VAGINAL METASTASES FROM HYPERNEPHROMA

A REPORT OF FOUR CASES

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Vaginal metastases from hypernephroma are rare. A review of the literature reveals only 16 such cases. Yet in the last twenty-eight months we have seen 4 cases. Lubarsch, in mentioning the various probable sites of metastasis in hypernephroma, includes the vagina as a rare location, though he believes that this form of metastasis is more common than is generally supposed, many cases appearing in the literature as carcinoma, sarcoma, hemangioma, and hemangio-endothelioma. This seems to be true, for bleeding from a vaginal metastasis may be the first indication of a renal tumor, and it is quite possible that under these conditions a more complete examination might frequently reveal a primary kidney tumor. The first case presented here is an excellent example of just such a possibility.

CASE I (No. 11875): A woman of sixty-five years was admitted on May 12, 1934, with a history of vaginal bleeding of three months' duration. There was no history of previous disease. The menopause had occurred at forty-five years. One year prior to admission, the patient noticed a lump the size of a plum in the right side of the back, tender at first. There was no history of trauma. Lying on the right side was painful, as were deep breathing and coughing. The vaginal bleeding was spotting in character and occasionally moderately severe. The patient had been hospitalized in a city institution, and a papillomatous, cyanotic, red, easily bleeding growth was discovered on the anterior vaginal wall just behind the urethral orifice. An x-ray examination at that institution revealed a destructive process in the tenth right rib with fusiform dilatation of the shaft in that area. The vaginal growth was removed and reported as an "adenocarcinoma of the vagina (melanoma to be ruled out)." A final diagnosis of adenocarcinoma of the vagina with metastasis to the tenth rib was made.

On admission the patient was pale and undernourished. A soft, slightly tender mass, 4 cm. in its longest diameter, was present in the right posterior axillary line of the thorax and appeared to be part of the tenth right rib; crepitation was observed in this area. Examination of the abdomen revealed a large, nodular, firm mass in the left upper quadrant, below the hypochondrium. The mass could not be distinctly delineated, but was easily ballotable from the left costovertebral angle. It was not tender. Vaginal examination disclosed an ulceration in the midline of the anterior wall of the vagina, 1.5 cm. behind the external urethral orifice. The edge of the ulcerated area was raised, dark red in color, irregular, soft, bleeding easily on palpation.

A biopsy taken from the ulcerated area and a slide obtained from the former hospital were both typical of metastatic hypernephroma of the clear-cell type (Fig. 1). There were areas containing numerous dilated blood capillaries suggestive of hemangioma, and large areas of hemosiderin were observed (Fig. 2). All specimens of urine examined contained a few erythrocytes. A roentgenogram of the chest and ribs revealed a fusiform dilatation of the right tenth rib with destructive changes; no other metastatic changes were noted in the chest or remainder of the skeleton. An intravenous pyelogram revealed the lower pole of the right kidney on a level with the fifth lumbar vertebra. There was a large area of increased density on the left side, corresponding to the region of the left kidney, which ex-
Fig. 1. Case I: Vaginal Tumor, Biopsy Specimen

Fig. 2. Case I: Vaginal Tumor, Biopsy Specimen, Showing Numerous Blood Capillaries

The large, irregular, dark-staining areas are hemosiderin.
tended from the twelfth thoracic vertebra to the sacrum. In films the calyces of the right kidney appeared normal; those of the left were distorted and dilated.

The blood glucose, urea nitrogen, and creatinin were normal. A blood count revealed hemoglobin, 55 per cent (Sahli); red cells, 2,400,000; white cells 8,200.

When the patient was last seen, June 10, 1934, there was a bright red nodule, the size of a cherry, in the vagina, a recurrence of the earlier tumor (Fig. 3). The mass in the left upper quadrant of the abdomen was larger and more easily palpated. Death occurred Nov. 1, 1934. No autopsy could be obtained.

Case II (No. 10242): The patient was admitted Feb. 17, 1933. In April 1932 she had first noticed a mass in the left upper quadrant of the abdomen. This had increased in size, and the patient went to a city hospital. There was no history of hematuria, but the urine examined on admission to that institution showed a few red blood cells. An attempt at left nephrectomy was made in October 1932, when a large retroperitoneal mass occupying the greater portion of the left abdomen was seen. The tissue removed for biopsy was reported as a hypernephroma.

On admission in February 1933 the patient was bedridden, complaining of dyspnea and lower back pain. Physical examination revealed a large, nodular, non-tender mass filling the left upper quadrant of the abdomen. On the anterior vaginal wall, behind the external urethral orifice, was a soft, friable, pedunculated mass, 3 × 3 × 4 cm., bleeding readily to touch. The pedicle was quite thin and long. Extensive metastatic involvement of the lungs and pelvic bones was revealed by x-ray examination. The urine showed a few red blood cells. A blood count revealed hemoglobin 60 per cent (Sahli); red cells 3,100,000; leukocytes 6,700. Blood chemistry: glucose 105, uric acid 35, urea nitrogen 15.

The pedunculated mass was removed from the vagina, and histologic examination revealed a typical metastatic hypernephroma, not unlike that encountered in the preceding case (Fig. 4).

The patient died April 21, 1933. At autopsy the left kidney was found replaced by a tumor mass 14 × 10 × 9 inches in size, presenting grossly the typical picture of hypernephroma, with large, yellow and hemorrhagic areas interspersed by areas of necrosis. The left adrenal contained a metastatic nodule. Numerous metastases were found in the liver and lungs. The pelvic lymph nodes were enlarged and contained metastases. The vaginal mass was identical histologically with that removed from the left kidney area.
CASE III (No. 11857): A colored woman, fifty-seven years of age, was admitted May 9, 1935, complaining of occasional frank hematuria of two years' duration and severe dysuria for seven weeks. The past history was essentially negative. The menopause had appeared at thirty-nine years. Just prior to admission the patient had been hospitalized for five weeks at another institution, where the diagnosis of inoperable hypernephroma of the right kidney was made.

The liver and spleen were not palpable. A large, firm, irregular mass, the size of a man's head, was palpated in the right upper quadrant of the abdomen. The mass filled the right flank, and was ballotable from the right costovertebral angle. Some tenderness was elicited on palpation of this mass. Inspection of the vagina and manual examination of the pelvis at this time were negative. The blood pressure on admission was 202/108. Urinalysis showed frank hematuria with numerous red cells microscopically. Blood chemistry figures for glucose and non-protein nitrogen were within normal limits. A blood count showed hemoglobin, 50 per cent (Sahli); red cells, 1,850,000; leukocytes, 6,700. The blood Wassermann test was negative. An intravenous pyelogram, taken May 15, 1934, showed marked hydronephrosis of the right kidney. The left kidney pelvis was moderately dilated. X-ray examination of the chest and skeleton revealed nothing remarkable. Cystoscopy performed June 7, 1934, showed the urinary bladder normal in appearance. Bloody urine could be seen coming from the right ureteral orifice. The patient was considered a poor operative risk, and was given palliative x-ray therapy only. Following a blood transfusion, June 15, 1934, she was permitted to return home.

The patient was readmitted March 30, 1935, in a much weakened condition, emaciated, and complaining of vaginal bleeding and a mass in the vulva. The mass in the right upper abdomen was considerably larger. A pedunculated tumor, about 6 x 7 cm., was seen on the right labium minor about 1.5 cm. from the external urethral orifice. The pedicle was short and broad, 2 cm. at the base. The mass was excised on April 8, 1935, and reported as metastatic hypernephroma. Within one month a recurrence appeared which grew to about three-quarters the size of the original mass. The patient died May 27, 1935.

The essential autopsy findings were as follows. A large mass involving the upper two-thirds of the right kidney, 9 x 11 x 7 cm., was seen. The descending portion of the duodenum was firmly adherent to the upper pole of this tumor. The center of the neoplastic mass was necrotic, containing a considerable amount of purulent material. The central necrotic cavity communicated with the right kidney pelvis. An area of perforation 1.5 cm. in diameter was present in the descending portion of the duodenum, which was adherent to

**Fig. 4. Case II: Biopsy from Pedunculated Vaginal Node**
the tumor. This communicated directly with the central necrotic cavity of the kidney tumor. Large metastatic lymph nodes were present in the retroperitoneal space, beginning at the celiac plexus and extending into the thoracic cavity, filling the hilus areas of both lungs. Several metastatic nodules were present in the liver and lungs, the largest 2.5 cm. in diameter. Grossly, there was no evidence of metastatic involvement of the para-aortic, para-iliac or parametrial lymph nodes.

The genitalia were removed in toto, including the kidneys, ureters, bladder, and urethra. Grossly the metastasis in the vulva, described above, did not invade the deeper structures. There was no evidence of metastases in the urogenital tract.

Histologic study of the primary kidney tumor and the vaginal mass showed them to be identical. The mass in the vulva invaded the vagina only superficially and was sharply demarcated (Fig. 5). Serial sections were made of several portions of the vaginal wall. No evidence of direct or lymphatic extension was seen.

**Case IV (No. 12749):** A woman aged fifty-one was admitted Jan. 11, 1935, complaining of profuse vaginal bleeding, hematuria, weakness and loss of weight, of several months duration. A slight hemoptysis had occurred two weeks before admission. The patient stated that a year and a half earlier she had noticed a mass in the left upper quadrant of the abdomen, which had steadily increased in size. She had also had occasional pain in the left side of the abdomen and frequency of micturition. A diagnosis of hypernephroma of the left kidney had been made at a city institution. Operation for the removal of the left kidney had been performed Nov. 20, 1934, but due to extensive growth, nephrectomy was not done. A biopsy taken at the operation confirmed the clinical diagnosis. The patient had been discharged three weeks following operation, and referred for x-ray therapy, which she refused. Soon after her discharge, she began to notice continuous vaginal bleeding, which subsequently became more profuse. For this she was readmitted to the hospital on Jan. 5, 1935, and immediately referred to our institution.

The patient was emaciated and the conjunctivae and mucous membranes of the oral cavity were quite pallid. An oblique well healed scar was seen in the left flank, about 6 inches in length. A firm irregular mass, the size of a child's head, was palpated in the left upper quadrant of the abdomen. The mass moved slightly with respiration. Vaginal examination showed a bulky, bluish red mass filling the entire right fornix of the vagina and extending onto the right half of the portio, completely covering the latter. The left half

![Fig. 5. Case III: Sharp Demarcation of Metastasis in Vaginal Wall](image-url)
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appeared normal. The mass bled easily upon manipulation. A biopsy taken at this examination was reported as a metastatic hypernephroma of the clear-cell type. X-ray examination of the chest and skeleton, Jan. 14, 1935, revealed no pathology in the bones or lungs. Intravenous urography showed a slight hydronephrosis of the right kidney pelvis, while the left kidney showed no excretion of the dye. A dense mass was seen in the left kidney area. A cystogram taken Jan. 22, 1935, revealed nothing of note. All specimens of urine showed many red blood cells and large quantities of albumin.

The patient continued to bleed profusely from the lesion in the vagina in spite of palliative x-ray and radium therapy, and died March 10, 1935. No autopsy was obtained.

DISCUSSION

The almost identical location of the vaginal metastases in 3 of the 4 cases here described seems more than mere coincidence, and of unusual interest, especially since our statistics show that only 6 cases of hypernephroma in women were seen at our institution since January 1933. Of these 6 patients, 4 are dead, the 4 with vaginal metastases described in this paper. The review of the cases published in the literature would seem to strengthen this observation on the occurrence of vaginal metastases from hypernephroma.

In 1906, F. Henke, reported the case of a sixty-nine-year-old woman with multiple vaginal nodes and a pedunculated skin tumor. Post mortem a hypernephroma of the left kidney was found. The histologic pictures of the kidney tumor and vaginal nodes were identical.

In the same year H. Peham reported the case of a fifty-nine-year-old woman who gave a history of vaginal bleeding of several months' duration, with hematuria observed on one occasion. A large irregular mass was found in the left upper quadrant of the abdomen. On the anterior wall of the vagina, just behind the introitus and to the left of the urethral meatus, was a lobulated mass the size of a hazelnut. A biopsy proved the lesion to be a metastatic hypernephroma.

E. Hoffmann in 1907 reported the case of a woman of sixty who complained of a vaginal discharge. In the introitus, in the region of the urethra, was a growth the size of a walnut, cauliflower-like in appearance, with an ulcerated, easily bleeding surface. The original diagnosis was carcinoma of the vulva, but histologic examination later revealed metastatic hypernephroma. A mass was subsequently palpated in the left upper quadrant of the abdomen. Cystoscopy showed a urinary bladder metastasis. Autopsy confirmed the clinical findings.

In the same year A. Doran reported the case of a forty-year-old patient who complained of a swelling of the abdomen and slight vaginal discharge. An oval elastic growth the size of a cricket ball was found in the right iliac region and a pedunculated lobulated grape-like growth was noticed on the anterior vaginal wall, a little to the right of the mid-line and 2 inches above the vulva. The pedicle was 3/4 inches in length. Three sessile growths were observed in the posterior vaginal wall, the largest 1/2 inch in diameter. A clinical diagnosis of vaginal sarcoma with an abdominal tumor was made. At operation the tumor was found to be renal in origin, the primary growth being situated at the upper pole of the right kidney. Histologically the renal and vaginal tumors were similar in character and "suggested suprarenal growth." Autopsy showed further metastases in the lungs and liver.
Also in 1907 B. Overy described a patient with a polypoid mass attached to the anterior vaginal wall. The growth was removed and later a large tumor was discovered in the right side of the abdomen. The vaginal growth recurred after two months. Post-mortem examination showed a right "adrenal tumor" with metastases to the liver and lungs.

In 1908 E. Gräfenberg reported 2 cases. His first patient was a sixty-year-old woman who had passed the menopause ten years prior to the onset of illness. The chief complaints were irregular vaginal bleeding and a foul smelling discharge of one year's duration. On examination a lobulated, brown-black, pedunculated tumor was found arising from the left labium minor. The mass was excised and a diagnosis of hypernephroma was made. At autopsy, a hypernephroma of the left kidney was discovered. No other metastases were found. Gräfenberg's second patient was a woman of fifty-four with a tumor in the left hypochondrium and a node the size of a hazelnut on the posterior vaginal wall just behind the vulva. Histologically both nodes proved to be typical hypernephroma. There were no demonstrable metastases.

R. Freund in 1908 reported the case of a fifty-six-year-old woman whose chief complaint was vaginal bleeding of six months' duration. A year and a half prior to admission a left nephrectomy had been performed for a mass the size of a child's head. The vaginal bleeding came from a growth the size of a cherry near the urethral orifice on the anterior vaginal wall. Histologically this growth was the same as the primary tumor.

In 1915 C. Fleischmann reported the case of a sixty-two-year-old female with a history of vaginal bleeding of seventeen days' duration. The point of bleeding was a cyanotic red tumor the size of a half a plum at the apex of the posterior columna rugarum. The mass was radically excised and histologically the diagnosis of metastatic hypernephroma was made. Movable masses were subsequently observed in both loins. The author believed the mass in the left loin to be a kidney tumor.

At a meeting of the Obstetrical and Gynecological Society in Vienna, in March 1918, W. Latzko demonstrated a vaginal metastasis from a hypernephroma in a patient whose left kidney had been extirpated nine months previously. The exact location of the metastasis is not mentioned in the report.

G. Gellhorn in 1918 reported the case of a fifty-four-year-old patient who complained of abdominal pain and a brown, offensive vaginal discharge. A large, hard, immovable mass was found in the left hypochondrium. Vaginal examination revealed two rounded growths springing from the anterior vaginal wall immediately behind the introitus. One was situated in the median line, the second was just behind the first. These growths were the size and shape of raspberries, soft in consistency, and attached to the vaginal wall by a broad base. Histologically the diagnosis of "hypernephroma-like growths" was made and upon autopsy, which was restricted to the abdomen, a hypernephroma was found in the upper pole of the left kidney.

In 1928 H. U. Hirsch-Hoffmann reported the case of a seventy-one-year-old woman whose chief complaint was a bloody vaginal discharge. A firm node the size of a hazelnut was found just behind the external urethral orifice.
The histological diagnosis was metastatic hypernephroma. At autopsy a tumor the size of a man's fist was found in the left kidney.

C. Fleischmann described a second case in 1929. The patient, aged fifty-five, complained of vaginal bleeding. Upon examination a small ulcerated nodule was discovered on the anterior wall of the vagina, as well as several smaller nodules on the posterior wall, all just behind the introitus. Though the entire area was widely excised, a definite histologic diagnosis could not be made at that time. Four months later a large mass could be palpated in the left hypochondrium. A diagnosis of malignancy of the left kidney was then made, and removal of the organ was attempted. Soon afterward several nodules reappeared in the vagina. Histologically the tumor tissue from the kidney and that of the vaginal nodes were identical. The final diagnosis was a hypernephroma of the left kidney, with multiple vaginal metastases.

O. Gragert in 1929 reviewed the cases mentioned above, including in the group one that he had observed in a fifty-three-year-old woman. The patient was referred to the hospital with the diagnosis of carcinoma of the vagina. The chief complaint was vaginal bleeding. On the anterior vaginal wall, just below the external urethral orifice, was a dark red, pedunculated node the size of a hazelnut. The growth was radically excised, and a year and a half later the patient returned with no recurrence in the vagina, but complaining of a mass in the left loin. A tumor the size of a child's head could be palpated in the left upper abdomen. A left nephrectomy was performed and the mass removed. A diagnosis of hypernephroma was made on both specimens.

In 1932 J. Szymonowicz reported the case of a patient who gave a history of hematuria, and pain in the left hypochondrium of ten weeks' duration. In addition she had noticed a small growth in the vulva which bled upon the slightest friction. The node in the vulva had been removed at another institution and a recurrence had appeared soon afterward. Upon examination, a mass the size of a child's head was noted in the left hypochondrium. The growth in the vulva was the size of a walnut and covered the external urethral orifice. Cystoscopy revealed a tumor the size of an egg, similar in appearance to that in the vulva, on the right wall of the bladder. The nodule in the vulva was excised and histologically suggested the appearance of hypernephroma of the large clear-cell type.

The last case described in the literature is that of K. Bowes in 1935. A fifty-two-year-old woman complained of an offensive vaginal discharge and a lump in the region of the vulva. The latter was described as "a necrotic ulcerated mass growing from the anterior wall of the vagina, extending from the mid-line towards the left side. It was immediately posterior to the urethra and just inside the introitus." A biopsy showed this lump to be hypernephroma. No abdominal mass or masses were found at the first examination. Subsequently, a tumor of the left kidney was discovered and nephrectomy was performed. The vaginal mass recurred within a short period.

Summarizing all of the cases presented, we find that of the 20, 13 showed single nodules on the anterior vaginal wall, all situated near the external
urethral orifice or in closed proximity to it. In 5 cases multiple vaginal nodes were found, and in 3 of the latter the largest nodule was situated near the external urethral orifice. In one case a single node was found in the posterior columna rugarum just behind the introitus. In another instance a single vaginal nodule was seen, but its location was not described. In all, 16 cases presented large metastatic nodules on the anterior vaginal wall, in the region of the external urethral meatus.

E. Gräfenberg was the first to offer an explanation for these metastases. He suggested the theory of retrograde hematogenous metastasis, assuming that the path taken by the hypernephroma cells must be by way of the left ovarian vein, which empties directly into the left renal vein, so that a direct path exists from the left kidney to the pampiniform plexus. An anastomosis must also exist between the pampiniform plexus and the vena obturatoria, and so to the pubic veins. The pubic veins empty into the vena obturatoria. To support his theory Gräfenberg refers to the investigations made by E. Kownatzki, reported in his Die Venen des weiblichen Beckens. Kownatzki was able to demonstrate such an anastomosis, most commonly, however, when an inflammatory condition of the pelvis had previously existed. Gellhorn accepts this explanation.

Gräfenberg's theory would suffice to explain vaginal metastases from left-sided kidney tumors. In cases of right-sided kidney tumors, however, it is difficult to accept, since the ovarian vein empties into the interior vena cava directly. Of the cases mentioned here, we find three instances of right-sided primary kidney tumors with single vaginal metastases.

Lubarsch has suggested the theory of retrograde lymphatic invasion, to explain metastases in the ureters and bladder, but this explanation has not been offered for vaginal metastases. Although involved pelvic lymph nodes were found on autopsy in 2 of the 20 cases here described, this rather vague explanation would seem difficult to apply to secondary lesions near the external urethral orifice and the vagina. For this purpose a thorough histological investigation of the vagina of our Case III (No. 11857) was made in an attempt to find any possible involvement of the lymphatics of the vagina, but without success. The possibility of retrograde lymphatic metastasis, however, cannot be entirely discounted.

The remaining, and more likely explanation is that suggested by J. Szymonowicz, a possibility conceived by the present authors independently. The suggestion is that the hypernephroma cells carried by the urine are implanted into the vaginal wall. The theory of implantation metastasis by way of the urinary tract has been proposed before. In 1898 Switalski described what he believed to be an instance of true implantation metastasis. He reported the case of an adenoma of the urinary bladder with a similar growth in the vulva. He was of the opinion that the viable adenoma cells of the bladder were washed out with the urine and that these cells implanted themselves in the vulva. H. G. Pleschner, in 1913, also suggested the urinary path from hypernephroma of the kidney to the ureter. Lubarsch mentions this theory, but considers it rather improbable. He is of the opinion that the hypernephroma cells are too seriously damaged for successful implantation.

We may assume, therefore, that these authors believed that tumor cells are
constantly being washed out with the urine in cases of hypernephroma. P. Albrecht, in 1905, attempted to prove this when he examined the urinary sediment of 28 cases of hypernephroma for tumor cells. He reported that in only two instances were cells seen which were suggestive of tumor cells, and added that there was no thought of a definite diagnosis. We must admit the difficulty of finding and recognizing the few tumor cells that may be washed out with the urine in these cases of renal hypernephroma. The authors have made numerous attempts to find hypernephroma cells in the urinary sediment of their patients and came to the same conclusions as Albrecht.

More recently N. Shinohara (1934) demonstrated experimentally that tumor cells are excreted in the urine of rabbits with Kato sarcoma having metastases in the kidneys. The rabbit urine was removed from the bladder and injected into normal rabbits, in which identical tumors then appeared.

If we assume that these cells are to be found in the urine—a fluid medium at body temperature—it seems more than likely that they can remain viable long enough to deposit themselves in some excoriated or macerated area along the urinary tract and external genitalia. Here they find a suitable bed to sustain themselves, and grow. Such suitable areas are less likely to be found in the kidney pelvis, ureters, and urethra, where the mucous membranes are less apt to be traumatized and where there is a constant flow of urine, leaving the cells little opportunity to deposit themselves. A greater opportunity is present in the urinary bladder, where the urine is delayed and the solid particles form a sediment at the base of the bladder. That portion of urine is expelled last. The most suitable areas, however, are the external urethral orifice, vulva, and vagina in the female. The urine as it leaves the female urethra is washed over the immediate epithelial surface. This continual wetting gives rise, very easily, to maceration and excoriation of the immediate epithelial surface, a condition frequently observed clinically. It is in just such areas that viable hypernephroma cells could easily implant themselves, especially since the last portion of urine is that containing the cellular elements and no other urine follows immediately to wash the sediment away.

It is interesting to note that in all our cases both the ureter and urethra were free from metastases, although ureteral metastases have been described in the literature. The cases themselves would seem to bear out the assumption that the most likely area for implantation metastasis is the region of the external urethral orifice and vulva. As we have seen, in 16 of 19 cases there were nodules in close proximity to the external urethral orifice. In the remaining 3 instances there were (1) metastases in the urinary bladder; (2) a nodule on the posterior vaginal wall. In one instance the exact location of the nodule in the vagina was not described.

**Summary and Conclusions**

(1) Four cases of hypernephroma with vaginal metastases are reported.
(2) Sixteen cases appearing in the literature are reviewed.
(3) The various theories seeking to explain this occurrence are discussed.
(4) The most probable explanation seems to be implantation metastasis by way of the urinary tract.
BIBLIOGRAPHY