died.

Anatomical summary.—Adenocarcinoma of the prostate with metastases in the ureters, lungs, pleural, abdominal and mediastinal lymph glands; bilateral pyonephrosis; hypertrophy of the heart; arteriosclerosis; dilatation of the first part of aorta.

Prostate.—Sections show a very diffuse overgrowth of glandular loops replacing a great part of the normal prostatic tissue. The loops show a very marked increase of their lining epithelium. In a great many places large

acini are practically filled with growth. The cells are large, pale staining, with deeply staining round or oval nuclei. In parts the fibrous stroma of the prostate is infiltrated by small groups of these cells arranged in irregular nests; the larger the nests the more definitely glandular formation is seen. *Diagnosis*: adenocarcinoma of prostate (Fig. 1).

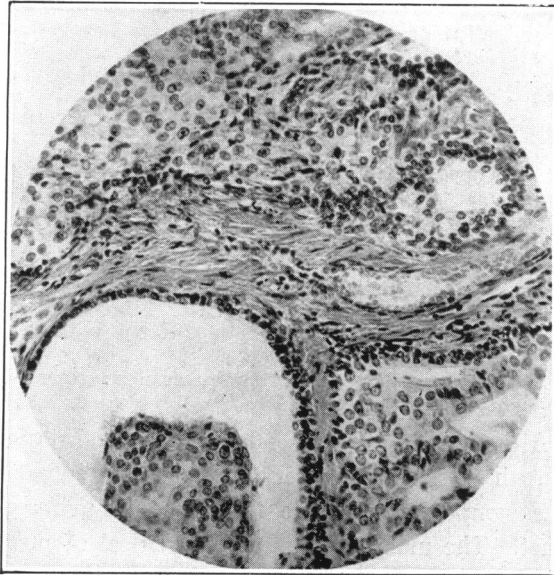


FIG. 1.—Case 1. Adenocarcinoma of the prostate. Acini filled with large pale staining epithelial cells which have dark staining round or oval nuclei.

Ureters.—The left was considerably dilated in the upper part and is almost obliterated in parts in the lower half. On opening the lower half the wall showed very irregular thickenings. The right ureter showed a pedunculated mass, the size of a green pea about its middle. For about two centimetres below this the ureter was free. The lumen was then blocked by a more irregular larger mass which did not appear pedunculated. This extended for two or three centimetres. *Microscopic*: the growth was firmly attached to and grew out, right



FIG. 2.—Case 1. High power photomicrograph of a metastatic growth of the right ureter, secondary to an adenocarcinoma of the prostate.

and left, from the ureteral walls, which showed invasion of all their coats by the carcinomatous growth (Fig. 2). Cancer cells can easily be demonstrated in the perivascular lymphatic spaces of both ureters (Fig. 3). *Diagnosis*: metastatic adenocarcinoma of both ureters.

This case is a most interesting one. Although the patient died from a carcinoma of the prostate with multiple metastases, yet the clinical picture was that of cardiac failure and renal insufficiency. Except for the slight nocturnal frequency and a smooth firm prostate there was nothing to indicate a carcinomatous lesion of either the prostate or ureters. The partial obstruction of the lumen of each ureter resulting from the metastatic growth undoubtedly played a major part in the formation of the bilateral pyonephrosis. Cancer cells were easily demonstrated in the perivascular lymphatic spaces of the ureters, thus proving the metastatic character of the growth.

CASE 2

P. R., a male, aged 61 years, was admitted to the surgical department in November, 1927, complaining of pain in the epigastrium, belching of gas, constipation and vomiting.

History of present illness.—The history dated back to February, 1927, when the patient began to be troubled with the above symptoms. The vomiting was not a constant symptom. There were no symptoms referable to the genito-urinary tract.

Personal and family history.—Irrelevant.

Examination.—The general physical examination was essentially negative.

Laboratory findings.—Urine: cloudy, straw, acid, 1015; albumin ++; sugar 0; pus ++; amorphous uretes +; epithelial cells; no casts.

Blood count.—Red blood cells, 4,600,000 per cubic mm.; white blood cells, 7,400 per cubic mm.; hæmoglobin, 70 per cent (Sahli).

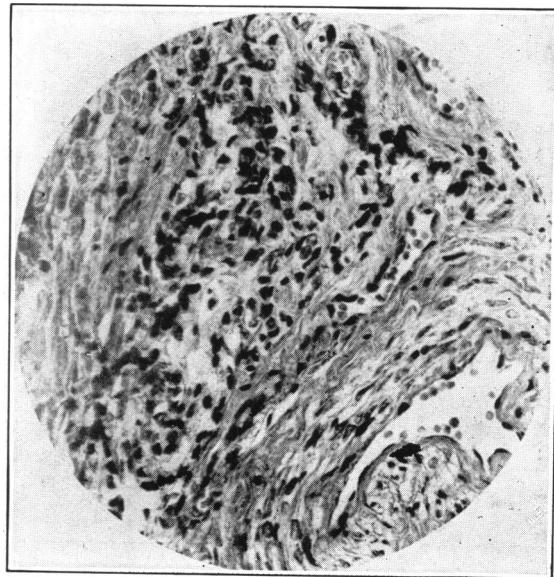


FIG. 3.—Case 1. Perivascular lymphatic invasion of left ureter by cancer cells, secondary to an adenocarcinoma of the prostate.

Blood Wassermann test.—Negative.

Barium series.—This revealed a lesion of the body of the stomach, probably an ulcer, but a carcinoma could not be ruled out.

A laparotomy was performed and an inoperable carcinoma of the lesser curvature of the stomach was

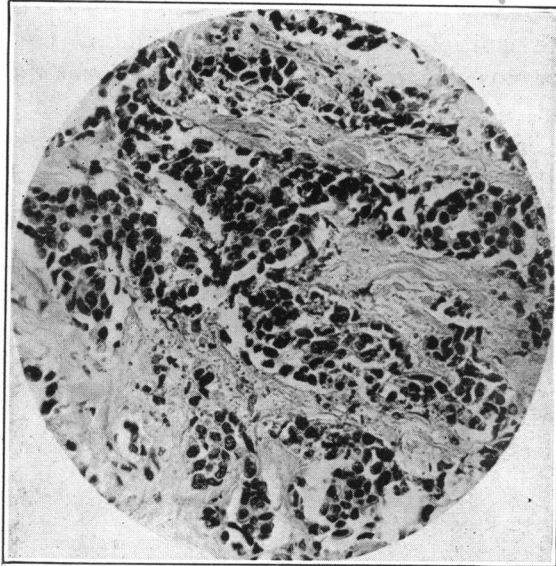


FIG. 4.—*Case 2.* Adenocarcinoma of the stomach. Note the immature glandular epithelial cells forming irregular small acini and columns. There is also present a diffuse fibroplastic stroma.

found. As the stomach was still emptying, nothing further was done at that time. The patient was discharged on November 30, 1927. In June, 1928, he returned. He was now vomiting everything he ate. A jejunostomy was therefore performed. Patient died two months later.

Anatomical summary.—Adenocarcinoma (scirrhous) of the stomach, with metastases in the right ureter and ileum. Also pyonephrosis, right; myocarditis; hydro-

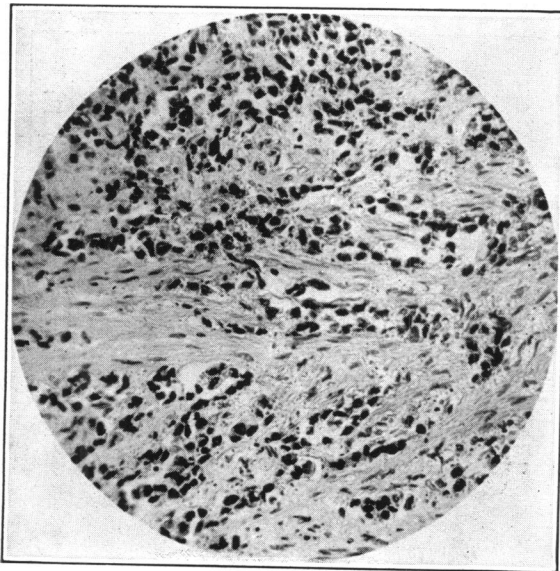


FIG. 5.—*Case 2.* Metastatic growth of right ureter secondary to an adenocarcinoma of the stomach. The nests of immature glandular epithelial cells are similar to those found in the growth of the stomach.

thorax; fibromyoma of the prostate; and passive hyperaemia of liver and lungs.

Histology.—Stomach: Sections showed a marked thickening of the mucosa due to a diffuse proliferation of immature glandular epithelial cells. These cells formed irregular small acini and columns. There was a diffuse fibroblastic stroma proliferation, most marked in the submucosa. The muscularis appeared thickened. Small nests of cancer cells could be seen infiltrating through all the coats, and were always associated with a diffuse fibroblastic stroma, which in some areas was mature, showing extensive fibrous tissue thickening (Fig. 4).

Diagnosis.—Adenocarcinoma (scirrhous) of the stomach.

The upper half of the right ureter was moderately dilated and filled with thick purulent material. The surface was red and finely granular. There were no definite masses in the lumen. Microscopically the muscular coats were infiltrated with small nests of immature glandular epithelial cells, similar to those found in the stomach. The mucosa was intact. Fibrous stroma was abundant (Fig. 5). Cancer cells also invaded the perivascular lymphatic spaces (Fig. 6).

Diagnosis.—Metastatic adenocarcinoma scirrhous of the right ureter.

Although this patient had a definite metastatic growth of the ureter, yet there were no subjective symptoms referable to the genito-urinary tract. The urine did show a great deal of pus, which was explained by the right pyonephrosis. Here too the growth in the ureter was undoubtedly the cause of the destroyed right kidney. The finding of cancer cells in the perivascular lymph spaces definitely proved that the growth was a true metastatic one.

CASE 3

N. B., a female, aged 34 years, was admitted to the gynaecological service of the Royal Victoria Hospital on August 26, 1929, complaining of pain in the left side of

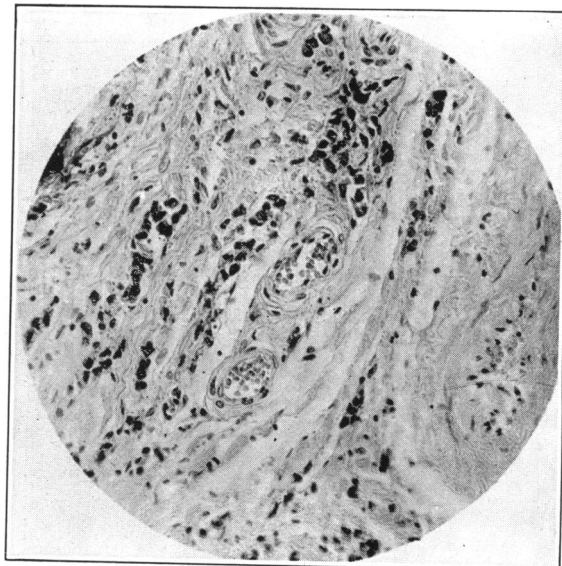


FIG. 6.—*Case 2.* Definite perivascular lymphatic invasion by the cancer cells in a metastatic growth of the right ureter secondary to an adenocarcinoma of the stomach.

the abdomen, brownish vaginal discharge, and bleeding at times.

History of the present illness.—The above symptoms first began in July, 1929, and gradually became more marked.

Personal history.—Married, with three normal pregnancies.

Family history.—Negative.

Examination.—The general physical examination was negative, except for a lesion found in the anterior lip of the cervix. A portion of this was removed for pathological examination.

Histological examination.—Sections showed muscle and connective tissue, with an overlying epithelium. The greater part of this tissue was replaced by a dense round-cell infiltration in which are nests of embryonic epithelial cells. Numerous mitotic figures were seen. Many eosinophiles were also present. The picture was that of a diffuse infiltrating squamous carcinoma of low maturity (Fig. 7).

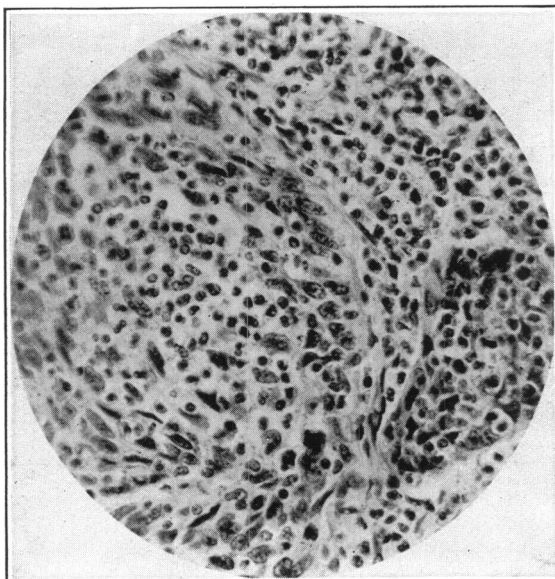


FIG. 7.—Case 3. Carcinoma of the cervix. Note the dense round-cell infiltration in which are nests of immature epithelial cells. Many eosinophiles could be seen in the original preparation.

The patient was given a course of radium and was kept under observation. The last pelvic examination, in September, 1930, did not reveal any recurrence of the growth. On September 3, 1930, she was admitted to the urological service of the hospital complaining of frequency of urination, pain in the left loin radiating downwards and forwards to the left lower quadrant of the abdomen, anorexia and loss of weight.

History of illness.—The history dated back to May, 1930, when she first began to have a dull ache in the left loin. In July she began to be troubled with acute attacks of pain, and also with frequency and urgency of urination. She never noticed any gross hæmaturia.

Examination.—The general physical examination revealed tenderness and resistance in the left flank and in the left lower quadrant of the abdomen. There was also considerable tenderness in the left loin. No masses or enlarged glands were palpated.

Laboratory findings.—Urine: cloudy straw, acid, 1008; albumin +; sugar none; pus +; red blood cells +; epithelial cells; no casts. One cubic centimetre of phenolsulphonphthalein given intramuscularly: excretion, 1st hour 60 per cent, 2nd hour 20 per cent, total 80 per cent.

Blood chemistry.—Non-protein nitrogen, 21.3 milligrams per 100 c.c.; creatinine, 1.39 milligrams per 100 c.c.

Blood count.—Red blood cells, 3,950,000 per cubic millimetre; white blood cells, 6,250 per cubic millimetre; hæmoglobin (Sahli), 60 per cent.

Blood Wassermann test.—Negative.

X-rays did not reveal any metastases in the lungs or bones.

Cystoscopy.—This examination revealed a definite obstruction at the junction of the middle and upper third of the left ureter. A uretero-pyelogram on the left side showed a definite constriction about the middle of the ureter. There was also evidence of a dilated upper ureter with destruction of the corresponding kidney.

Diagnosis.—A diagnosis of an obstructed ureter with a destroyed and infected left hydronephrosis was made.

Treatment.—Patient was operated upon and a nephrectomy and partial left ureterectomy was performed. At operation the kidney was very adherent and there were found a double pelvis and branched ureter for the upper third. Where the two ureters joined was a hard mass the size of a large grape. This was markedly adherent to the spine. It was removed together with the kidney and double ureter.

Pathological report.—The gross specimen consisted of a pale kidney measuring 12 by 6 cm. Two ureters emerged from the pelvis and joined, after running separately for 7 cm. At the point of junction the walls

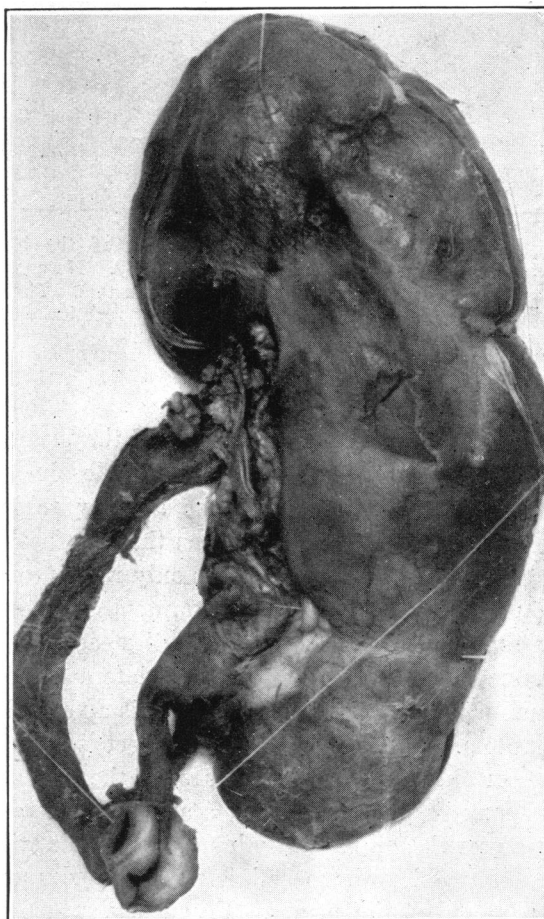


FIG. 8.—Case 3. Metastatic growth at the point of junction of the two ureters. The growth was secondary to a carcinoma of the cervix.

were greatly thickened by a diffuse circular growth (Fig. 8).

Histology.—Sections from the nodule at the junction of the ureters showed the ureters to be embedded in fibrous scar tissue which was the seat of a malignant growth of immature epithelial cells, lying in small clusters in the lymphatics and perivascular lymphatic spaces. There was considerable exudative inflammatory reaction with many eosinophiles. The lining epithelium of the ureters was for the most part well preserved, and there was no evidence that the growth has originated from this source. The cancer cells grew in solid fashion without keratinization (Figs. 9 and 10).

Anatomical diagnosis.—Carcinoma solidum (metastatic from carcinoma of the cervix).

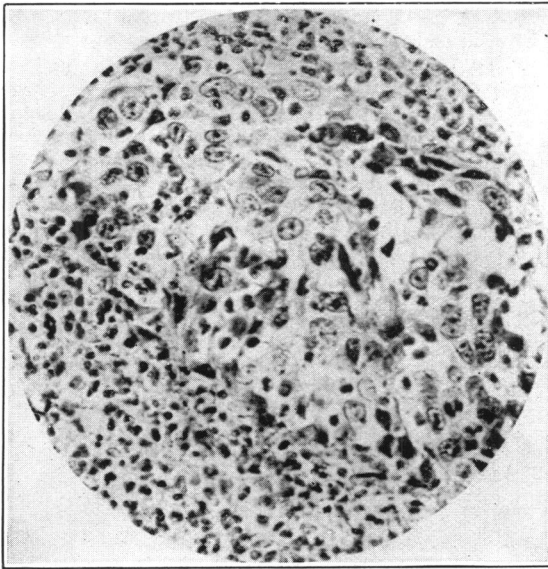


FIG. 9.—Case 3. Metastatic growth of the left ureter secondary to a growth in the cervix. Note the immature epithelial cells lying in small clusters. There is also considerable exudative inflammatory reaction with many eosinophiles.

Cystoscopic examination gives us the most information. Ureteral catheterization usually reveals a stricture at the site of the growth, and a ureterogram demonstrates the narrowed portion of the ureter and the dilatation just above it. This patient (No. 3) had all the symptoms and signs just described. In addition she had a history of a carcinoma of the cervix. In spite of these aids a diagnosis of a growth in the ureter was not made. We must confess that we

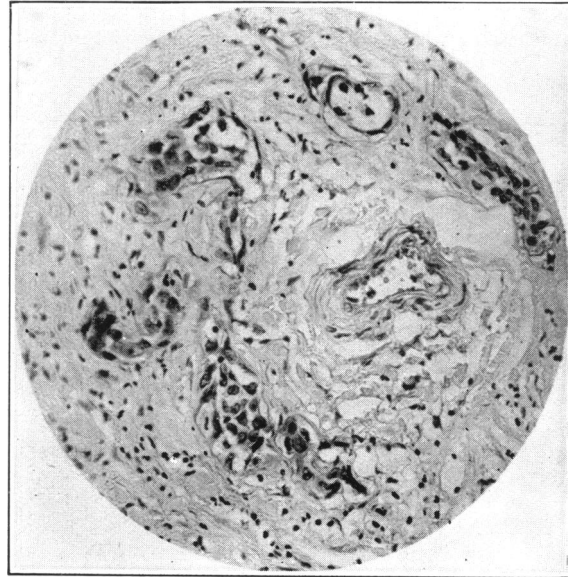


FIG. 10.—Case 3. Definite perivascular lymphatic invasion by cancer cells in a metastatic growth of the left ureter secondary to a carcinoma of the cervix.

DISCUSSION

The diagnosis of a new growth of the ureter, whether primary or metastatic, is made almost always at operation or on the autopsy table. There are no symptoms or signs that are pathognomonic, and the condition is only rarely considered. The outstanding symptom is pain. This may be represented by a dull steady ache on one or other side, or may simulate a severe renal or ureteral colic. Hæmaturia is a variable symptom. In primary growths it occurs at one time or another during the course of the disease, and may be profuse or very scanty. In metastatic growths, on the other hand, hæmaturia will not occur unless the growth has encroached upon the lumen of the ureter. Frequency, urgency of urination and dysuria are occasionally complained of, and usually result from a secondary infected hydronephrosis and hydro-ureter.

considered the stricture of the ureter as due to the radium therapy.

CONCLUSIONS

1. True metastatic growths of the ureters are extremely rare.
2. We must not confuse metastatic growths of the ureter with those resulting from direct extension of tumours of adjacent organs.
3. In metastatic growths of the ureters malignant cells can always be demonstrated in the perivascular lymphatic spaces or in the blood vessels about the ureter.
4. A diagnosis of a new growth of the ureter, whether primary or metastatic, is almost always made at operation or in the post-mortem room.

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