THE DIFFUSELY INFILTRATIVE CARCINOMA OF THE URINARY BLADDER

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Carcinoma of the urinary bladder is usually papillary in type and protrudes into the cavum. Necrosis and consequent bleeding from the vascular stalks account for the hematuria, which often is the only symptom noticed by the patient. French urologists for many years have recognized, also, a diffuse infiltrating type of carcinoma of the urinary bladder, in which there is neither a projecting tumor mass nor obvious hematuria. This type occurs rarely and may be confused with some other malignant growth of the bladder or regional tissues. The tumor cells infiltrate the bladder wall widely, and it is markedly thickened.

According to Albarran (1), some of these growths are small, but most of them involve large portions of the bladder wall. They have a granular surface or ulcerate, and the ulcers have raised borders and granular rough bases. According to Clado (2), there is no obvious tumor in the bladder lining, and the entire wall or a large part is as much as 2 to 4 cm. thick, depending upon the extent of infiltration. The thickest regions are usually at the base or trigone. Clado described small villi on the surface of these carcinomas, which in some cases were seen only when the tissues were floated in water. He further described the thickened wall of the bladder as tough and fibrillar, resembling fibrous tissue, and the cavum as markedly decreased in size. Voillemier (3) observed this infiltrative form of carcinoma in three patients.

Ashhurst (4), in 1872, reported painful polyuria and spasmodic cramps of the abdomen of seven months' duration in a man aged forty-five years, and a hard suprapubic mass that had been noticed for five weeks. The suprapubic mass was considered a malignant growth of the bladder. The prostate was not enlarged. A urethral catheter drained only a small volume of urine, indicating a contracted cavum. There was no hematuria. Death occurred nine months after the onset of symptoms. Post-mortem examination disclosed a primary carcinoma of the urinary bladder which extended into the abdominal wall and involved the rectum and

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several loops of the small bowel. The wall of the bladder was uniformly thickened, the lining was unbroken, and the cavum was markedly diminished. The histologic diagnosis was fibrocarcinoma. Ashhurst emphasized the absence of pain and hematuria.

Legueu (5) recorded the surgical excision of a hard thick infiltration of the upper and anterior portions of the urinary bladder without an appreciable growth projecting into the cavum. This tumor was diagnosed alveolar carcinoma. Hematuria had been the main clinical symptom.

English (6), in agreement with previous authors, reported that infiltrating carcinoma of the urinary bladder penetrates extensively and thickens the bladder wall but presents no appreciable projecting tumor of the lining epithelium. In the late stages of the disease, the mucosa shows papillary or polypoid folds, and seldom nodules. English stated, also, that the thickening of the bladder wall is an important clinical sign and that the disturbances of bladder function depend upon the extent of infiltration. When the urinary bladder is diffusely infiltrated, it has the form of an hypertrophied bladder, the wall is markedly resistant, and the capacity of the cavum is small. Tenesmus is more severe with this carcinoma than with simple hypertrophy, with which the lesion is likely to be confused. It increases in severity until finally the patient has no sensation of relief after urination. The urine at first is clear but later contains exudates and blood, as in cystitis. In this infiltrating form of carcinoma hematuria is rarely the initial symptom.

English recorded examples of infiltrating carcinoma of the urinary bladder in two patients. Only one was examined post-mortem. The symptoms in this case, in a man aged sixty-nine years, had been difficult painful urination and hematuria. The anatomic diagnosis, following post-mortem examination by Paltauf, was "carcinoma infiltratione vesicae urinariae, subsequente infiltratione textus cellulosi periprostatici et retroperitonealis et glandularum lymphaticarum; cystitis necrotica; pyelitis bilateralis et pyelonephritis purulenta." The tissues above the symphysis were indurated, the urinary bladder was rigid, and the peritoneum of the minor pelvis and in front of the spine as far as the renal veins was thickened and contained gray nodules. The wall of the urinary bladder was made up of hyperemic gray tissue 17 to 20 mm. thick. The prostate was enlarged but not diseased, and the lining of the rectum was unchanged. The histologic diagnosis of the
bladder tumor was carcinoma. Wolff (7), in 1901, described a diffuse carcinoma of the urinary bladder removed postmortem from a man aged sixty-three years. This man had had urinary retention about three years and clinically was considered to have carcinoma of the prostate with involvement of the urinary bladder, prevesical tissues, and pelvic lymph nodes. The wall of the bladder, except for a small area near the prostatic urethra, was 3 to 4 cm. thick. The lining was extensively ulcerated but showed no circumscribed growth. In histologic preparations, the bladder wall was diffusely infiltrated by epidermoid carcinoma.

Only brief comments are recorded by American urologists on these diffuse infiltrating carcinomas of the urinary bladder. Barney (8) removed all of the urinary bladder above the urethra and ureters from a woman, aged forty-seven years, who had observed hematuria about a year before. Cystoscopic examination at that time disclosed no changes of the bladder lining. Shortly afterward, during the second attack of hematuria, a fine stream of blood was observed coming from a small ulcer in the dome of the bladder. This ulcer was cauterized. Hematuria ceased, but recurred after four months, at which time the same ulceration was found and again cauterized. Examination six months later disclosed that this region was slightly elevated and resembled a small papilloma. After four more months two small papillomas were found, and the bladder was excised. Dr. J. H. Wright reported that the growth was an undifferentiated carcinoma. An emergency laparotomy shortly before death, about a year following the bladder operation, disclosed disseminated carcinoma of the peritoneum. Barney stated that the condition corresponded to the infiltrating form of carcinoma described by Geraghty (9).

According to Geraghty, there is an infiltrating type of carcinoma of the urinary bladder which shows no growth on the mucosa. The bladder wall may thicken to 4 cm., depending upon the extent of infiltration. The lining surface is irregular and nodular, and sometimes shows small ulcers, changes which usually characterize a severe ulcerative cystitis; the walls may be cartilaginous in consistency. Dean (10) reported that flat carcinomas of the urinary bladder have extensive submucous infiltrations but no tumor projecting from the lining. Where such a growth is suspected, he states, the lining of the bladder should be examined carefully for gray or yellow ulcers.
The foregoing references are quoted as an introduction to a description of a case of diffuse infiltrating carcinoma of the bladder in a patient whose symptoms, except for the last few days of his life, did not suggest carcinoma of the urinary bladder, although the presence of a malignant pelvic tumor had been established by physical and roentgen examinations.

**Case Report**

G. P., a white man, aged forty-two years, entered St. Luke's Hospital July 24, 1929, because of pain in the left hip of one year's duration. It had first been noticed after a long game of golf, and had gradually become worse; the left sacro-iliac joint was tender, and on motion the pain radiated down to the heel. A firm mass at the attachment of the left gracilis muscle to the pubic bone, slightly enlarged inguinal and femoral lymph nodes, and a nodule of tissue behind the center of the superior ramus of the left os pubis were demonstrated by external examination. By rectal examination a mass on the left side of the pelvis that reached but did not involve the prostate was found. A satisfactory diagnosis was not made, although pelvic sarcoma and lymph gland dyscrasia were considered. Roentgen examination did not disclose changes in the spine, sacrum, pelvis, or left hip, or filling defects of the colon. An inguinal lymph node showed no evidence of tumor. Erythrocytes numbered 4,500,000, and leukocytes 10,200 per c.mm. The hemoglobin was 85 per cent. The urine and feces showed no unusual elements.

Before leaving the hospital on Aug. 1, 1929, the patient received two roentgen ray treatments over the affected parts. Within two weeks the pain in the back and left leg had disappeared, the swelling in the left groin decreased, and in three months the patient had gained thirty pounds in weight. After eight months, however, the pain returned and he re-entered the hospital Nov. 14, 1930.

A malignant growth of the prostate was considered at this time, since the left lobe of the gland seemed involved by an infiltration that extended to the pelvic wall. The urine contained 5 mgm. of albumen per 100 c.c., a few epithelial cells, erythrocytes, leukocytes, and bacteria. There were 3,780,000 erythrocytes per c. mm. of blood; the hemoglobin was 70 per cent.

Between Dec. 3, 1930, when the patient left the hospital, and May 5, 1931, his third admission, his physical status showed no change. He had severe pain in the left sacro-iliac joint, the left thigh, and the left leg. He also suffered from nocturia, voiding as often as six times in a night, though on each occasion he had the sensation of having emptied the bladder. By June 21, 1931, this had increased to ten urinations. Slight urinary incontinence and rectal tenesmus were observed July 5, 1931. Death occurred on July 6, 1931, the patient having been irrational for six days. This was two years after his first admission and three years after the appearance of symptoms.

The head, neck, and trunk were examined post mortem. The
essentials of the anatomic diagnosis were: diffusely infiltrative carcinoma of
the urinary bladder with destructive invasion of the left side of the
pelvis; metastatic carcinoma of the diaphragm, lungs, and parietal
pleura; slight bilateral obstructive hydronephrosis and hydro-ureter.

The body was that of a white man, weighing 124 pounds and measuring
174 cm. in length. The only changes observed externally were an old
laparotomy scar, a biopsy scar in the left groin, and a decubitus ulcer, 20
by 8 mm., opposite the left ilium. The abdomen contained about 150 c.c.
of clear, yellow fluid. The urinary bladder measured 6 cm. in diameter
and extended 7 cm. above the symphysis pubis. It had the contour of
a contracted, hypertrophied urinary bladder. The glistening peritoneum

covering it contained small tumor nodules. Similar nodules 1 to 8 mm.
in diameter roughened the peritoneum of the right leaf of the diaphragm.
The pelvic viscera were bound firmly to the floor and anterior wall. On
the left side, the tumor extended from the neck of the urinary bladder to
the lateral wall of the pelvis. The bones were extensively eroded, and the
tumor had penetrated the acetabulum. The bladder, prostate, seminal
vesicles, and some extra-vesical tumor formed a mass 14 × 11 × 7 cm.
The lumen of the bladder was markedly contracted and contained a
gray viscid material. The thick folds of the mucosa were mottled with
recent hemorrhages. There was no papillary tumor or ulceration of the
epithelium. All parts of the bladder wall were markedly thickened, in
the vertex to 12 mm., and ventrally near the neck to 23 mm. The cut
surfaces of the wall were resistant, gray, and fibrillar, and resembled
fibromyoma. The extensions of the tumor behind and on the left side surrounded the prostate, seminal vesicles, vasa deferentia, and ureters. The primary growth did not originate in them. The lining of the rectum was unchanged.

Fifteen discoid gray metastases 2 to 13 mm. in diameter were observed on the pleura of the right lung, and a few were seen in the parenchyma. There were ten nodules on the pleura of the left lung. Four others, two on each side, were found under the parietal pleura near the spine.

*Histology:* The tissues of the urinary bladder were infiltrated extensively by carcinoma. The tumor cells were 10 to 15 μ in diameter. Of the few larger cells, some had two to four nuclei. The cytoplasm was granular and the nuclei were vesicular. In representative areas the arrangement of the cells was papillary (Fig. 1). The papillae had slender stalks of vascular fibrous tissue and broad mosaics of cells without stroma, reaching to a depth of eight to fourteen layers. Where the papillary structure was not maintained in the tumor structure the cells were in cords and alveoli separated by thin septa of fibrous tissue or held in an interwoven mesh of connective-tissue fibrils. The subperitoneal tissues were infiltrated diffusely by carcinoma cells in small clusters or cords (Fig. 2). The carcinoma had extensively invaded the tunica propria of the bladder mucosa, although much of the surface epithelium was unchanged except by mechanical displacement. There were large areas of necrosis in the carcinoma and in the muscular tissue of the
bladder wall. In some of these necrotic areas the papillary arrangement of the carcinoma was especially distinct. The papillary arrangement was also present in the metastases of the lungs (Fig. 3).

![Photomicrograph Illustrating the Papillary Structure in the Subpleural Metastases](image)

**Comment**

The diffuse infiltrating type of carcinoma of the urinary bladder according to the experience of urologists, and as illustrated by the case reported, has an insidious clinical course. The usual bladder symptoms, especially hematuria, may be absent. The marked infiltration of the bladder wall and its thickening, the absence of a conspicuous tumor of the lining epithelium, and the contracted cavum are the outstanding anatomic features. The tumor cells in the case reported were small, and in regions where compression, necrosis, and deep penetration of the bladder wall had not masked the structure, the arrangement was papillary. This papillary form aligns the infiltrative carcinomas of the urinary bladder with other papillary tumors of the urinary tract. Unless this papillary arrangement is recognized in the examination by the pathologist, the small size of the carcinoma cells and their diffuse infiltration of the bladder wall may lead to the histologic diagnosis of round-cell sarcoma or lymphosarcoma.
REFERENCES

3. Voillemier. Quoted by English (7).