CONSERVATIVE TREATMENT OF CANCER OF THE PROSTATE: SOME CLINICAL OBSERVATIONS

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MANY statistical reviews have reported the results of various methods used in the treatment of cancer of the prostate. This report presents some typical cases as well as general observations of the effectiveness of conservative measures in the treatment of prostatic carcinoma. Conservative therapy is mainly hormonal treatment, but it also includes simple orchiectomy (in 20 per cent of patients) and even an occasional transurethral resection for the relief of obstructive urinary symptoms.

It is generally agreed that only about 10 per cent of patients are suitable candidates for so-called "radical prostatectomy." Thus, the remaining 90 per cent of patients must be treated by conservative measures. Experience also suggests that these measures may give results in the other 10 per cent of patients which compare favorably with those obtained following radical operation.

Diagnosis

Diagnosis is first made from digital rectal palpation of the prostate; the experienced finger is remarkably accurate. A roentgenogram of the pelvis is useful to rule out (or in) prostatic calculi. When necessary, we obtain a histologic diagnosis from tissue obtained by needle biopsy. Biopsy occasionally has not been done, as in cases of typical advanced cancer or in certain instances of radiographically demonstrable metastasis.

Categories of Cancer

In reviewing the records of patients with cancer of the prostate, one is impressed by the fact that this is not a uniform disease. Cases may be roughly separated into three groups: (1) slowly growing cancer that runs a chronic course; (2) rapidly growing cancer, often far advanced when first seen, which swiftly progresses to fatal termination in spite of all treatment; and (3) an intermediate group of hormone-dependent cancers that may be controlled for long periods by appropriate treatment.

The following is a typical example of cases in group 1.

A 57-year-old man was first examined by us in 1951, at which time a general physical examination revealed a questionable nodule in the left lobe of the prostate. His history indicated that this was first observed six years previously but was disregarded. Three years before our examination, in another city, a urologist noted this nodule and recommended that the patient take stilbestrol. The advice was followed for six weeks, but there was no apparent change in the nodule, and medication was discontinued. In view of this history, we advised continued observation without treatment. He returned in

November, 1953, with the prostatic findings essentially unchanged, but there were pressing reasons for definitive histopathologic diagnosis. Accordingly, a needle biopsy was performed and the specimen of tissue was reported as adenocarcinoma, grade 3. The patient was given stilbestrol, 5 mg. each day. He returned for three follow-up examinations in 1954, apparently in excellent health and with good clinical response to estrogens.

In July, 1956, he returned, in excellent health, but he had voluntarily discontinued taking stilbestrol some six months before, because his breasts became sore. There was no detectable change in the prostate, and the results of the roentgen studies were negative, so we consented to observe him closely while omitting the estrogen therapy; he was warned of the risk involved. In February, 1958, he returned in excellent health, reporting that he was vigorously active in a thriving business. Recent word finds him in continued good health, *now 14 years after a nodule was first palpated in the prostate, histologically verified as adenocarcinoma.*

At the other extreme we may summarize a case representing group 2 (rapidly growing, irreversible cancer).

A 67-year-old man was first examined in November, 1952. Palpation revealed a hard, nodular, fixed prostate from which a perirectal mass extended. A specimen obtained by needle biopsy revealed undifferentiated prostatic carcinoma. There was no roentgen evidence of bony metastasis. A bilateral orchiectomy was performed and the patient was given stilbestrol. Six months later he returned because of pain in the hip and the back. A roentgenogram of the spine and the pelvis showed extensive metastatic lesions in all bones. He was given palliative roentgen therapy, but when last examined in July, 1953, *eight months after his first examination,* he was approaching a terminal phase.

These two cases illustrate the extremes in clinical behavior of prostatic cancer. Between these extremes is a large group of cases in which conservative treatment can be successfully employed. There is at present no complete unanimity of opinion as to the most satisfactory conservative measures to be adopted or the order in which they should be employed. For example, is castration immediately necessary once the diagnosis is established, or will intensive estrogen administration be sufficient, or when is castration most beneficial?

It has been shown, and we have observed in some of our patients with carcinoma of the prostate, that stilbestrol in adequate doses produces a castration effect as measured by the androgen excretion products in the urine. Birke, Franksson, and Plantin[1] studied androgen excretion in patients with carcinoma of the prostate after stilbestrol treatment and orchiectomy. They concluded that the androgen-depressing effects of stilbestrol and of orchiectomy were the same. Stilbestrol, 30 mg. daily for five days, or 10 mg. for two to three weeks, will produce a full castration effect. These studies support our clinical experience and form the rationale for first giving adequate doses of estrogen before advising orchiectomy. This surgical procedure may be held in reserve, as we have seen palliative benefit from orchiectomy in some patients who no longer show favorable response to

stilbestrol. The following case history demonstrates this course of events.

A 62-year-old man was first examined in January, 1957. The diagnosis was cancer of the prostate; it was verified by histologic study of specimens from a needle biopsy. The pathologic report was adenocarcinoma, grade 2. Roentgenograms of the lumbar spine and the pelvis showed evidence of changes suggesting osteoblastic metastasis or Paget's disease. He was immediately given a course of stilbestrol and did well until December, 1958, when he noted increasing pain in the back. An increase in dosage of stilbestrol brought no benefit. In January, 1959, roentgen examination revealed evidence of extensive, mixed, osteolytic and osteoblastic metastasis. Bilateral orchiectomy was performed and the patient experienced remission of the pain.

Metastatic Disease Controlled by Estrogens

The response of metastatic masses to estrogen therapy is often truly dramatic, as in the following case.

A 52-year-old man was referred to Dr. George Crile, Jr., in February, 1956, because of a tumor in the neck. Examination revealed a large mass of lymph nodes filling the entire posterior triangle on the left side of the neck. Study of specimens from a biopsy of a node led to the diagnosis of metastatic carcinoma. Prostatic examination revealed a firm nodule in the left lobe of the prostate. Needle biopsy of the prostate was performed and the report was adenocarcinoma, grade 2. He was given stilbestrol, 10 mg. a day. Three weeks later the mass in the neck had regressed sharply, and in July, 1956, it was "gone." In May, 1958, the referring physician reported the patient to be well with no evidence of recurrence. On November 1, 1959, a phone report indicated that he is well with no recurrence now almost four years after the initial examination. *It should be noted that orchiectomy was not performed in this case.*

We have had patients in whom a large mass extending from the prostate has produced ureteral obstruction. In several the mass was clearly palpable as an abdominal mass.[2]

A 58-year-old man was examined in November, 1954, because of mild obstructive symptoms. Digital examination of the prostate revealed a fixed, hard, nodular gland with a mass extending upward from the right lobe. An intravenous urogram showed evidence of delayed and diminished function on the right side, with grade 3 hydronephrosis noted in the 60-minute film. He was advised to take stilbestrol, 5 mg. per day. Prompt clinical improvement and relief of the obstructive symptoms ensued. Within eight weeks the mass above the prostate receded, and an intravenous urogram repeated nine months later showed evidence of prompt and normal right renal function with complete disappearance of the hydronephrosis. The patient remained well for four years and died suddenly apparently of a heart attack.

Metastatic disease in bone may likewise show marked regression under hormonal management; one of our most outstanding examples follows.

A 49-year-old man when first examined in December, 1942, by Dr. Charles C. Higgins, had a stony hard, nodular prostate; there was evidence on roentgenograms of

metastatic disease in the lumbar spine and the pelvis. In order to relieve obstructive symptoms, a transurethral resection was performed. The pathologic diagnosis of tissue removed was adenocarcinoma, grade 3. Bilateral orchiectomy was performed and the patient was advised to take stilbestrol. When he was examined in January, 1945, the patient was in good health, and a roentgenogram of the lumbosacral spine and the pelvis revealed no evidence of metastasis. He reported in good health for periodic follow-up examinations, and in April, 1958, he returned for removal of a stone in the bladder. Roentgenograms of bone again showed no evidence of metastasis. The patient was examined in November, 1959; he felt well, and the result of the roentgen study was negative, *17 years having elapsed since the original diagnosis of cancer of the prostate with bony metastasis.*

Certain unusual types of cases deserve special mention.

A 50-year-old man was first examined in the Department of Dermatology by Dr. George H. Curtis, in February, 1956, because of a skin eruption on the face, and great generalized weakness to the point of inability to move the arms. A diagnosis of dermatomyositis was made. Physical examination revealed an enlarged supraclavicular lymph node, which was removed for biopsy. It was diagnosed as metastatic adenocarcinoma. At first examination the prostate had excited no suspicion, but re-examination revealed suggestive nodularity with fixation. A specimen removed by needle biopsy was diagnosed as adenocarcinoma with perineural lymphatic invasion. The patient was treated with intravenous estrogens, and later stilbestrol. There was prompt improvement with clearing of the skin eruption and the return of normal full use of his arms. The patient was still well at the time of the last follow-up report in January, 1959.

Dr. Arthur L. Scherbel, in the Department of Rheumatic Disease, has under observation five patients who were examined because of pain diagnosed as typical of rheumatoid arthritis. Each patient had carcinoma of the prostate, as verified by histologic study of tissue removed at needle biopsy. After administration of stilbestrol, and no other hormone, all had prompt and complete remission of their arthritic symptoms and have remained well for from one to four years. In none of these patients was there roentgen evidence of bony metastasis.

Discussion

The above-mentioned isolated case reports, of interest in themselves, assume more significance when we realize that they are illustrative of larger groups of patients. The cumulative effect of observing the favorable response to hormonal therapy in some of the advanced cases of prostatic cancer raises the question: If this is so good for the advanced cases, why is it not equally good or better for the so-called "early" cases? There is some difficulty in knowing when a case is truly early in a surgical sense. Franks,[3,4] in studying the spread of prostatic cancer, found invasion of the capsule in 75.4 per cent of 69 cases of unsuspected cancer. Invasion of lymphatic and blood vessels was common, and perineural infiltration was found in 31.9 per cent of cases.

There is divided opinion as to when estrogen therapy should be started even in proven carcinoma of the prostate. We have chosen to start therapy when the

diagnosis is made, though some physicians believe that it should be reserved until troublesome symptoms develop. Neither is there general agreement as to when orchiectomy should be performed. Since administration of estrogens has been shown to produce a castration effect, there appears to be no need to include orchiectomy as a part of the original plan of treatment. We have performed orchiectomy in only 20 per cent of patients, and many of these have followed full courses of stilbestrol administration.

Mention should be made of the use of cortisone in conservative treatment. We have used cortisone in a small group of patients who have deteriorated after administration of estrogens or after castration, or after both types of therapy. Transient improvement may be noted and the use of cortisone is recommended, although dramatic and long-term improvement cannot be expected.

Conclusion

It is estimated that from 80 to 85 per cent of prostatic cancers are hormone-dependent, and that benefit from conservative or hormonal treatment may be expected. There is no reliable and simple method for determining which tumors are sensitive, or their degree of sensitivity. At present, this can be determined only by empirically using estrogens on each patient.

The benefits of hormonal treatment of cancer of the prostate are more keenly appreciated if one's experience goes back to pre-stilbestrol days. Today it is uncommon to see the painful and prolonged terminal illness commonly seen in past years. With increasing frequency our records show that patients with prostatic carcinoma who are on hormonal treatment, die of other diseases. It has been said that there is no case on record of a permanent cure with hormonal therapy, yet there are many cases in which normal life expectancy has been given to the patient, and death was not related to his prostatic disease.

References

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