

DEEP ROENTGEN-RAY THERAPY IN THE TREATMENT OF CARCINOMA OF THE BLADDER *

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In 1923, and again in 1924, I presented before the American Roentgen Ray Society the results obtained in the Brady Urological Clinic, in bladder carcinoma, by means of deep roentgen-ray therapy.

The basis of the present report comprises 120 cases of bladder tumors divided as follows:

1. Papillomas, benign and malignant.
2. Noninfiltrating papillary carcinomas.
3. Infiltrating carcinomas, superficial and deep.

The foregoing groups of tumors have been observed over a period of four years.

One of the most serious complications in the treatment of bladder tumors, following irradiation of any kind, is a burn. In a certain number of instances, local and systemic reactions which, at times, reach alarming proportions undoubtedly occur.

It is well known that when a patient is exposed to a series of roentgen-ray treatments a cumulative effect is produced, and this should be closely watched for from day to day by the urologist himself. It has seemed to me that the cumulative effect of roentgen rays on a patient occurs in direct proportion to the debilitated physical condition of the patient. Thus, an old man with a papillary carcinoma of the bladder, greatly debilitated from long continued suffering, requires more careful watching during the course of his deep roentgen-ray therapy than would a younger and a stronger man.

Among the earliest symptoms of radiation intoxication may be mentioned nausea, vomiting, prostration, diarrhea, rectal burning, and tenesmus. Repeated examinations of the blood should be made to determine the effects on the white blood corpuscle count in particular, though counts of the red blood cells and hemoglobin estimations should also be made. The number of white blood cells is reduced much more rapidly following irradiation than is that of the red cells. It is rarely safe to treat a patient further when his white count has fallen below 4,000.

The necessity of careful and close cooperation of the urologist with the roentgenologist is therefore obvious. Many of the ill effects could be avoided if the roentgen-ray treatments were more closely observed by the roentgenologist and the urologists, and not left so largely to mere technicians.

Despite the disturbing reactions that are not wholly avoidable, the relief afforded to two symptoms of bladder cancer, namely, root pains and hematuria, justifies the treatment. Even when no other benefit is obtainable, these two distressing symptoms rarely fail to be relieved with roentgen-ray therapy.

There is no subject in urology concerning which opinion has differed more from time to time than that of the treatment of bladder tumors. For many years the sole treatment consisted of excision, when possible, of the tumor, with or without some portion of the bladder mucosa. Later, a more radical procedure, which consisted of resecting the surrounding bladder wall, was carried out. Thus Young, in 1913, reported the results obtained in 117 cases in the Johns Hopkins

Hospital, and I mention his report simply to allow comparison with the results of methods that can be employed today. Of his tumors, 83 per cent were malignant, and excision as practiced then was nearly always followed by recurrence; this was true not only of the malignant growths, but of the benign as well.

After the introduction of fulguration by Beer in 1910, it was shown that both the benign and the malignant papillomas could be successfully handled by this intravesical method with results much superior to those obtainable by any surgical procedure. It was soon found, however, that though fulguration was successful in the handling of papillomas, it was worse than useless in the treatment of papillary carcinomas (either superficial or infiltrating).

With the introduction of radium therapy (by Pasteau and Degrais, and by Schüller, in 1913) and later of deep roentgen-ray therapy, and still more recently of diathermy, a new chapter has been added to the treatment of bladder tumors, and by the application of these measures it has been possible in a considerable number of cases to destroy extensive infiltrating growths that were hopelessly inoperable.

Experience has shown that with the use of intravesical applications of radium, superficial papillary carcinomas (which comprise about 15 per cent of all bladder tumors seen) can be handled successfully; yet no success is to be obtained by this method of irradiation when the tumor is deeply or extensively infiltrating. Nor when a superficial or noninfiltrating papillary carcinoma involves a large extent of bladder surface is intravesical treatment with radium satisfactory, owing to the fact that too large an area has to be treated.

It has been the experience in our urologic clinic that about 10 per cent of the infiltrating carcinomas are either sufficiently circumscribed or so situated as to permit a successful radical resection. But not infrequently a tumor, even though comparatively small, is located on the trigon, or involves the vesical orifice in such a way that the performance of radical excision with any hope of success would mean the transplantation of the ureters, the removal of the posterior portion of the prostate, and the excision of the trigon—a surgical procedure that is technically difficult, and now rarely justifiable.

Today, by a combination of fulguration with the application of radium to the surface of tumors through the urethra, on the one hand, and by destruction of the carcinoma by the cautery after suprapubic incision, on the other hand, about 75 per cent of tumors can be removed. This leaves about 25 per cent of hopeless tumors that occupy positions which render them inoperable, or involve such extensive areas of the bladder wall that neither surgery nor intravesical radium treatment offers any chance of success.

In the later development of radium therapy, it has been demonstrated that in a certain percentage of the hitherto hopeless infiltrating cancers the tumor can be destroyed by opening the bladder suprapubically and implanting either radon tubes or radium element in the tumor area. Recently, because of the sloughs from deep radium burns produced by bare radon tubes, we have discontinued their use, and have been employing in the type of case mentioned only thoroughly screened radium needles.

From the statistics quoted, it is clear that there still remain many cases unsuitable for fulguration, for intravesical radium treatment, for resection, or for

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treatment by radium needles; in such cases, if benefits are to be obtained, some other measure must be applied. It is just here that deep roentgen-ray therapy, with its modern and improved methods of application, seems to offer real help.

In 1923 I studied a series of sixty-seven cases of vesical carcinomas treated by different means of radiation, as follows:

1. Twenty-five cases treated by implantation with emanation points or needles.

2. Twenty-one cases treated with deep roentgen ray alone.

3. Twenty-one cases treated with a combination of deep roentgen ray with intravesical applications of radium.

I shall discuss only the results in the series treated by deep roentgen ray alone. Of these twenty-one cases, all but four were extensive infiltrating papillary carcinomas.

One of these four cases was an extensive superficial noninfiltrating papillary carcinoma, which received two complete series of roentgen-ray treatments, the dose amounting to 130 per cent each time without any benefit.

A third series of deep roentgen-ray treatments, in combination with radium applied to the surface of the tumor through the urethra, caused a rapid disappearance of the growth.

In another case, a large papillary mass responded promptly to roentgen-ray treatment, and later was seen cystoscopically to be made up of four separate tumors which had superficially fused.

A third case was that of a large noninfiltrating papillary carcinoma covering the whole posterior bladder wall, which responded promptly to roentgen ray, and the tumor disappeared.

The fourth case of this series was a superficial papillary carcinoma in a very elderly man, 88 years old.

Of these four superficial noninfiltrating carcinomas covering a large area of the bladder, three were apparently destroyed under roentgen-ray therapy alone, but the first case mentioned was a complete failure under roentgen ray alone. In this case, however, a prompt response was obtained to roentgen-ray treatment in combination with a small amount of radium applied to the growth through the urethra.

Seventeen cases were all extensive infiltrating carcinomas, many of the patients being almost moribund, and only a fractional part of the roentgen-ray treatments could be given. In none of these cases did we secure any results from the deep roentgen-ray treatments alone, with but two exceptions. One patient was explored with the possibility of implanting the growth with radium needles, but the carcinoma was found to have invaded at least two thirds of the bladder wall with an extensive extravascular growth. The wound was closed, the bladder not being opened. Ten days later, roentgen-ray therapy was started. On completion of the roentgen-ray treatment, the patient left the hospital with no improvement in his symptoms. He was voiding every few minutes with agonizing spasms, although he was receiving about 12 grains (0.8 Gm.) of morphine daily. Two months later the patient's son reported that his father was well on the road to recovery, urinating without pain and at normal intervals, and that he required no morphine. The patient was not examined by cystoscope. The improvements, in this case, can be attributed only to the deep

roentgen-ray therapy, and the patient lived fourteen months in comparative comfort. In the other case, a large papillary carcinoma, which failed to respond to intravesical radium therapy over a period of several years and which became an extensive infiltrating growth with a palpable mass above the symphysis, promptly responded to one series of deep roentgen-ray treatments, and the patient has remained perfectly well for two years—the mass above the symphysis disappearing along with the marked frequency of urination and pain. This result can also be attributed only to the roentgen ray.

In five of these seventeen cases, in which no improvement was obtained from the roentgen-ray treatments, the bladder was subsequently opened and the tumors implanted with radium. In two of these the cancer disappeared, and no tumor could be found cystoscopically. In two, no benefit was obtained; five cases were lost sight of.

CONCLUSIONS

Our experience up to this time would seem to warrant the following conclusions:

1. The best treatment for superficial papillary carcinoma, whether localized or extensive, is a combination of deep roentgen-ray therapy with applications of radium applied directly to the surface of the growth. Radium alone has been very successful in handling this type of case, but frequently so much radiation is required that the destruction of the tumor is followed by a severe radium ulceration. In our experience, the results obtained by the combination of deep roentgen ray with radium are better when the tumor has received from 600 to 800 milligram hours of radium before the roentgen-ray treatment is started.

2. By the combination of radium with roentgen-ray treatment as outlined, most of these tumors can be destroyed with a minimum amount of injury to the bladder, and in many instances with but little or no irritation of the bladder mucosa.

3. When the growth is an infiltrating carcinoma, though still operable, we believe that radical resection should be carried out, since it offers the greatest chance of complete cure.

4. Twenty-five per cent of the infiltrating growths in our series occupy positions that render them inoperable, or they are so extensive that radical removal is impossible. In this group, when it is possible to apply radium directly to the growth, both radium and deep roentgen-ray treatments should be given a trial, for in a certain number of the cases favorable results can be obtained by this method alone. But in cases in which this procedure does not yield the results hoped for, or in cases in which one feels that the growth is sufficiently localized to warrant implantations of radium needles, the bladder should be opened suprapubically, and screened radium needles should be implanted throughout the growth. But if the growth is so extensive that a total of more than 2,500 milligram hours is necessary, in order thoroughly to destroy the cancerous areas by implantations, this method should not be considered. Within the last few years, diathermy has been used in a number of clinics. Our experience with this form of therapy is too recent to warrant the drawing of any definite conclusions.

5. Finally, the great tendency to recurrence of tumors of the bladder, following their apparent destruction by fulguration, irradiation or deep roentgen-ray treatment, makes it imperative that patients return at frequent intervals for cystoscopic examinations. In at least

five of our patients, in whom recurrences ultimately resulted in death, complete cures might well have been obtained had they returned regularly for observation and treatment before the recurrences had become too extensive. In a few cases in which the patients have returned for observation, the recurrences, when found, have responded well to radium alone. This is especially true of the noninfiltrating papillary carcinomas. Even in cases that are incurable, regardless of the treatment employed, deep roentgen-ray treatment is an excellent palliative measure, in that it tends to control hemorrhages and to decrease nerve root pains.

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THE TREATMENT OF CARCINOMA OF THE BLADDER BY RADICAL SURGICAL METHODS*

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The idea that carcinoma originates in a single area is borne out in the case of carcinoma of the bladder. Furthermore, carcinoma beginning in the tissues of the bladder usually remains confined to these tissues. Only in rare instances does it metastasize to distant regions or extend beyond the confines of the bladder and perivesical tissues. Death occurs indirectly from the effects of carcinoma of the bladder but directly from secondary infection in the surrounding tissues and in the kidneys. Because of the tendency for carcinoma of this organ to remain local, it should especially lend itself to radical resection, and the results of radical surgical treatment in these cases should be better than they are at present.

The functioning mechanism of the bladder depends on the sphincter muscles controlling the outflow, the ureteral orifices through which the urine enters the bladder, and, in operations on the bladder, a sufficient amount of bladder wall to contract and expel the urine. If the bladder is to be of any use, the sphincter control must be preserved. So far as the ureters and ureteral orifices are concerned, one or both of these structures may be transplanted to other parts of the bladder; or, if malignancy involves the lower end of one ureter, it would be justifiable to ligate this ureter, provided the opposite ureter is functioning. Under these circumstances a permanent ligature should be used, and the removal of the kidney later will be necessary in only a small proportion of the cases, probably those in which considerable renal infection existed. Carcinomas of the bladder most often start near one of the ureteral orifices, so that removal of the lesion involves some method of disposing of the ureter. Transplantation into some other quadrant of the bladder should be the procedure of choice, but for some reason, in the cases in which we followed this plan at the clinic, the percentage of recurrence was higher than in those in which the ureter was ligated. It is possible that, in preserving the lower end of the ureter in order to reimplant it, we unknowingly left in a small amount of carcinomatous tissue. Whenever one ureter can be ligated without serious consequences in cases in which the renal function is known, and whenever it seems to offer a much better outcome, we have been inclined recently to remove the lower few inches of the ureter

with the growth in those cases in which subtotal cystectomy is performed. This is carried out only in cases in which the ureter's proximity to the growth makes its preservation a much less radical operation.

The question of whether resection of the bladder should be carried out by an extraperitoneal or by a transperitoneal approach, it seems to me, depends entirely on the situation of the neoplasm and on whether it is necessary to open the peritoneum for better exposure. Formerly, in many cases, I opened the peritoneal cavity widely and packed it off during resection of the bladder. Some time ago it was found that a better plan, when it was an advantage and a necessity to open the peritoneum, is to open the peritoneal cavity first and excise the involved portion of the peritoneum attached to the growth. The peritoneal flap at the base of the bladder is freed from the bladder and surrounding tissues, and then sutured to the flap from the anterior parietal peritoneum, in this way closing the peritoneal cavity again before resection of the bladder is carried out. When we first developed this transperitoneal method of resecting the bladder we thought it was original, but we later learned that the same method had been used in some of the Russian and French clinics. One should not hesitate to perform a transperitoneal resection if anything may be gained by it. Many times we have opened the peritoneum and excised large pieces, and convalescence has been practically the same as when the extraperitoneal route was employed. The peritoneal cavity should be closed completely and not drained after transperitoneal resection.

The results of radical operations for carcinoma of the bladder have not been as good as expected, and yet they are about the same as those obtained in radical operations for carcinoma of the breast, stomach, colon and other regions. Carcinoma originating about the head, face and neck is in some ways comparable to carcinoma of the bladder, particularly in that it remains a local disease. Less than 1 per cent of cases coming to necropsy following death from carcinoma of the head, face and neck show any extension of the disease below the clavicle. Death is usually due to infection and pneumonia. The ultimate results in certain cases of carcinoma of the face are good because they are less malignant at the onset; on the other hand, some of the more virulent malignant growths in this region show about the same proportion of satisfactory results as carcinomas of the bladder.

A review of the literature shows that the results of surgical treatment of tumors of the bladder are not altogether discouraging. Young and Scott,¹ in reviewing 380 cases treated at the Brady Institute, state that resection of the tumor with removal of a wide margin of bladder wall gives good results in the vertex and anterior and upper lateral walls, and that good results also follow resection of the trigon and ureteral areas. They had 27 per cent of five-year cures in fifty-one cases in which the wall of the bladder was resected. If the growth is extensive they consider the risk of operating too great, and say that 95 per cent of patients with benign papillomas, 75 per cent with malignant papillomas and 25 per cent with infiltrating carcinomas are probably curable by the judicious use of fulguration, radium, the electrocautery and careful radical resection.

* From the Division of Surgery, Mayo Clinic.
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1. Young, H. H., and Scott, W. W.: The Results Obtained by Various Methods in the Treatment of Tumors of the Bladder, New York M. J. 118: 262-268 (Sept.) 1923.