HODGKIN'S DISEASE INVOLVING THE BLADDER

REPORT OF A CASE

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Though Hodgkin's disease has been found in practically every organ and tissue of the body, reports of its occurrence in the bladder are few and meager, while careful search of the literature fails to disclose a single case of the transformation of a Hodgkin's granuloma in the bladder to a sarcoma.

CASE REPORT

E. G., a white man forty-one years old, was admitted to the Saratoga Hospital on April 6, 1935, complaining of intermittent hematuria, urgency, frequency, and nocturia accompanied by chills and fever, of four months' duration. Except for a gastric ulcer ten years earlier, diagnosed by x-ray, the past history was of no significance.

The patient was well developed and well nourished, with an irreducible right inguinal hernia and an atrophied right testicle. Cystoscopy revealed a thickened bladder mucosa, an easily bleeding trigone, and an inflamed prostatic urethra. Near the upper and inner side of the left ureteral orifice was a papilloma which was considered benign, though no biopsy was done. The patient was treated with silver nitrate irrigations (1:5000) and instillations of 10 per cent argyrol. Hematuria ceased soon after treatment but recurred June 1, 1935. The patient was then seen at the Albany Hospital by Dr. J. E. Heslin, who observed on physical examination (July 22, 1935), in addition to the above findings, a fullness of the left prostatic lobe with evidence of induration in the region of the left seminal vesicle.

Cystoscopy (July 22, 1935) showed: slight congestion of the trigone, with diffuse congestion of the entire mucosa; no evidence of stone, tumor, or diverticulum; large veins in the mucosa about the left ureteral orifice. The right ureteral orifice was normal and easily admitted a No. 6 French catheter; the urine was clear and the rhythm normal. The left ureteral orifice was swollen and pouting; the urine was discontinuous and pale. Staphylococcus aureus was cultured from the left kidney and bladder urine; the right kidney urine was sterile.

The impression at this time was: prostatitis, vesiculitis, left pyelitis with hydronephrosis and left hydro-ureter.

About one year later, July 6, 1936, the patient returned to the Albany Hospital complaining again of hematuria of three days' duration and of burning and nocturia for the past year. General examination showed frank bleeding from the external urethral meatus; bladder dulness about 3 cm. above the symphysis pubis, pressure on this area evoking a sense of pressure on the urethra; bilateral enlargement of the anterior cervical lymph nodes, especially on the right. No lymph nodes were palpable elsewhere. The liver and spleen could not be felt. There was no tenderness at the costovertebral angles and no abdominal tenderness on deep pressure.

Cystoscopy by Dr. Heslin on July 6, 1936, showed a deformed bladder. The ureteral orifices could not be identified. Several bleeding areas were present at the bladder neck. A biopsy of the posterior bladder wall showed chronically inflamed vesical mucous membrane. An intravenous pyelogram revealed some evidence of dilatation of the right renal pelvis. The left kidney showed complete loss of function at this time.

Cystoscopy was again done on July 10, 1936. The bladder was deformed. The ureters were easily catheterized. Right kidney function was excellent but that of the left kidney was very poor. A punch biopsy of the prostate showed a minute blood clot.
The impression was extravesical involvement of the bladder, possibly malignant.

The patient was discharged from the Albany Hospital with a diagnosis of chronic prostatitis, vesiculitis, contracted bladder, and bilateral hydronephrosis more marked on the left. He was again seen at intervals, but with no real change in his condition except remission of the hematuria. Proctoscopy on Aug. 8, 1936, revealed nothing of note. On Aug. 20, 1936, the patient complained of an "ammonia taste." His ankles were swollen and the urine was blood-tinged. The prostate was again examined digitally and though enlarged did not feel malignant. Malignancy was considered but could not be established.

On Aug. 28, 1936, the patient was admitted to the Saratoga Hospital in convulsions and coma, presenting a typical picture of uremia. He died thirty-six hours later without recovering consciousness. He was well nourished and did not look as if he were harboring a malignant growth. No enlarged lymph nodes could be found, nor could the liver or spleen be felt.

Only the typical and significant laboratory findings need be given here. The urine on July 5, 1936, showed albumin 3+ and a large number of red and white blood cells. On Aug. 28, 1936, the findings were: specific gravity 1.010; albumin 0.075 per cent; sugar 0.2 per cent; indican, negative; an occasional epithelial cell; several pus cells per high-power field; no red blood cells.

Blood chemistry tests, Aug. 28, 1936, showed 122 mg. urea nitrogen per 100 c.c. of blood; 5.6 mg. creatinine per 100 c.c. of blood.

The blood count, July 10, 1936, was: hemoglobin 80 per cent; red cells 4,200,000; white cells 7,800.

Guinea-pig inoculation with urine, July 1935, was negative for tuberculosis.

The complement-fixation test for syphilis was negative on several occasions.
Autopsy (limited to the abdomen): The body was that of a normally developed, well nourished, white man. No enlarged superficial lymph nodes could be found. Except for a right inguinal hernia there were no changes of note externally.

Section of the abdominal wall showed the musculature and subcutaneous adipose tissue to be normal in amount and appearance. The peritoneal cavity contained no free fluid and the visceral and parietal peritoneum was for the most part smooth and glistening except in the pelvis, where the bladder was strongly bound by dense, tough, fibrous adhesions to the symphysis pubis and its rami anteriorly, the muscles and fascia of the pelvic walls laterally, and the rectum posteriorly. Intermingled with the adhesions were small, hard, well defined, round or ovoid masses, some discrete and some matted together, which on cut section were flat, smooth, and gray-white. The bladder wall was rigid and thickened, measuring 2 cm. in thickness for the most part, except for an area 3 cm. in diameter in the fundus where it was 0.6 cm. The thicker portion was made up of a uniform, dense, yellowish gray-white, slightly granular tissue, while the thinner portion was composed of fibrous tissue containing opaque, gray-white nodules. The bladder lining was yellowish gray, fairly smooth, with some wrinkles and ridges and a number of small, knobby projections. Neither the trigone nor the ureteral orifices could be identified. The capacity was 200–250 c.c. In spite of the adhesions, the organ was not especially deformed.

The ureters after they crossed the pelvic brim were surrounded and compressed by the pericystic masses and adhesions already mentioned, and on traversing the bladder wall, their walls were so infiltrated by the yellowish gray-white tissue that they could not be identified. Above the pelvic brim the ureters were dilated, thinned, and filled with turbid, yellow urine mixed with amorphous granular and particulate material.

The left kidney (Fig. 1) measured 8 x 4 cm. and weighed 110 gm. The capsule was fibrous and 0.2 cm. thick. It stripped easily, exposing a fairly smooth surface, dark red mottled with black and red, slightly pitted and roughened in a few places. The pelvis was
greatly dilated and compressed, and the renal parenchyma thinned so that in places cortex and medulla together measured but 0.9 cm. Cut section was flat, dark red with blackish mottlings, and deep within the cortex was a sharply circumscribed, hard, uniform gray white nodule 1 cm. in diameter. The right kidney measured $14 \times 8$ cm., weighed 190 gm., and except for some compression of the medulla by the moderately dilated pelvis was essentially normal.

The prostate was firm but not hard. The prostatic urethra was patent and the bladder could be emptied freely through it by pressing on the fundus. Hemisection of the prostate showed pearly gray-white tissue with a few discrete, round, raised, well delimited but not encapsulated, dense yellowish gray-white nodules. Though the prostate was firmly bound to the bladder, no continuity could be established between the prostatic nodules and the massive infiltration of the bladder wall.

![Image of bladder wall showing marked activity of cellular elements](image)

**Fig. 3. Another section of the bladder wall from a more cellular area, showing marked activity of the cellular elements. $\times 400$**

Note the mitoses in the Reed-Sternberg giant cells.

The seminal vesicles were embedded in a mass of dense fibrous tissue through which were dispersed nodules similar to those in the prostate.

The rectum was partially surrounded by tough fibrous adhesions intermingled with hard, yellowish gray-white nodules, such as those already described, invading the muscularis propria, leaving the mucosa and submucosa free. The rest of the alimentary tube was normal.

The liver was increased in size and weighed 1800 gm. Beneath the capsule of Glisson were a small number of isolated, well defined, raised, rounded, umbilicated, reddish gray, slightly granular masses ranging from 1 to 3 cm. in diameter. Cut section showed similar masses deep within the liver substance.

In the mesentery an occasional discrete, hard, gray-white nodule, averaging 0.5 cm. in diameter, was found.

The abdominal aorta was partially encased in 2 long chains of hard gray-white masses.
some isolated and some matted together, embedded in a dense fibrous matrix. These masses were merely adherent to the adventitia of the aorta.

The nodes of the pancreaticocolienal chain were discrete, hard, gray-white, and encapsulated, the largest measuring 4 cm. in diameter.

Because of autopsy limitations, the thoracic organs were not examined. They were palpated through the diaphragm but no masses were felt in them.

Microscopically the changes in the bladder were most striking, and were characteristic of the same lesion in other organs and tissues.

The bladder wall was invaded and destroyed by a dense infiltrate of more or less free cells supported by a widespread, heavy, poorly vascularized, granulomatous, fibrous and reticular network. This process extended well into the pericystic adipose and connective tissue and destroyed most of the mucosa, though it stopped short in the submucosa in places, the epithelium being fairly well preserved over long stretches. Within the meshes and interstices of the granulomatous stroma were lymphocytes, plasma cells. Reed-Sternberg giant cells, endothelial cells and eosinophils. The lymphocytes and plasma cells predominated. Mononuclear and multinuclear Reed-Sternberg giant cells were also numerous; they varied greatly in size and shape and staining reaction, and mitoses were extremely frequent. In places there was a diffuse overgrowth of endothelial cells. The eosinophils were scant (Figs. 2 and 3). Where the stroma meshes were large and had massive collections of cells casual examination under low magnification gave the impression of an actively proliferating lymph follicle, the whole picture suggesting a reticulum-cell type of lymphosarcoma. Careful scrutiny of the section under a higher power, however, revealed that, although the lesion was neoplastic, it had no organized structure and many Reed-Sternberg giant cells and granulomatous elements indicated the true nature of the process.

Where the bladder mucosa was present, it was fairly well preserved and showed a lymphocytic infiltrate and a few intra-epithelial cysts filled with acidophilic débris.

The nodules and masses in the ureters, prostate, seminal vesicles, left kidney, liver, pelvic muscles and fascia and the mesenteric, pelvic, periaortic, and pancreaticocolienal lymph nodes presented essentially the same picture.

There were no changes in the spleen except an acute passive hyperemia.

**Anatomical Diagnosis:** Hodgkin's sarcoma involving the bladder, ureters, prostate, seminal vesicles, left kidney, liver, pelvic fascia and musculature, and the pelvic, mesenteric, periaortic, and pancreaticocolienal lymph nodes; chronic suppurative pyelonephritis, bilateral, especially marked on the left; bilateral hydro-ureter; cystitis cystica; acute seminal vesiculitis; fatty metamorphosis of liver, slight; accessory spleens (2) with acute passive hyperemia; subacute catarrhal gastritis.

**Review of the Literature**

Fraenkel and Much (1) in their review of Hodgkin's disease report one case in a twenty-eight-year-old white male who had three isolated, submucous lymphogranulomatous nodules, each the size of a lentil, in the bladder. Terplan and Mittelbach (2), who describe Hodgkin's disease in practically every organ, report lesions the size of a pea in the bladder mucosa of a twenty-four-year-old woman. Ginsburg (3), who believes that Hodgkin's disease and lymphosarcoma are identical, in giving the autopsy findings in the case of a fifty-four-year-old white woman merely says, "Bladder: Grossly no evidence of tumor growth. Microscopically the wall of the bladder is infiltrated with Hodgkin's tissue." Szenes (4) gives the most detailed findings in the case of a woman thirty-five years old who, along with marked involvement of the bladder, had extensive lesions in the internal genitalia. Wallhauser (5) in a recent, comprehensive review of Hodgkin's disease does not mention the bladder except to refer to Szenes' paper. Krueger and Meyer (6) collected 60 proved cases of Hodgkin's disease from the records of the Wisconsin State
Hospital from 1924 to 1934 and found the condition only once in the bladder. No case of the transformation of a Hodgkin's granuloma to a sarcoma could be found in the literature.

**Discussion**

The invasiveness, destructiveness, and marked anaplastic and neoplastic character of the cellular elements in the case here reported warrant a diagnosis of sarcoma, while the presence of Reed-Sternberg cells and the widespread granulomatous stroma point to transformation from a Hodgkin's granuloma.

There is considerable disagreement about the nature of Hodgkin's disease. Mallory (7) for many years has maintained that it is a malignant neoplasm and classifies both Hodgkin's disease and lymphosarcoma as lymphoblastoma. Ewing (8), on the other hand, voices the more commonly accepted belief that Hodgkin's disease is a granuloma which may, however, undergo sarcomatous degeneration. Among the more recent workers, Terplan and Mittelbach (2) also believe that there is a blastomatous type of Hodgkin's disease. Luse and Grave (9), quoting K. Ziegler, conclude that there is a tumor form also and report 2 such cases. Karsner (10) states that Hodgkin's disease must be considered as a "chronic granulomatous inflammatory process which may undergo transformation with assumption of malignant characters." Ginsburg (3), however, agrees with Mallory (7).

Wallhauser (5) asserts that there are no standard histological criteria for the diagnosis of Hodgkin's disease. Even Reed's (11) and Sternberg's (12) descriptions of the giant cell that bears their names and is considered so characteristic of Hodgkin's disease differ. Sternberg described a large cell with abundant clear cytoplasm and one or more large, variously shaped hyperchromatic nuclei, while Reed pictured a large cell with homogeneous cytoplasm with one or more disproportionately large, round, bean-shaped or irregularly indented acidophilic nuclei with prominent chromatin network. Dudits (13) believes that Roulet's (14) "Retothelsarkom" and Ahlström's (15) "reticulo-endothelioma of lymph nodes" are caused by the same agent as Hodgkin's granuloma and that these conditions therefore may be regarded as a tumor form of Hodgkin's disease. Brandt (16) does not even believe that Hodgkin's disease is a disease entity but merely represents the reaction of the reticulo-endothelial system to various stimuli. Medlar's (17) concept of Hodgkin's disease as a megakaryocytoma is the newest hypothesis and is a radical departure from all conventional beliefs. However, as Ahlström (15) says, "as long as the etiology of Hodgkin's disease is unknown any discussion of its morphological limits must be more or less theoretical."

**Summary and Conclusions**

A sarcomatous lesion of the bladder is described and classified as a Hodgkin's sarcoma, a term which best fits the known facts in the present state of our knowledge.
BIBLIOGRAPHY