The Treatment of Adenocarcinoma of the Prostate

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SUMMARY

Substantial progress has been made in the treatment of adenocarcinoma of the prostate. The various modalities of curative and palliative treatment used in this disease are discussed. The combination of these various methods plus the comprehensive treatment of these patients — including the diagnosis and treatment of concomitant medical complications — is stressed. Some of the more recent developments in the treatment of this disease are mentioned.


Adenocarcinoma of the prostate gland is one of the 3 commonest neoplasms affecting males (together with bronchogenic and colonic carcinoma). Prostatic carcinoma is currently the second most common cause of death from cancer in the male—second only to carcinoma of the bronchus and lung and exceeding that of any portion of the digestive tract. It occurs in approximately 20% of men over 60 years of age, and it is the leading cause of death in men over 75 years of age. It is estimated that in 1969, 16,900 males died as a result of adenocarcinoma of the prostate in the USA. What can be done for patients suffering from this disease? I propose to discuss the treatment of carcinoma of the prostate under the following headings:

1. Classification of carcinoma of the prostate.
2. Surgery.
3. Endocrine control.
4. Radiotherapy.
5. Oncochemotherapy.
6. Recent advances.
7. Treatment of concomitant medical complications.
8. The prognosis.

CLASSIFICATION OF CARCINOMA OF THE PROSTATE

The following classification is that adopted by the Cooperative Study of Radiotherapy for Carcinoma of the Prostate.¹

Stage I

(a) Occult carcinoma (microscopic foci of carcinoma found in specimens of prostatic tissue removed for benign conditions).
(b) Latent carcinoma (microscopic foci of carcinoma found in prostatic tissue at necropsy).

Stage II

Carcinomas confined within the prostatic capsule without elevation of the serum acid phosphatase.

Stage III

(a) Carcinomas apparently confined within the prostatic capsule that are accompanied by an elevation of the serum acid phosphatase.
(b) Carcinomas that are no longer confined within the prostatic capsule or those that have extended into the extracapsular structures (seminal vesicles, urethra, bladder, etc.) with or without an elevation of the serum acid phosphatase.

Stage IV

Carcinomas with demonstrable bony metastases or any extrapelvic involvement.

Surgery

Surgical measures which are of use in the treatment of prostatic carcinoma may be either curative or palliative.²

Curative Surgery

Only a minority of carcinomas are curable by surgical means. Such carcinomas are those that are still confined within the capsule—and are at stages I and II of the above classification. Only 5 - 10% of carcinomas are still resectable at the time of diagnosis.

The following operations may be used for curative surgery:

Radical perineal prostatectomy: This is the prostatovesiculoprostatectomy of Young,³ which includes the surgical removal of:
- prostate plus capsule;
- facia of Denovillier;
- vesical neck;
- much of the trigone;
- seminal vesicles and the ampulla of the vas deferens.

Retropubic Prostatectomy: If this operation includes the extirpation of the regional lymph nodes it is known as a radical retropubic prostatectomy.

Cystovesiculoprostatectomy: This consists of complete excision of the bladder, prostate and seminal vesicles together with ureterocolostomy (operation of exenteration).

Palliative Surgery

Numerous palliative procedures may be employed in those patients in whom the prostatic carcinoma is too advanced for attempts at curative surgery—stages III and IV of the above classification. Among these palliative procedures are the following:
Transurethral resection for severe urethral obstruction. Cryosurgery may be used instead of transurethral resection.

Anuria or oliguria due to urethral obstruction may be relieved by suprapubic urinary diversion techniques such as suprapubic cystostomy and urethral reimplantation.

The following other measures are also used (see 'Endocrine Control'): (a) orchidectomy or seminectomy, (b) bilateral adrenalectomy, and (c) hypophysectomy.

ENDOCRINE CONTROL

Carcinoma of the prostate is a hormone-dependent or hormone-sensitive neoplasm and therefore responds to endocrine therapy. As early as 1941 Huggins showed that androgen control could be used in palliation of incurable patients with advanced carcinoma of the prostate. For this work he was awarded the Nobel Prize for Medicine in 1966. Androgen control consists of:

(i) elimination of the source of androgens by either orchidectomy or seminectomy, and
(ii) neutralization of androgens by means of oestrogens (diethylstilboestrol, chlorotrianisene, oestradiol, stilphos- terol). Anti-androgenic progestational steroids, e.g. cyproterone acetate may also be used.

More than 85% of prostatic carcinomas are androgen dependent. With androgen control remarkable clinical improvement may be obtained, as well as softening and regression of local tumours and soft tissue extensions, lymph node metastases, and osseous metastases. There is often a decrease in serum acid phosphatase.

Controversy exists as to exactly when in the course of prostatic carcinoma androgen control should be instituted. The Veterans Administration Co-operative Urological Research Group has shown that the administration of oestrogens (at present the most commonly used endocrine control measure) results in a substantially increased risk of death in these patients from cardiovascular disease. Ackerman and del Regato feel that androgen control measures should not be applied to the asymptomatic patient, regardless of the extent of the disease. However the Veterans Administration Co-operative Urological Research Group indicates that the advantages of immediate oestrogen therapy in stage IV patients appears to be of greater importance than the danger of cardiovascular disease. The use of the nonoestrogenic, nonandrogenic steroid cyproterone acetate does not result in the abovementioned increase in cardiovascular disease.

When the tumour loses its initial endocrine responsiveness, recurrence occurs. The following endocrine control measures may then be employed:

1. Bilateral adrenalectomy.
2. Medical adrenalectomy, which consists of the administration of adrenocortical steroids in an attempt to depress the action of the adrenal cortex.
3. Hypophysectomy.
4. Implantation of radioactive yttrium (Y) seeds into the hypophysis.

RADIOThERAPY

Radiotherapeutic measures which are of use in the treatment of prostatic carcinoma may be palliative or, as has recently been claimed, curative.

Palliative Radiotherapy

Prostatic adenocarcinoma spreads eccentrically to the seminal vesicles, vesical wall and ureters. Furthermore, it metastasizes both haematogenously and via the lymphatics. Many radiotherapeutic measures are used in the palliation of advanced incurable prostatic carcinomas. The following procedures are available:

1. Irradiation of the prostate in inoperable carcinoma of the prostate with or without distant metastases—stages III and IV of the above classification. 2
2. Irradiation of localized bone metastases for palliative purposes.
3. Use of radioactive phosphorus (P) either orally or intravenously for the palliation of widespread diffuse bone pain. Recently the use of parathormone (parathyroid hormone) followed by radioactive P in widely disseminated prostatic carcinoma unresponsive to endocrine control measures, has been advocated.
4. The interstitial implantation of radioactive gold (Au), P, Y or radium seeds into the prostatic tumour in patients with locally advanced carcinomas.
5. Implantation of radioactive Y seeds into the hypophysis.
6. Before the administration of oestrogens, direct X-ray therapy to the region of the areola of the breast, prevents painful gynaecomastia.

Curative Radiotherapy

Flocks et al. have indisputably shown that prostatic carcinoma is radiosensitive. Adequate external pelvic irradiation either by means of supervoltage roentgentherapy, or by means of "Co teletherapy may prove to be the treatment of choice for the majority of patients with prostatic carcinoma.

ONCOCHEmOTHERAPY

In those patients with prostatic carcinoma who have relapsed after the use of all the abovementioned measures, oncochemotherapy may be attempted. The following cytotoxic drugs are used in the treatment of patients with advanced prostatic carcinoma unresponsive to all other modalities of treatment in a final attempt at palliation: alkylating drugs (e.g. cyclophosphamide), 5-fluorouracil, and ancyte.

RECENT ADVANCES

Lymphographic studies have shown a high incidence of lymph node involvement in prostatic carcinoma (up to
85% or higher). Extended wide-field irradiation involving the abdominopelvic nodes, the prostate gland plus adjacent regions, and in certain patients the mediastinum and supraclavicular nodes, has resulted in a significant increase in the survival rate of patients with stage III of the above classification. Clinical trials of extended-field irradiation for prostatic carcinoma showed tumour-free, 3-year survival rates of 93%.

Taking into consideration the recent advances in the use of curative radiotherapy in stages I and II, and curative radiotherapy plus extended-field irradiation in stage III in patients with prostatic carcinoma, it is quite conceivable that the future of the treatment of prostatic carcinoma lies more within the field of the radiation therapist than that of the urological surgeon.

IMMUNOLOGIC ASPECTS OF PROSTATIC CARCINOMA

Much research has been done concerning the immunology of neoplasms. Few studies have been reported concerning the immunological characteristics of prostatic carcinoma.

In view of the extensive evidence of immunologic aspects of various neoplasms, it is certain that immunologic mechanisms (and in particular cell-mediated immunologic mechanisms) play an important role in the biogenesis of prostatic carcinoma. Further research in this field may yield methods of immunotherapy which can be used in the treatment of prostatic carcinoma.

THE TREATMENT OF CONCOMITANT MEDICAL COMPLICATIONS

Prostatic carcinoma may be manifested clinically by unusual symptoms and syndromes. These bizarre symptoms and signs are known as paraneoplastic syndromes. The following paraneoplastic syndromes have been associated with prostatic carcinoma:

1. Hypercalcaemia.
2. Cushing's syndrome.
3. Neuromyopathies and other non-metastatic effects of prostatic carcinoma on the nervous system.
4. Coagulopathies.
5. Thrombophlebitis.
6. The syndrome of inappropriate secretion of antidiuretic hormone.
7. Psychiatric disturbances.

It is beyond the scope of this review essay to discuss the treatment of each of these paraneoplastic syndromes. However, these syndromes must be searched for and appropriately treated in every individual with prostatic carcinoma.

THE PROGNOSIS

According to Bumpus the average length of life from onset of symptoms to death in untreated patients with prostatic carcinoma is 31 months. In patients with prostatic carcinoma who have been treated by radical perineal prostatectomy Vickery and Kerr reported a 5-year survival rate of 79% and a 10-year survival rate of 49%, and Jewett reports a 15-year survival rate of 33%. The study of the Veterans Administration Co-operative Urological Research Group revealed the following results: Patients with stages I and II operable prostatic carcinoma had a 5-year survival rate after prostatectomy of approximately 70%. In inoperable prostatic carcinoma without distant metastases: (stage III) the 5-year survival rate for all patients who received various palliative procedures was approximately 50%, and in inoperable prostatic carcinoma with osseous or distant metastases: (stage IV) the 5-year survival rate for all patients receiving palliative measures was approximately 25%.

CONCLUSION

It is clear from the foregoing discussion that the earlier in its course the prostatic carcinoma is diagnosed the better the prognosis. Therefore it is essential that all men over the age of 50 years should as a routine undergo 6-monthly rectal examinations. The rectal examination is the principal resource in the diagnosis of prostatic carcinoma.

The various modalities of treatment available, and described in this essay, should be used in both the curative and palliative treatment of prostatic carcinoma. The use of these various modalities of treatment, either individually or in any possible combination, has resulted in a steadily increasing number of patients who are free of any signs of prostatic carcinoma 5, 10, and 15 years after the diagnosis of prostatic carcinoma has been made. Furthermore, in those patients with incurable, advanced prostatic carcinoma the quality of life has been improved and the time of survival has been lengthened by these methods.

In conclusion I would like to express the belief that prostatic carcinoma will, hopefully, in the not too distant future be, if not curable, at least controllable.

REFERENCES

Torticollis

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SUMMARY

The classification of torticollis in general is given. Muscular torticollis is discussed from the point of view of pathology and treatment. Spasmodic and ocular torticollis are briefly discussed.


Torticollis is a contracted state of the sternomastoid muscle, usually unilateral but occasionally bilateral, which produces a tilting of the head to that side, with torsion of the neck and deviation of the face. The first tenotomy was performed by Isaac Minnius of Amsterdam in 1641. In 1826 Hensinger described tumour of the sternomastoid.

There are many causes of torticollis, the commonest being fibrosis of the sternomastoid muscle.

Classification*

Torticollis may be classified as being either congenital or acquired.

Congenital: (a) congenital postural—present at birth, no tumour, self-correcting; and (b) congenital muscular torticollis.

Acquired: (a) skeletal disorders—Trauma to cervical spine or inflammatory disease of cervical spine; (b) neurological and psychological disorders—spasmodic, ocular, habitual, paralytic peripheral or central nervous system lesion, or as a reflex from glands in the neck; and (c) soft tissue contractions.

CONGENITAL MUSCULAR TORTICOLLIS

Pathologically, striated muscle is replaced by fibrous tissue—endomysial fibrosis.1,3 There is no dense collagen and no evidence of recent haemorrhage. There are numerous theories on the cause of torticollis but the most likely seems to be that venous occlusion during intra-uterine life, possibly due to malposition, produces the muscle change. Similar changes were produced in the sartorius muscle by Bowden and Guttmann.4 There is a higher incidence of breech presentation in established cases. Von Lackun5 quotes 3 siblings with torticollis. MacDonald6 in an excellent survey of 100 cases found a family history in 9 cases.

Clinically, the sternomastoid tumour is not present at birth but presents in the first 7 - 21 days. Jones7 quotes an incidence of 0.4% of births. In 50% the tumour gradually disappears and the neck is normal by the 6th or 7th month. In 30% there may be slight residual fibrosis with some asymmetry or tightening. In 9% the tumour grows and gives rise to torticollis. In 75% of cases the right side is affected, most commonly the clavicular head of the sternomastoid.8 The shortening of the sternomastoid produces a lateral inclination of the head with the chin rotated up and out to the opposite side. The rare bilateral cases have an extended head.

The affected muscle is hard and tight and there is limitation of rotation to that side.

Secondary Effects

Cranial asymmetry—plagiocephaly—commences once the torticollis is established. Facial hypoplasia on the affected side soon becomes evident. Jones has noted that there is constant atrophy of the ipsilateral trapezius muscle. A late development may be a compensatory thoracic scoliosis.

Treatment

Mothers can be trained to put the baby’s head through a full range of movement 3 or 4 times aday. Once contrac-

*Date received: 20 August 1971.