

CARCINOMA OF THE MALE BREAST WITH AXILLARY METASTASIS FOLLOWING STILBESTROL THERAPY

REPORT OF A CASE TREATED BY RADICAL MASTECTOMY*

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ESTROGENS HAVE BEEN SUSPECTED of being carcinogenic for the human being since the work of Lacassagne⁸ in 1932, when he demonstrated that the incidence of carcinoma in certain strains of mice can be increased by the administration of estrogens.

A decade ago at least three cases appeared in the literature in which carcinoma of the female breast was suspected to have resulted from prolonged estrogen therapy.^{2, 3, 10}

Since the advent of estrogen therapy for carcinoma of the prostate by Huggins in 1941, it has been noted that most of the patients developed gynecomastia as a side effect of the treatment. Foote and Stewart⁶ made a study of this problem and reported in 1945 that the hyperplasia of this type of gynecomastia was not related to neoplastic changes. Rose¹¹ made a study of side effects of estrogen therapy for carcinoma of the prostate and concluded that they were not harmful and that the only ill effect of the gynecomastia was to discourage the patient from taking the drug.

It is only within the past three years that five cases have been reported in the literature in which carcinoma of the male breast has followed estrogen therapy for carcinoma of the prostate or bladder. None of these cases have presented themselves before there was metastasis to the bone. The nature of the resulting breast lesion

was not determined early enough in any case to allow surgical treatment.

In January, 1948, Abramson and Warshawsky¹ reported a case of a 51-year-old Negro man who was first seen with carcinoma of the prostate and metastatic bone lesions. He was put on 1 mg. of stilbestrol daily and improved with weight gain for two years, but then began to have weakness and weight loss again. Masses developed in both breasts and both axilla. An orchiectomy was done and some improvement occurred. The patient died six and a half years after diagnosis and the onset of estrogen therapy. At autopsy, sections were taken from only one breast, which proved to be carcinoma.

In June, 1948, Harold Entz⁵ reported a case of a 49-year-old white male truck driver who came in with the complaint of back pain and was found to have metastatic lesions in the bones of the pelvis and a hard nodular prostate. The patient was put on 9 mg. of stilbestrol daily, but after a week the dose was reduced to 4 mg. daily and taken for a month. At the end of this period the breasts became large and tender. The dose was reduced to 1 mg. daily, and the patient died 17 months after the diagnosis. A limited autopsy was done, and sections were taken from the right breast. Examination revealed a small-celled carcinoma, which was reported by Colonel J. E. Ash at the Army Institute of Pathology as probably coming from the prostate.

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In 1949 Howard and Grosjean⁷ reported a case of a 71-year-old man who took .1 mg. of stilbestrol from 1943 to 1946 for carcinoma of the prostate. At the end of this period he was found to have a hard nodular breast and bone metastasis. The dose was first increased to 5 mg. daily and then

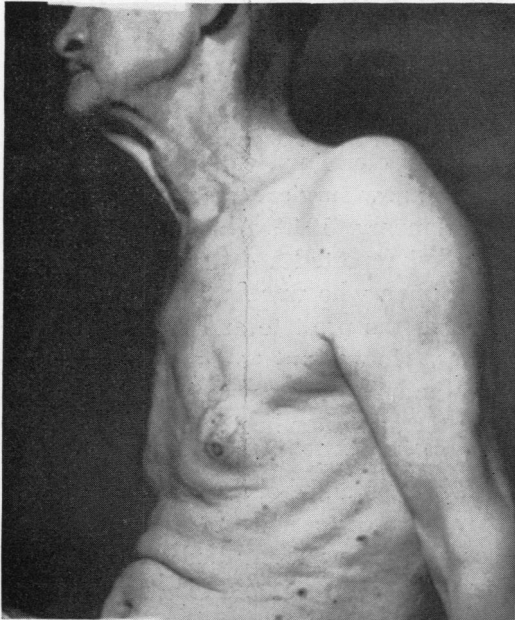


FIG. 1.—Photograph of patient taken one month after estrogen therapy was discontinued. The breast is hard, nodular, and fixed to the skin.

120 mg. daily, with subsequent reduction to 80 mg. daily. He received a total of 120 mg. the first three years, and 40,160 the last two years of life. Autopsy in January, 1948, revealed scirrhous carcinoma in both breasts. Microscopic study revealed the tumor to be in sheets and cords with only abortive attempts at acini formation.

In August, 1950, Corbett and Abrams⁴ reported the case of a 65-year-old man with a carcinoma of the prostate and evidence of bony metastasis in the pelvis and dorsal spine. He was put on 3 mg. of stilbestrol daily. After eight months the breasts were so large and tender that the dose was reduced to 1 mg. daily, and he remained on

this dose for two years. He died four years after the onset of estrogen therapy and a total of 3240 mg. of stilbestrol had been given. The breasts were found to be bilaterally hard and nodular during the last year of life. Autopsy revealed adenocarcinoma of the prostate with metastasis to the lung, pleura, skeleton, adrenal glands, left kidney, liver, brain, breasts and lymph nodes. Several pathologists reviewed the sections but could not determine whether the breast lesion was a primary carcinoma or a metastatic growth.

In May, 1951, McClure and Higgins⁹ reported a case of a 56-year-old man with carcinoma of the bladder, who had been treated with 1770 mg. of stilbestrol over a period of 126 days. The breasts became swollen and tender six weeks before the drug was discontinued. A roentgenogram of the skull revealed a metastatic tumor, and biopsy revealed carcinoma simplex in both breasts. The patient had a family history of carcinoma. He died before treatment of the breasts could be instituted.

Having briefly reviewed the five previously reported cases, we wish to add a case of our own which was diagnosed early enough so that no metastasis from the prostate could be determined and which was treated by a radical mastectomy followed by deep roentgen ray therapy to the chest.

CASE REPORT

B. E. B., a 78-year-old white male, was first admitted to the hospital on November 5, 1948, with an acute urinary retention. A diagnosis of carcinoma of the prostate was made and confirmed on microscopic section following a transurethral resection. No evidence of bone metastasis was found on roentgen ray examination. He made an uneventful recovery from the resection and was discharged from the hospital November 16, 1948, with instructions to take 6 mg. of stilbestrol daily. He was seen in the office at 3-month intervals. He gained weight and strength until the end of the first 6 months, when he began to complain of nausea, anorexia, and painfully enlarged breasts. He continued to take 5 mg. of stilbestrol daily

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until August 28, 1950, when the symptoms increased to the extent that he was taken off estrogen therapy. An estimated total of 4400 mg. of stilbestrol had been taken over this period of time. It was noted that the prostatic tumor had extended into the seminal vesicles and that he was having increasing evidence of urinary obstruction. An

essentially normal, and the acid phosphatase level was reported as one unit. On October 25, 1950, a bilateral orchiectomy and a radical mastectomy on the left breast was done. The breast, pectoral muscles, and axillary contents were removed in one mass, and the closure carried out with difficulty. The pathologist reported adenocarcinoma of the

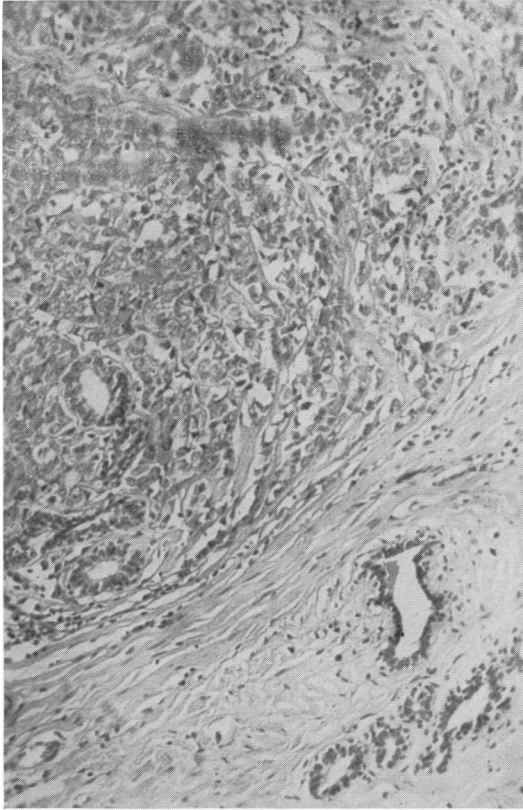


FIG. 2

FIG. 2.—Microscopic section of the breast tumor removed by radical mastectomy.

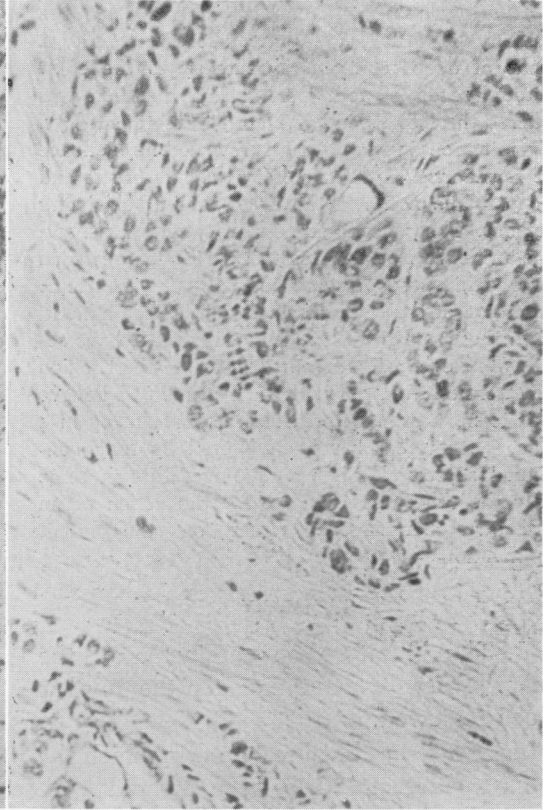


FIG. 3

FIG. 3.—Microscopic section of the tissue removed from the prostate, showing a poorly differentiated carcinoma.

orchiectomy and second resection were advised, both of which he refused.

A month after the stilbestrol had been discontinued, the swelling and tenderness in the right breast had disappeared. However, a hard, nodular, nontender mass approximately 4 cm. in diameter was found in the left breast. The mass was attached to the skin, but not to the deeper structures. A nodule was in the subcutaneous tissue just medial to the breast, which measured 2 cm. in diameter. There were several enlarged and hard, but freely movable axillary glands on the left, but there were none in the right axilla or supraclavicular regions. The blood picture was

left breast with axillary metastasis. The microscopic report was that of fairly well-circumscribed masses of tumor tissue made up of cords and sheets of undifferentiated cells, which in some places showed an attempt at acinar formation. The cells were irregularly polyhedral with basophilic cytoplasm and round oval nuclei containing irregularly dispersed chromatin and prominent nucleoli. Mitoses were very numerous, and many were atypical. The testes were reported to show atrophy of the tubules. A week later a transurethral resection of the prostate was carried out with removal of 25 Gm. of tumor tissue. This tissue was reported as carcinoma of the prostate and described as anaplastic in

type, with large cells containing little cytoplasm and large, hyperchromatic, oval nuclei. The architecture was poorly differentiated and somewhat distorted by the electro-dessication. The patient made an uneventful recovery from both operations and was discharged from the hospital on November 6, 1950, with no urinary symptoms, and with wounds of the chest and scrotum well healed.

During the period from November 29, 1950, to January 12, 1951, the patient received 2400 R units of deep roentgen ray therapy to the chest through each of four ports. This radiation was filtered through air and given on 24 treatment days. Examination on May 9, 1951, revealed no evidence of recurrence of the tumor in the left breast and no palpable nodes in the axilla or supraclavicular regions. The patient had no urinary symptoms, and the urine was clear. Rectal examination revealed a very thin hard prostatic bed without evidence of extension of the carcinoma. Monthly examinations, with the last one on November 15, 1951, have revealed no evidence of recurrence in the chest region or extension from the prostatic capsule. We believe this to be a primary breast carcinoma arising in a duct system that has been altered by long continued stilbestrol therapy. We feel that in some way the stage has been set for the action of an unknown carcinogenic agent on the breast epithelium.

SUMMARY

1. The literature on carcinoma of the male breast following estrogen therapy has been reviewed.

2. A case has been reported in which the breast carcinoma has been treated with apparent success.

3. Insofar as we can find in the literature this is the first case to be reported of carcinoma of the breast following estrogen therapy in which metastasis could not be demonstrated elsewhere in the body. This is the

first case that has presented itself early enough to be treated by radical mastectomy.

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