TREATMENT OF THE MALIGNANT PROSTATE

BY

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Whilst the treatment of urinary obstruction due to innocent forms of enlargement of the prostate has made great progress during the last twenty years, the treatment of obstruction due to carcinoma still remains disappointing. The fact that malignant disease of the prostate is by no means so rare a condition as was thought at the end of the last century makes our lack of progress particularly unfortunate. Exactly what is the ratio between innocent and malignant enlargement is difficult to determine, but various figures ranging from 13 to 25 per cent. have been given. The incidence of prostatic carcinoma is at any rate sufficiently high to justify a general survey of the present position of its treatment.

Surgical Treatment

This may be subdivided into radical and palliative, by radical treatment being implied an attempt to extirpate the carcinoma, and by palliative, surgical measures that limit themselves to relieving symptoms. As in the case of carcinoma elsewhere in the body complete removal of the carcinomatous tissue by the scalpel would be the ideal form of treatment. This being so, many attempts have been made during the last twenty years to cure carcinoma of the prostate by this means. Prominent among those who have made efforts in this direction has been H. H. Young of Baltimore. As an exponent of perineal prostatectomy, it was by the perineal route that his attack was carried out. In a paper published in the *American Journal of Surgery* (April, 1935) he analyses his results.

Fifty patients were submitted to operation and of these four died, giving an operative mortality of 8 per cent. Thirty-three of the survivors were alive and well five years or more after leaving the hospital, and thirteen had survived for a period of seven years or more without a recurrence. Eleven patients died with recurrences or metastases.

The statistics supplied by operators using the suprapubic route are less complete, and would appear to show less satisfactory results. Nevertheless Marion, writing in 1928, expresses the opinion that the suprapubic route is in no way inferior to the perineal for the removal of a malignant prostate. He points out that neither by the perineal nor by the suprapubic route can the lymphatic glands be dealt with, and the suprapubic permits of excision of the vesicles as easily as does the perineal. Most surgeons have come to the conclusion, however, that the results of radical operation are disappointing, and few are prepared to attempt it except in the earliest stages of the disease.

Lymphatic Spread

This abandonment of an ideal, although it may be unfortunate, is fully justified, for the fact that the lymphatics cannot be dealt with puts a narrow limit on the surgery of the malignant prostate. Had the surgery of the malignant breast been subject to the same limitations its results would have been equally poor. The secondary invasion of the lymphatics would appear to be as rapid in the case of the prostate as it is in the

case of the breast. E. R. Mintz and G. G. Smith, in the *New England Journal of Medicine* of September, 1934, state that in sixty out of a hundred cases of malignant prostate examined in the post-mortem room there was an obvious involvement of the retroperitoneal glands. Pasteau also reports extension to the lymphatics in 80 per cent. of necropsies.

There is another point to be borne in mind when we survey the claims made by the exponents of the radical operation—namely, that carcinoma of the prostate is, as a rule, of very slow growth. It is by no means uncommon for a patient once he has been relieved of his obstruction to survive for a period of five years or more. As Young's series includes many early cases one cannot help speculating how long they would have lived had no radical operation been undertaken. Moreover, the fact that clinically no recurrence has been detected is no guarantee that such is actually the case, for who can be certain when palpating the indurated site of a prostatectomy that the induration is due only to the presence of fibrous tissue and not to the existence within that tissue of islands of carcinomatous cells?

In apparently discounting Young's results and his advocacy of radical operations, I have no desire either to show lack of appreciation of his brilliant surgery or to suggest that radical operations have no place in the treatment of the malignant prostate. I am simply emphasizing the fact that it is only the very earliest cases that are amenable to such a form of treatment. It is, above all, the secondary type of carcinoma—that is to say, the prostate which, once innocent, now arouses a suspicion of malignancy—that should be promptly extirpated. Recent statistics have shown that 14 per cent. of innocent enlargements suffer malignant change, so that even if surgery were confined to this type alone it would still have an important place in the treatment of malignant disease.

Early Diagnosis

Since success in surgery depends on early diagnosis it is important to know what signs should arouse a suspicion of malignancy. The most important is the presence of a hard area within the prostate. If this is discovered it can only be due to one of three causes: (1) a malignant deposit, (2) a prostatic calculus, and (3) a collection of distended acini surrounded by induration. The second of these three causes can be confirmed or disproved by an x-ray, and a pelvic radiograph should always be asked for. Not only is this necessary in order to exclude the presence of a calculus, but also in order to make certain that deposits in the bones of the pelvis do not already exist. Together with the vertebrae, the pelvic bones are the commonest site for secondary deposits. On three occasions in my experience, in spite of the fact that the diagnosis of carcinoma was in doubt owing to the insignificance of the signs noted on rectal examination, extensive disease of the pelvic bones was revealed by a radiograph. In one of these cases the nodule in the prostate was so small that had the patient not been examined under an anaesthetic it would probably have been missed.

A second sign of importance in diagnosis is induration of a vesicle. It is true that vesicular hardening is frequently found in association with an innocent prostate, but such a discovery should always be regarded with suspicion. The extraordinarily high incidence of vesicular extension in cancer of the prostate has long been known, and Young and Frontz have estimated that this organ is invaded in forty-two out of sixty-three patients operated upon for malignant disease of the prostate.

Prostatic Secretions

The third aid to early diagnosis, the value of which has not yet been confirmed by other writers, may be the character of the expressed prostatic secretions. S. W. Mulholland, in the *Proceedings of the Staff Meetings of the Mayo Clinic* (December 16th, 1931), states that if the secretions obtained by massage from a malignant prostate are examined microscopically they will be found to contain a cell which is about two or three times the size of an ordinary polymorphonuclear leucocyte. These large cells tend to occur in clumps, and they are often so closely packed together that their outline is distorted. This observation of Mulholland's has not received much attention, and it is to be hoped that other observers will confirm or contest it. Difficulty is sometimes experienced in differentiating a fibrous prostate from one that is the site of scirrhous carcinoma. The characteristic cell obtained by massage of a fibrous prostate is the leucocyte, and if these clumps of larger cells can be shown to be pathognomonic of carcinoma, examination of the expressed prostatic fluid should prove a valuable aid to differential diagnosis.

Such well-known characteristics of the malignant prostate as fixation, asymmetry, disappearance of the central sulcus, and changes in the overlying vesical mucosa seen through the cystoscope occur, of course, so late that they are of little value in establishing an early diagnosis.

Once the suspicion of malignancy has been aroused immediate operation is indicated, however trifling may be the symptoms of which the patient complains. In cases where the surgeon is so much in doubt that he hesitates to advise an immediate operation, he would be well advised to insist on an examination under an anaesthetic, since with good muscular relaxation a more careful palpation and appreciation of the texture of the prostate can be obtained.

Operative Technique

It is usually the prostate that has started as an innocent one and undergone malignant change that is subjected to removal. In this type of case infiltration of the capsule occurs later than in a primary carcinoma starting in the posterior lobe. Even if the prostate cannot be enucleated entirely by the finger it can generally be removed by a combination of enucleation and dissection. Sometimes it is the difficulty in enucleation and the cartilaginous feel of the prostate that confirms what, up till that moment, has been only a suggestion of malignancy. When this happens every effort should be made to remove not only the whole of the gland but also the vesicles, since extension to these structures occurs early in the disease.

Surgery and Radiotherapy

The question arises whether, after extirpation of a malignant prostate, treatment by means of radium or deep x-ray therapy should be instituted. It is almost certain that, if the prostate has proved difficult to enucleate, the prostatic capsule itself will be the site of malignant infiltration. The treatment of this residual focus is therefore a necessity if the patient is to be safeguarded from an early recurrence. Two methods of treating the capsule are possible: radium and deep x-ray therapy. I agree with Marion when he states that a satisfactory introduction of either needles or radon seeds into the capsule is not only difficult after prostatectomy but also gives very poor results. I have not found, however, that rapid extension is encouraged by such

treatment. But whilst there are difficulties in applying radium to the capsule there are none attached to the use of x rays, and a course of deep x-ray therapy should be prescribed as soon as the patient has recovered from his operation. At present it is too early to be able to assess the precise value of supplementary deep x-ray therapy, but since employing it I have had none of those rapid recurrences of symptoms that previously made the removal of an obviously malignant prostate so disappointing a procedure.

Treatment of Inoperable Carcinoma

In these cases surgery is confined to the relief of obstruction. Advances in the technique of per-urethral resection have placed at our disposal a measure that has many advantages over the establishment of a permanent suprapubic drain. Patients show marked differences in their reaction to a suprapubic drainage tube. At one end of the scale are those who readily accept its imposition, and may even assert that the artificial method of emptying their bladders is as satisfactory as the natural one. At the other are the patients who complain that they would sooner die than continue to live with such an encumbrance. These differences depend not only on the social position of the sufferer, his enjoyment of leisure, and his possession of the means of obtaining good nursing, but also on his psychological make-up. It is therefore an advantage to be able to offer the alternative of an attempt to restore natural micturition by means of a per-urethral operation. Only one condition must be satisfied in order to make this possible—namely, that the urethra should admit the passage of a McCarthy electrotome. Distortion of the prostatic urethra is often more marked and always more unyielding in the case of a malignant than in that of an innocent prostate, and as a result difficulty is often experienced in instrumentation. Sometimes this can be overcome by means of a preliminary dilatation with metal bougies, but it may necessitate the use of an instrument of smaller calibre than that usually selected. It has been advanced as an argument against attempts to restore micturition by per-urethral resection that cutting through malignant tissues with a diathermy current may stimulate the growth of the carcinoma. This objection is, however, a theoretical one, and there is nothing to lead one to suppose that it is of practical importance. Experience does not show that resection provokes activity in the growth, and as a rule the sufferer from a malignant prostate supports his operation well. Haemorrhage is less likely to prove a complication than in the case of an innocent enlargement, and since carcinoma of the prostate is usually of slow growth, early obliteration of the channel is not often noted. It must, of course, be realized that restoration of micturition by per-urethral resection is generally only attempted in the scirrhous type of malignant prostate, where the total increase in volume is small and the extension of growth slow. For the larger type of prostate suprapubic drainage is preferable.

Surgical Relief of Pain

Some reference should be made to surgery undertaken purely for the relief of pain. The amount of pain occasioned varies markedly in different individuals, and sometimes, when nerve trunks are involved, may become agonizing. For the relief of pain in such cases two procedures have been advocated: resection of the pre-sacral nerves and chordotomy. In my experience the results of the first-named operation are erratic and unreliable, as is to be expected when we consider how different may be the causes of the pain. It is only by

chordotomy that complete freedom from pain can be promised, but as the operation is a severe one it should be reserved for exceptional cases. In my own experience the necessity for chordotomy has only arisen once.

Treatment by Radiotherapy

Two alternative lines of treatment are here available: radium and deep x -ray therapy. If the former be selected the radium is applied as needles or as radon seeds, inserted into the substance of the gland, the old methods of application by means of a receptacle in the posterior urethra or rectum having been abandoned. I prefer to insert seeds by means of an introducer thrust through a perineal incision. It must, however, be confessed that the results are disappointing, and Young's comment that "in some cases the duration of life appears to be distinctly lengthened, and it may be that a few cures have been obtained" represents the optimum to be expected.

A more promising line of treatment is by means of deep x -ray therapy. Writing in the *Journal of Radiology* in 1926, Sir John Thomson-Walker published an account of forty-eight cases of malignant prostate treated by means of massive doses of x rays. In five of these cases fairly advanced carcinomata disappeared for a sufficiently long time to encourage the hope that they would not recur. In another fifteen cases a temporary improvement was produced followed by recurrence, making altogether twenty cases, or 41.6 per cent., where the growth was profoundly altered by the x rays. Since the publication of Thomson-Walker's paper great advances have been made in the technique of this form of treatment, and I believe that with these advances there will be an equal improvement in the results obtained. That this opinion is not supported by statistics in the present paper is due to the fact that the number of malignant prostates I have submitted to modern methods of deep x -ray therapy is not yet sufficient (some dozen cases) to justify the publication of statistics, nor can I find reliable figures from other sources with which to supplement these. But although figures are at present lacking it is still possible to draw certain conclusions on the subject.

Conclusions

The first of these is that, if possible, patients should be referred to the radiologist without having been submitted to suprapubic drainage. The presence of a drainage tube and the inevitable infection of the bladder associated with it adds enormously to the discomfort of the reaction provoked by the treatment. If the difficulty in micturition or the amount of residual urine is such that relief of the obstruction is necessary, per-urethral resection is infinitely preferable to suprapubic drainage. Another conclusion that can be drawn is that there exist wide variations in the response of different patients. I have had two advanced cases of malignant disease which when examined two months after the conclusion of a course of deep x -ray therapy appeared to have normal prostates. Other cases treated by the same radiologist, with the same intensive doses, remained exactly as they were, even though some improvement in symptoms had been noted. What determines this difference, and whether it lies in some unknown factor in the patient himself or in some difference in the radio-sensitiveness of the cancer cells, it is impossible to say. Perhaps, as Thomson-Walker has stated in the publication already referred to, some means will be found of estimating the radio-sensitiveness of a patient so that unpromising cases may be spared the disappointment of an ineffectual and irritating treatment. It is indeed to be hoped that closer co-operation

between the urologist and the radiologist will lead not only to a more accurate estimation of the value of radiotherapy in carcinoma of the prostate, but also to an actual improvement in the technique and management of the cases during treatment. In the meantime, I believe that radiotherapy is the most valuable agent at our disposal in the treatment of inoperable carcinoma of the prostate, and is, too, a valuable supplement to surgical removal.

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PROSTATIC RESECTION

A SIMPLIFIED TECHNIQUE

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Having performed diathermic resection by the suprapubic route in ten cases, with apparently completely satisfactory results, I feel encouraged, in spite of the small number of cases, to place a short description of this simple method of prostatic resection on record. It has occurred to me that it might prove of interest to those surgeons who, through lack of the requisite type of operating cystoscope or of sufficient opportunities to acquire skill in cystoscopic methods, feel themselves unable to carry out the orthodox operation per urethram. It has been my experience that about 40 per cent. of cases of prostatic obstruction are not fit to stand the shock, sepsis, and loss of blood entailed in the performance of a complete prostatectomy at the time when they first come to a surgeon for advice. Perhaps half of these are unfit as the result of exceptional delay in seeking advice for their urinary difficulty. The remaining half may be unfit from a variety of other morbid conditions which, either alone or in conjunction with the results of prolonged urinary back-pressure, render them definitely unfit for radical operation by any method.

I have found that the use of the diathermic method of partial resection allows about half of these otherwise inoperable cases to receive the benefit of surgical relief without subjecting them to any unduly high risk. The greatly diminished shock, the lessened post-operative pain, the almost complete bloodlessness of this operation, and the very small area of damaged bladder surface are the factors which contribute to the greater safety of diathermic methods in cases presenting high surgical risk. Perhaps the largest single factor contributing to the low mortality of this type of operation is the lessened element of septic absorption resulting from the small area of damaged tissues and the fact that all the vessels and lymphatics are automatically sealed during the process of resection. This is evidenced by the smooth and afebrile convalescence enjoyed by all the cases I have so far dealt with.

Pre-operative Treatment

In preparing the patient for operation, cases requiring preliminary drainage should have this done by the use of a urethral catheter in preference to the employment of a suprapubic tube if they are destined to have their prostates resected by the suprapubic route. My reason