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THE ROLE OF ORCHIECTOMY IN THE MANAGEMENT OF ADVANCED MALE BREAST CANCER

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Nine men with advanced carcinoma of the breast were evaluated after orchiectomy at the National Institutes of Health over 19 years. Of patients followed for greater than one year, five had complete remissions, one had a partial remission, and two patients did not respond to orchiectomy. The average disease-free interval was 20 months; the average survival from the time of orchiectomy in those who responded was 55.8 months and in non-responders was 26.7 months. Orchiectomy appears to be a safe and effective way to produce an objective response and prolong survival in over 50 percent of men with advanced breast cancer.

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THERE ARE APPROXIMATELY 600 NEW CASES of male breast cancer in the United States each year, and about 250 deaths.² The generally accepted treatment of the primary lesion consists of radical mastectomy, modified radical mastectomy, or simple mastectomy plus irradiation. When the tumor recurs or is initially inoperable, the choices of therapy include irradiation, chemotherapy, and/or hormonal manipulation. Irradiation is suitable only for localized areas of malignant disease and chemotherapy may have significant toxicity even with optimal management. The ideal palliative therapy for a metastatic tumor would be one with minimal morbidity, but one that gives the patient the best chance for regression or remission.

Castration has been performed in premenopausal women for many years as the initial therapy for recurrent or initially inoperable breast carcinoma. Poor response groups include those with extensive CNS, pulmonary, or hepatic metastases;¹¹ most series have an objective response rate of 30-40%.⁸ This report describes the experience at the National Institutes of Health with orchiectomy in the management of advanced male breast carcinoma and reviews the literature concerning this therapeutic modality.

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CLINICAL MATERIAL

Between 1955 and 1974, there have been nine men with advanced breast cancer who have undergone evaluation at the National Institutes of Health (NIH) following orchiectomy; eight of the orchiectomies were performed at the NIH and one (J.W.) was performed elsewhere and previously reported.⁹ Pathologic review of the original slides was carried out in all instances; all nine patients had infiltrating ductal carcinoma. The first eight patients have died; the ninth patient only recently underwent orchiectomy and followup data is not yet available.

A complete response was defined as complete clinical and laboratory elimination of disease. Relapse was defined as clinical evidence of recurrent disease. Patients whose disease remained stable or did not completely regress were considered to be non-responders. Five of the eight (62.5%) patients had objective responses (Table 1). The average interval from orchiectomy to relapse was 20 months in the responding group (range 13-24 months). One of the non-responding patients (C.G.) continued to have progression of disease after orchiectomy; another patient (R.B.) had his disease stabilize for a year before progressing. The third patient who did not have a remission completely healed his pulmonary disease for 12 months, although he continued to have subcutaneous local recurrences de-

TABLE 1. Patients Undergoing Orchiectomy for Advanced Breast Carcinoma

Patient	Age at Dx.	Primary Rx.*	Date Primary Rx.	Date Orch.	Resp. to Orch.	Recurr.	Disease-free Interval (months)	Followup
C.G.	52	S.M.	1945	1/53	None		0	d. 8/54
R.B.	61	S.M.	1951	11/55	None		0	d. 11/57
G.S.	66	S.M.	1959	9/59	Healing soft tissue	9/61	24	d. 9/63
A.N.	37	R.M.	1956	12/58	Healing bone	11/60	23	d. 9/65
W.B.	68	S.M.	4/53	10/59	Healing of pulm., soft tissue progression	10/60 — pulm. recur.	0	d. 11/62
J.W.	43	R.M.	7/51	12/59	Healing of pulm. mets.	10/61	22	d. 4/66
D.E.	65	R.M.	6/61	12/62	Healing of bone & soft tissue	6/64	18	d. 9/65
C.K.	26	B.R.M.	5/66	8/69	Healing of bone	9/70	13	d. 1/73
M.S.	64	M.R.M.	6/74	8/74	Too early to evaluate			

* S.M.—Simple mastectomy.
R.M.—Radical mastectomy.

B.R.M.—Bilateral radical mastectomy.
M.R.M.—Modified radical mastectomy.

velop and then spontaneously regress at the mastectomy site during the year following orchiectomy and was, therefore, not considered a responder. Average survival of all patients from the time of orchiectomy was 44.9 months; averaged survival was 55.8 months in the group that responded, but only 26.7 months in the non-responders. Two patients underwent hypophysectomy when their disease recurred after orchiectomy (J.W., A.N.); both responded to this secondary endocrine ablative procedure. Chemotherapy and additive hormone therapy was used in all patients after relapse or disease progression.

One patient (A.N.) received an infusion of pituitary gonadotropin prior to his orchiectomy which was associated with an exacerbation of his bony pain. He had a good response to orchiectomy. Another patient (G.S.) was treated with diethylstilbestrol following his original mastectomy; when metastatic disease occurred the estrogen therapy was discontinued. He then had a two-year response before requiring orchiectomy, to which he also had a good response.

The ninth patient in our series (M.S.) had estrogen binding activity present in his metastatic tumor.¹² Although it is too early to document his response, it was interesting that pre-orchiectomy he was unable to sit or walk without severe discomfort due to vertebral disease and hip pain. Following orchiectomy,

his requirement for analgesics was immediately decreased and he was able to walk and sit without difficulty within two days. Another patient (G.S.) had similar vertebral disease; within four days after orchiectomy, he rapidly progressed from a state of being completely bedridden to a state of ambulation completely pain free. His response lasted 24 months.

DISCUSSION

Orchiectomy was first described in the treatment of advanced male breast carcinoma by Farrow and Adair in 1942.⁴ Morbidity from the operative procedure is minimal and it is our experience that the insertion of testicular prosthesis would appear to decrease the associated psychological problems. Since the original report, there have been few studies concerning the efficacy of this procedure.^{3,5-7,10}

The reported response rates to orchiectomy vary according to the criteria used by each author. Treves¹⁰ described a subjective response in 31 of 41 patients and an objective response in 28 of 41 patients. However, the criteria used to define a response were not stated. In a partially overlapping group of patients reported from the same institution, Holleb⁵ described an objective response in 17 of 38 (45%) patients. Donegan³ has reported responses in five of six patients; four of the

five responders did not have adjunctive therapy while one patient received estrogens after the orchiectomy. Huggins⁷ and Houttuin⁶ have also reported objective responses in a majority of patients (Table 2). Other reported series are small, often do not mention the results of orchiectomy, and the criteria for evaluating the possible response are not always clear.² We have had remissions in five of eight patients and a mixed response in a sixth patient (Table 1). Although there have been few males reported with Paget's disease of the breast, it appears that they may not respond well to orchiectomy. Coley and Kuehn¹ have reported five patients who underwent orchiectomy; only one responded.

The mean survival of patients in this series (44.9 months from the time of orchiectomy) compares strikingly with that of women following oophorectomy for metastatic breast cancer (14 months⁸). Male responders survive twice as long as non-responders, which is similar to the situation in women. Although many authors state that men with breast cancer have a worse prognosis than women,^{2,5} the mean survival in this series was eight years from the time of initial diagnosis, although these patients were all seen at the NIH with metastatic disease. This compares with a mean survival of all women with breast cancer of five to six years.⁸ Even if a patient fails to respond to orchiectomy, he may well respond to adrenalectomy or hypophysectomy. Al-

though the number of reported cases is small, three of four have responded to adrenalectomy even after failure to respond to orchiectomy.^{6,10,14} Similarly, responses to hypophysectomy after orchiectomy failure have been reported (1/4).⁹ It is interesting that men with visceral involvement may respond well to endocrine ablative procedures,⁶ although women with extensive visceral involvement have a poor response rate.¹¹ Additive therapy with estrogens, progesterone, or androgens has limited effectiveness^{2,5} and may well allow the tumor to increase its growth rate as was seen in two of our cases.

Assay of malignant tissues for hormone receptors may become a more useful test in evaluating patients for possible endocrine therapy. Those patients who lack hormone receptors may not respond to hormonal manipulation. It has been reported in women with advanced breast cancer that 55-60% will respond to therapeutic hormonal procedures if estrogen receptor activity is present; however, if this activity is absent, the response rate is under 10 percent.¹³ There have been only two previous male patients assessed for estradiol receptor activity.¹⁵ * One patient with high estradiol receptor activity responded to adrenalectomy and orchiectomy;¹⁵ the other patient had receptor activity following no response to adrenalectomy.* The patient in our series who had estrogen receptor activity present is too early in the postoperative period to be able to objectively evaluate his response to orchiectomy.

It is still too early to assess the predictive role of estrogen receptor activity in males; however, even without this information there is a 50-70% remission rate to orchiectomy in patients with metastatic breast carcinoma. Considering the relative safety and effectiveness of this procedure, it should be performed in most patients at the time the tumor recurs or when the patient is shown to have initially inoperable disease.

TABLE 2. Reported Response Rates to Orchiectomy

Author	Pts.	No. Responding (%) [†]	Mean Duration of Response (Months)
Treves*	41	28 (68.3%)	29
Holleb* [‡]	38	17 (44.7%)	unknown [‡]
Donegan [‡]	6	5 (83.3%)	17
Houttuin ⁶	8	7 (87.5%)	26
Huggins ⁷	10	6 (60%)	16
Present series	8	5 (62.5%)	20

* Partially overlapping series.

[†] Criteria vary from series to series.

[‡] Range 3-40 months; 9 remissions > 12 months.

* Perlin, E. and Tormey, D., unpublished data.

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