

TREATMENT OF BLADDER TUMORS*

A COMPARISON OF RESULTS IN PEDUNCULATED AND INFILTRATING TYPES

A Report of 130 Cases

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INTRODUCTION

Tumors of the urinary bladder have been, and still remain, one of the most difficult problems of urology, particularly in the selection of proper treatment. My purpose is to show the value of the cystoscopic interpretation of a tumor as a criterion for the selection of treatment.

At the Cleveland Clinic, bladder neoplasms constitute about 4 per cent of all malignancies, and 35 per cent of all cases of malignant diseases of the genito-urinary tract. Of 512 cases of bladder tumor treated over a twenty-year period, only forty-five patients (8.7 per cent) survived for more than five years.

The 130 cases in this review were selected at random from a total of 160 cases seen at the Cleveland Clinic from 1931 to 1939. Thirty cases are not included because of the meagerness of clinical data. Prior to this relatively short period of years, cystoscopic interpretation did not receive the present emphasis, and transurethral excision of bladder tumors with the resectoscope, used extensively in our series of cases, was unknown.

Sarcoma of the bladder, which occurs in less than 1 per cent of the cases, and other rare forms of bladder tumor are not discussed in this report.

CLASSIFICATION

The majority of bladder tumors are epithelial in origin and papillary in form. All papillary tumors are considered as potentially malignant.

For clinical interpretation, bladder tumors are classified as pedunculated or infiltrating. Pedunculated tumors which may be single or multiple are villous growths surmounted on a stalk growing out from the pedicle. Infiltrating tumors are broad based, sessile, nodular or papillary, ulcerated growths, with evidence of invasion of the bladder wall. Little attempt is made to differentiate clinically the papillary from the more strictly infiltrating carcinoma, since both are malignant neoplasms necessitating radical treatment.

It is not within the scope of this paper to discuss the histology of bladder tumors. Dr. Allen Graham, of the Department of Pathology, in accord with the clinicians, bases his classification on the presence or

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absence of infiltration of the bladder wall. A classification which we tend to follow is given below.

A. Papillary

1. Non-infiltrating
 - a. Benign papilloma
 - b. Malignant papilloma
2. Infiltrating
 - a. Papillary carcinoma
 - b. Infiltrating carcinoma

B. Non-papillary

1. Infiltrating
 - a. Squamous cell carcinoma

Graham believes that grading the tumors according to their cellular differentiation is the best index of the inherent malignancy of the tumor. A grouping, combining the cystoscopic appearance, physical findings, and histologic examination, would be more practical.

In 75 per cent of our cases, the neoplasm involved the dependent portion of the bladder. In papillomas found in aniline workers, and in papillomas produced experimentally in dogs, the tumors occurred in that portion of the bladder in which urine collects, which supports the theory of a urogenous mechanism in the production of tumors.

In support of chronic irritation as a causative factor, one of our cases developed a carcinoma in a preexisting area of leukoplakia. Another case developed an infiltrating carcinoma at the seat of a lesion said to be a Hunner ulcer by the referring physician.

Fifty-five per cent of the cases of papilloma occurred in patients between sixty and eighty years of age. Seventy per cent of the cases of carcinoma were discovered in patients between the ages of fifty and seventy years. No case of malignancy was noted before the fourth decade, and only 7 per cent before the fiftieth year. Tumors in men outnumbered those in women three to one.

SYMPTOMATOLOGY

In all but thirty cases of bladder tumor, hematuria was the first symptom. Only seven patients related that there had been no blood in the urine; 37.6 per cent of the patients presented themselves more than one year following the initial bout of hematuria, which, in a number of cases, had been followed by a free interval for as long as three years. We found no characteristic features regarding the quantity or quality of the blood which in itself is diagnostic of bladder tumors.

When frequency appears before hematuria, the growth is usually near or at the bladder neck. Other urinary disturbances such as dysuria, hesitancy, intermittency, and sudden painless stoppage of the urinary stream, were occasionally present when the tumor occurred at the internal vesical sphincter. Pain and loss of weight or other constitutional

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symptoms appear quite late in the course of bladder tumors and then only in cases with extensive infiltrating carcinoma. Although obstruction of the vesical portion of the ureter was noted in 7 per cent of our cases, rarely were any subjective symptoms produced.

DIAGNOSIS

Cystoscopy is essential for the early diagnosis of vesical neoplasms. On occasion, however, roentgen examination, biopsy, and physical examination, in order of value, supply the examiner with more direct information than does the cystoscope. We place great stress upon the value of the cystoscopic and cysto-urethroscopic examination, which determines the size, character, and attachments to the bladder after the tumor is discovered. After a thorough search for other tumors, an effort is made to classify the lesion as either pedunculated or infiltrating.

Cystography and excretory urography are next in value to the cystoscope. The excretory urogram has two distinct advantages over the cystogram: (1) With the use of the excretion method, serial cystograms afford a better view of the location and type of tumor than does the single cystogram. A 5 per cent solution of sodium iodide, the media used in the cystogram, is so intensely radio-opaque that a filling defect may not be discernible. Diodrast, utilized in excretory urography, is less dense and more readily reveals the filling defect. (2) The state of the upper urinary tract and of the kidney function, and the primarity of malignant papillomas of the renal pelvis, with implants in the bladder, also may be established by excretory urography.

The value of biopsy is limited to borderline cases, in which a closed method of radiation alone is contemplated previous to cystectomy.

Rectal or vaginal examinations, although valuable, will not give any information about pedunculated growths of average size. Its greatest value is in determining induration of the bladder wall and the degree of perivesical extension rather than in establishing the presence of a neoplasm.

TREATMENT

We have found it difficult to set down any hard and fast rules concerning treatment as each case is studied and treated individually. At the Cleveland Clinic, the type of therapy is determined largely by:

1. Cystoscopic classification
2. Position of the tumor
3. Size of the tumor
4. State of the upper urinary tract

The cystoscopic classification is of paramount importance. Table 1, in correlating the cystoscopic classification and the survivals, shows the value of this procedure.

TABLE 1
CYSTOSCOPIC CLASSIFICATION AND SURVIVAL

<i>Time</i>	<i>Pedunculated</i>	<i>Infiltrating</i>	<i>Total</i>
Less than one year	15	6	21
One to two years	6	3	9
Two to three years	6	1	7
Three to four years	4	2	6
Four to five years	6	2	8
Five to six years	4	1	5
Six or more years	7	2	9
Total alive	48	17	65
Dead	6	49	55
Lost	6	4	10
	60	70	130

The position of the tumor greatly influences the selection of the type of treatment. In our series, growths on the lateral wall comprised 50 per cent, and tumors on the trigone and bladder neck, 26 per cent of the total. The Carcinoma Registry Committee points out that only 23.4 per cent of the tumors on the lateral wall can be excised without interfering with the urethra or ureters. Only a very small percentage of our cases required reimplantation of the ureter.

The size of the growth may be the deciding factor between an open and closed procedure, and between the use of surgery alone or supplementary diathermy and radiation.

Kidney infections, with dilated ureters and kidney pelves, is a contraindication to a long radical procedure, and the proceeding with uretero-sigmoidostomy. Before any radical operation is undertaken, roentgenograms of the chest, abdomen, and femurs should be negative. Metastases are more common in cases of bladder tumors than the average physician realizes.

Pedunculated tumors under 5 cm. should be treated by transurethral excision and fulguration. Fulguration alone practically has been discarded as a primary form of treatment, for with transurethral excision the tumor may be removed completely and thoroughly by one operation. Larger pedunculated tumors should be treated with cystotomy, excision, and fulguration of the base of the tumor. At this Clinic, the use of radium in the bladder has gradually decreased. The ulceration, increase in infection, and resulting symptoms offset any beneficial effect that the radium may give. High voltage roentgen therapy definitely will diminish the size and, in some cases, will destroy pedunculated tumors but will not prevent recurrence. In cases of multiple papillomas which are resistant to treatment, cystectomy should be considered. Table 2, in correlating the treatment of pedunculated tumors and survival, tends to substantiate the above beliefs.

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TABLE 2

TREATMENT OF PEDUNCULATED TUMORS AND SURVIVAL

Type of Treatment	Less than one year	1-2 yrs.	2-3 yrs.	3-4 yrs.	4-5 yrs.	5-6 yrs.	6 or more yrs.	With dis-ease	No evi-dence of dis-ease	Operative death within one month	Lost
Excision and fulguration	1	1	1	1			3 1 malignant papilloma	1			
Excision and radon		1	1 papillary carcinoma	1		1	1		1		
Partial resection							1 papillary carcinoma				
Transurethral excision	8	4	2 1 papillary carcinoma	1	6	1		1		1	6
Fulguration	6		1	1		2	1		2		
Total 60											

Of the sixty cases of pedunculated tumors treated at the Clinic, twenty-one (35 per cent) have survived three years, and eleven (18.3 per cent) have survived five years. All but four of these tumors were considered to be histologically benign.

Nine patients were treated by cystotomy and simple excision, followed by fulguration of the base. Of these, five are living more than three years and four are living six years or more without evidence of disease.

Of the six patients treated with cystotomy, excision, and radon, three (50 per cent) survived more than three years and two are living more than five years.

One patient who had a partial resection of the growth has survived for six years without recurrence.

In thirty-one cases with pedunculated tumors, transurethral excision was the procedure of choice. Because the method has been in use here for only seven years, the number of five year survivals will be low. Twenty-nine patients are still alive, eight of these for more than three years and one for more than five years. There has been no recurrence of tumor in thirteen cases. In the ten patients in whom recurrences developed, a second transurethral excision controlled the lesion.

Endovesical fulguration was used in thirteen cases with three survivals at the end of five years. However, eleven still are alive and all are free of disease. Two died of other causes.

The problem of infiltrating tumors is much more difficult and, accordingly, deserves more radical treatment. If the tumor is on the movable portion of the bladder, it may be resected with a wide margin of normal bladder wall.

TABLE 3
TREATMENT, TYPE OF TUMOR AND SURVIVAL

Treatment	Less than 1 year	1-2 years	2-3 years	3-4 years	4-5 years	5-6 years	6 or more years	Deaths		
								With disease	Operative death 1 month	Lost
Excision		1 infiltrating carcinoma						1 infiltrating carcinoma		
Resection		1 papillary carcinoma	1 infiltrating carcinoma							
Cystectomy	2 infiltrating carcinoma	1 infiltrating carcinoma			1 papillary carcinoma			1 infiltrating carcinoma	2 infiltrating carcinoma 1 papillary carcinoma	
Bilateral ureterosigmoidostomy									3 infiltrating carcinoma 3 papillary carcinoma	
Excision and radon	1 squamous cell carcinoma 1 papillary carcinoma						1 papillary carcinoma 1 infiltrating carcinoma	1 papillary carcinoma 1 malignant papilloma 1 infiltrating carcinoma	1 malignant papilloma	1
Resection and radon								3 infiltrating carcinoma		1
Radon						1 infiltrating carcinoma		9 infiltrating carcinoma 1 papillary carcinoma 1 squamous cell carcinoma		1
Transurethral excision	2 infiltrating carcinoma			1 papillary carcinoma				1 infiltrating carcinoma 1 papillary carcinoma 1 squamous cell carcinoma	1 infiltrating carcinoma	1
Endovesical radon				1 infiltrating carcinoma						
X-ray								14 unknown		
Total 70										

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We have used fulguration by the loop and ball electrodes through a suprapubic incision, or radon only as palliative measures.

Cystectomy should be performed in tumors about the base or in large tumors involving the movable portion of the bladder, but not in an elderly or enfeebled patient. One should not wait until all other methods have failed and the patient has a hidden metastasis before advising cystectomy. In advanced cases, usually with dilatation of the ureters, renal infection, and impairment of function, less radical procedures are, of necessity, employed.

Table 3 correlates the treatment, type of tumor, and survival. Of the seventy cases of infiltrating tumors treated, seven (10 per cent) survived three years and three (4.2 per cent) survived five years or more. Only seventeen (24.1 per cent) of the total remain alive.

Of three patients having cystotomy and partial resection of the bladder, all are alive with one surviving more than three years.

Of two patients treated by cystotomy and excision of the tumor, only one is alive two years postoperatively.

Cystotomy with excision and implantation of radon seeds was used in nine patients. Of these, four are dead and two have survived five years without recurrence.

Of four patients treated with cystotomy, resection and interstitial radiation, three died with the disease and no report is available on the other.

Cystotomy with the implantation of radon seeds was the method of choice in thirteen patients. Eleven are dead. One five year survival was procured.

Of eight patients treated exclusively by transurethral excision, none has survived five years and but one survived three years.

Fourteen hopeless patients were treated by roentgen therapy and all are dead.

Of the 130 patients studied, twenty-eight (21.5 per cent) survived three years while fourteen (10.45 per cent) survived five or more years. In 1936, the Carcinoma Registry Committee reported a crude five year survival rate of 23 per cent. Fifty-five (42 per cent) of the total number of patients have died. The majority of the deaths were in cases with infiltrating carcinoma, of which forty-one (74.5 per cent) of the cases died within the first year. The chief cause of death was usually a severe infection in the bladder and kidneys.

FOLLOW-UP

Operation constitutes only the first phase of the management. The patient should be warned of the marked tendency for bladder tumors to recur, and advised to come in at regular intervals for cystoscopic examina-

tion. Our routine is to have the patient come in three months after operation, and again three months later. If the bladder is clear in one year, yearly examinations are advised thereafter. Only by cystoscopic examination on each follow-up visit can small recurrences be recognized at a time when they can be destroyed easily.

CONCLUSIONS

1. The management of bladder tumors still offers many difficulties to the surgeon.

2. A cystoscopic classification of tumors, as pedunculated and infiltrating, based on the presence or absence of infiltration of the bladder wall, is offered. The classification is valuable in selecting the proper treatment and determining the prognosis. Pedunculated tumors offer a much more favorable prognosis than do infiltrating neoplasms. Eighty per cent of the patients with pedunculated tumors are alive as compared to 24.2 per cent with the infiltrating type.

3. All vesical neoplasms are potentially malignant.

4. The importance of painless, intermittent hematuria, the initial symptom in the majority of our cases, should be emphasized to the public; 37.6 per cent of our cases presented themselves more than one year following the initial bout of hematuria.

5. An effort has been made to demonstrate that no one method of treatment can be adapted to all cases.

6. Excellent results may be obtained by the transurethral excision of pedunculated tumors under 5 cm. in size.

7. Wide resection of infiltrating tumors is to be carried out whenever possible. Interstitial and external radiation has not controlled this type of neoplasm. Of twenty-eight patients treated by these methods, only two are alive. One has lived three years and the other five years.

8. Cystectomy should be done in less advanced and carefully selected cases. In the presence of upper urinary tract infection, cutaneous ureterostomy is the procedure of choice.

9. The majority of fatal cases die from severe bladder and kidney infection within a year. Rarely does one die a "cancer death."

10. Adequate follow-up examinations with the cystoscope are strongly advised.