

1957

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Bernie David Taylor
University of Nebraska Medical Center

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CARCINOMA OF THE BREAST

By

Bernie D. Taylor Jr.

College of Medicine,
University of Nebraska

1957

Omaha, Nebraska

INTRODUCTION

The therapy of advanced breast carcinoma by endocrine methods is based upon the concept of hormonal dependence. It has been demonstrated that carcinoma of the breast can be stimulated or inhibited by the administration or withdrawal of appropriate endocrine substances. Two new principles of medicine have been put forth in the development of this concept by Huggins and Hodges.

1. Carcinoma is not necessarily autonomous in its growth or intrinsically self-perpetuating. Some neoplasms retain sufficient characteristics of the normal cells from which they arose so that the tumor cells function like the normal tissue of origin. When the original tissue is dependent upon hormonal support for maximal activity, frequently its cancers are similarly dependent and atrophy when the hormonal support is withdrawn-- this by definition is a dependent tumor. The therapy of such a neoplasm is control by physiological means by altering or modifying the tumor--host relationship by administration of endocrine substances or by surgical removal of endocrine glands.
2. Breast cancer can be sustained and propagated by hormonal function that is not abnormal in kind or exaggerated in rate, but is operating at normal or subnormal levels. Only trace amounts of hormones need be present to support and stimulate their growth.

It has been demonstrated that some breast tumors do not respond to hormonal means of therapy. It is therefore essential that hormonal dependency be demonstrated before a patient is subjected to more radical hormonal therapy such as adrenalectomy and oophorectomy. Huggins and Dao⁽¹⁰⁾ have demonstrated that the histological appearance of the primary tumor can be used as an index of hormonal dependency.

A series of unreported cases managed by adrenalectomy and oophorectomy shall be reported with an attempt to correlate the histological appearance and tumor responsiveness according to Huggins and Dao's histological classification. A series of cases⁽¹⁰⁾ will be taken from the literature in an attempt to come to some definite conclusion as to whether this is an adequate index of hormonal dependency.

HISTORY

George Thomas Beatson⁽²⁾ in 1896, reported two cases of inoperable carcinoma of the breast in premenopausal women in which he was able to induce a remission by bilateral surgical removal of the ovaries. He further demonstrated histologically that the tumor cells underwent fatty degeneration and clinically tumor size decreased, pain in tumor area decreased and that patients began to gain weight.

Dr. Hugh Lett⁽³⁾ reported a series of 99 cases in 1905 which had been managed by bilateral oophorectomy. In his series of 99 cases, he demonstrated marked improvement in 23.2% of his

cases, with distinct though less improvement in an additional 13 cases. After this series of cases were reported, irradiation sterilization became the accepted mode of treatment on an endocrine basis.

In 1945 Charles Huggins and William Scott reported a series of four male patients with cancer of the prostate which were managed by bilateral adrenalectomy. This was before cortisone was available and post operative management was difficult. One patient survived 116 days after surgery and they were able to demonstrate marked tumor regression.

Since cortisone has been available, several series of cases of carcinoma in the breast have been managed by bilateral adrenalectomy and oophorectomy. Cade has reported objective remission in 45% of his series of 38 patients. Huggins in his series of 31 patients reports objective improvement in 22% with subjective improvement in 45% of his series.

At the present time adrenalectomy and oophorectomy are delayed in their use until the patient becomes refractory or fails to respond to more conservative type of management. Many of the patients are very poor operative risks at the time of surgery due to the far advancement of their disease process. Even though patients are very poor operative risks, Huggins reports an operative mortality of only 5% and Cade an operative mortality of 13%.

Since roughly 60% of the patients subjected to adrenalectomy and oophorectomy will be benefited by this procedure, an attempt to select patients which would respond to this therapy would be of considerable value. Jessamin and Moore have suggested that

the estrogen stimulating test could be employed to select these patients. The test is performed by administration of estrogen and measuring the urinary calcium excretion and combining this with the clinical picture of increased bone pain and general symptoms of increased tumor activity. They have also suggested that testosterone inhibition test may also be employed in a similar manner to demonstrate decreased urinary calcium output with the administration of the drug. The estrogen stimulating test carries with it the disadvantage of elevation of the plasma calcium level, especially with impaired kidney function.

Huggins and Dao suggest that the histological picture of the primary tumor may be used as an adequate index of tumor response to adrenalectomy and oophorectomy. ⁽¹⁰⁾ Cade reports that ⁽¹⁴⁾ tumor metastasis to the adrenal gland maintains the same histological picture as the primary tumor.

METHODS

All patients subjected to adrenalectomy and oophorectomy for carcinoma of the breast at the University of Nebraska Hospital and Immanuel D. Hospital were taken for study. A brief summary of their clinical course, history, physical examination, and response to therapy will be included. Two patients which died were autopsied and a brief autopsy report will be included. Histological sections were studied without knowledge of the case or therapeutic response and correlated afterward with the clinical course as near as possible. All sections were carefully reviewed with Dr. H. K. Giffen, Pathologist at Immanuel D. Hospital.

Knowledge of the case or response was not known at the time these sections were reviewed in order to eliminate improper grouping in questionable cases.

The classification suggested by Huggins and Dao was followed⁽¹⁰⁾ in evaluation of the histological picture of the tissue sections. In some instances it was difficult to adequately classify since the tumor pattern varied from area to area and in these instances they were evaluated as the predominant pattern without the knowledge of case or response to therapy.

Huggins and Dao's classification⁽¹⁰⁾ is as follows:

"The important consideration in determining response to adrenalectomy was maturity of cells with detritus in the false lumen, apparently due to central necrosis. We divided the histological material in four classes."

- A. Adenocarcinoma, defined as a preponderance of gland formation with secretion.
- B. Papillary carcinoma
- C. Duct cell cancers
- D. Undifferentiated carcinoma

Huggins and Dao⁽¹⁰⁾ have noted in their series of 43 cases studied that duct cell carcinoma responds poorly to this therapy--one case in eight responded. Undifferentiated carcinoma failed to respond in any of their 16 cases and 16 of the 19 patients with papillary and adenocarcinoma responded. They therefore postulated that undifferentiated carcinoma would fail to respond

to this therapy and duct cell carcinoma would rarely respond to this therapy.

Cases were taken from the literature and added to the series where the histological pattern was known in order to better evaluate and correlate the histological picture with the clinical response and attempt to come to a definite conclusion. The literature was also reviewed as to the current theory of this therapy and research.

DISCUSSION

One should first consider the degree of palliation offered by other forms of therapy. In a large series of patients treated by palliative irradiation the average survival time was 12 mo.; in a large series treated with testosterone the average survival was 7.5 mo.; in a large series treated with estrogens the survival ranged from 7.6mo.; to 12.3 mo. as reported to the council on Pharmacy and Chemistry in 1951.

It is quite gratifying to see the marked degree of palliation that is offered to a patient which responds to hormonal therapy by bilateral adrenalectomy and oophorectomy. The patient may have severe bone pain requiring narcotics for relief. Within two weeks and usually within two or three days after completion of surgery they require no analgesic for relief of bone pain. The pain in the tumor sites of the soft tissue disappear, the patient clinically feels much improved and is often euphoric. Their appetites improve, they gain weight and begin to take an interest in life once more. The remission may continue for as long as 36 months and when the relapse occurs they seem to grow rapidly worse and die within a short time. One case illustrates this very well (E. C.) whose remission lasted four months.

When first seen by Dr. Herbert Davis, she had flaccid paralysis of the left side of the face and ptosis of the left lid. There were extensive tumor metastases in skull, cervicle, dorsal and lumbo-sacral spine with severe pain in these areas, requiring analgesics for relief of pain. Three days following

surgery she required no narcotics for relief of pain in tumor areas. Facial paralysis and ptosis of left lid disappeared and patient felt considerably improved. The patient was quite comfortable for the following 3 1/2 months. When relapse occurred she grew worse rapidly and died within two weeks.

As one examines such a case one wonders why should a patient demonstrating such remarkable response to therapy, suddenly go into relapse? One asks many unanswered questions as to the actual mechanism of tumor response to hormonal treatment. Has accessory adrenal tissue hypertrophied to again support tumor growth or has actual tumor autonomy developed that has become independent of hormonal support for growth? What effect does cortisone alone have on tumor metabolism and is the pituitary also supporting some tissue growth through release of the growth, mammatrophic and gonadotropic hormones?

Graham demonstrated adrenal cortical tissue in the region
(11)
of the celiac plexus in 32% of 100 consecutive autopsies. The adrenal cortical tissue averaged 7x4x3 mm. and was similar in histological pattern to that of adrenal cortical tissue. Accessory adrenal glands are often found in the region of the normal tissue from the body is not done in the routine adrenalectomy and tissue may be left behind to secrete more hormone. The presence of accessory adrenal tissue may have been responsible for maintenance of life in the patient previously mentioned upon whom adrenalectomy was done for cancer of the prostate before cortisone was available. Pearson, West, and Hollander withdrew cortisone in twelve patients
(22)
who had been subjected to adrenalectomy and oophorectomy for

metastatic breast cancer. Ten of these patients went into adrenal crisis within three to seven days, the other two were maintained for several weeks without any hormonal replacement therapy and experienced only moderate asthenia and anorexia. The above two cases suggest that in some cases there is enough accessory adrenal tissue to maintain life following the routine adrenalectomy.

Greene reports that he was able to produce carcinoma of the breast in ⁽²⁴⁾95% of rabbits studied by the administration of a single massive dose of ESTRONE. Following administration of estrone an inflammatory process developed in the breasts and then subsided. This was followed later by a histological pattern comparable to that of fibro-cystic disease in the human breast. This was followed at a later date by malignant changes in 95% of rabbits studied.

Pearson and co-workers ⁽²²⁾demonstrated in two premenopausal women with bone metastases that urinary calcium excretion was markedly elevated at onset and continued to rise steadily with progress of the menstrual cycle. At the onset of menstruation, there was a prompt decline in urinary calcium but not to a normal level. Following oophorectomy, urinary calcium levels fell to normal within the first week. Administration of progesterone for a two week period produced no effect on calcium excretion. Administration of estradiol brought about prompt return of bone pain and marked elevated urinary calcium excretion and hypercalcemia. When estrogen was withdrawn, there was prompt subsidence of hypercalcuria and hypercalcemia with gradual decrease of bone pain, indicating tumor dependency of estrogen to support

the rapid growth of tumor.

It is probable that hormones would be required to stimulate and maintain a certain amount of mammary tissue before mammary carcinoma could develop. Attention has been focused on estrogen in such cases. However Gardner⁽⁷⁾ reports that he was unable to demonstrate any measurable difference in estrogen titers between mammary cancer-prone strains and non-mammary cancer-prone strains of mice. Struthers⁽⁸⁾ using the vaginal smear technique to determine estrogen level compared a series of 353 postmenopausal women whose average age was 56.1 years with a series of 57 postmenopausal women whose average age was 55.8 years in whom there was extensive carcinoma of the breast. He came to the conclusion that there is no greater estrogen production in patients with carcinoma of the breast after a natural or artificial menopause than in normal women after a natural or artificial menopause.

Ferguson⁽⁶⁾ experimenting with hypophysectomized and castrated rats noted that estrogen, progesterone and prolactin were necessary for lobule and alveolar mammary growth. He also noted that prolactin was more effective in producing growth when hormone and ACTH were present.

Hadfield and Young⁽⁴⁾ report in rats that full mammogenesis is a two phase process which depends on the synergistic action of two hormones and they suggest that estrone is responsible for growth phase and prolactin for phase of glandular differentiation. Maximal growth and differentiation depends on synergistic action of prolactin and estrone acting in optimal proportion with prolactin acting at far higher level of dosage

than estrone.

Olivecrma and Luft⁽¹⁵⁾ have reported improvement from hypophysectomy in patients with metastatic mammary carcinoma. The question arises whether hypophysectomy induces improvement simply by suppression of gonadal and adrenal function or whether there is in addition a pituitary hormone which is important in maintaining the growth of breast cancer.

Two women with active metastatic osteolytic mammary cancer, who had previously undergone oophorectomy and adrenalectomy with transient improvement, were subjected to hypophysectomy demonstrated improvement of anemia, cessation of osteolysis and calcification of osteolytic lesions. Remissions continued for three and seven months after hypophysectomy. Beef pituitary somatotropin was administered for 18 days, three months after hypophysectomy while patient was maintained on a metabolic balance regime. During growth hormone administration there was a steady rise in urinary calcium excretion. Nitrogen and potassium balance became slightly negative during growth hormone administration.

When somatotropin was stopped, urinary calcium and phosphorus excretion promptly returned to control levels. These data indicate that growth-hormone induced osteolytic tumor. This data suggests that pituitary somatotropin is an important growth factor for human mammary cancer.

Pearson et al reports objective improvement in 21 of a series of 41 cases treated by hypophysectomy. Eleven of these patients had previously been subjected to oophorectomy and

adrenalectomy with a remission and five of these eleven patients showed further remissions. He suggests that this group of five patients that responded to hypophysectomy had tumors that were stimulated by the mammotropic hormone alone.

Taylor and co-workers⁽¹²⁾ report that in a control study of eleven patients with advanced carcinoma of the breast that they were able to induce objective improvement in three of these patients by administration of 50-75 mg. of cortisone per day. They pointed out however that the objective improvement was not of the same degree as that in patients treated first by adrenalectomy and oophorectomy and the improvement was of a shorter duration.

Sezgo and Roberts⁽¹³⁾ suggest that cortisone also acts by competing with estrogen in peripheral blood for active sites on protein molecule which is a carrier for estrogens in the blood stream. They postulate that corticoids bind more weakly with this protein molecule than estrogens, which can only be replaced when cortisone is present in large excess. This would explain the escape phenomenon of disease from control by cortisone, for estrogen production increasing with time eventually exceeds the limit that can be bound by the standard dose of cortisone.

Pearson et al⁽¹⁴⁾ have shown that a further remission may be achieved by large doses of cortisone in patients who have relapsed after previous adrenalectomy and oophorectomy and hypophysectomy. Cortisone therefore must be acting directly on the disease itself in such cases.

Case Number 1---K. P.

Patient was a 62 year old white female who was first seen by U. N. staff in 1953. She had had a simple left mastectomy 18 years previously apparently for carcinoma and at the time she was seen by the hospital staff she had edema of both arms, left axillary adenopathy, a left supraclavicular mass whose surface was ulcerated; right breast indurated, fixed and contained a 10-12 cm. mass, right axillary adenopathy, right anterior cervicle chain adenopathy, and subcutaneous nodules in old incision and on anterior chest wall. At this time she had pain in her left shoulder and anterior chest. Breast biopsy revealed an undifferentiated type of carcinoma.

Patient was seen by Neuro-Surgical Department and felt to be a candidate for radon seed implantation of pituitary. In November 1953 radon seed was implanted through craniotomy incision by Neuro-Surgical Department. Within the next month the mass in the right breast had decreased to 1/3 of original size; it was soft and non-fixed, the axillary adenopathy had markedly decreased and edema of arms subsided, supraclavicular mass decreased in size and surface epithelialized, subcutaneous nodules on chest and in old scar had markedly decreased in size, and clinically patient gained weight and felt considerably improved.

Patient was followed in out-patient clinic and was in apparent remission until October of 1954 at which time was given Thio Tapa with some clinical decrease in size of skin nodules.

Patient was admitted to hospital January 1, 1955 at which

time previously described lesions were of size and appearance of before radon seed implantation. Supraclavicular mass was ulcerated and undurated, right breast was indurated, hard and fixed, and pain in left shoulder and anterior chest required narcotics for relief.

Patient was reviewed by surgery department and they felt that any palliation that could be offered was adenalectomy and oophorectomy. This was completed on 2-26-55. Post operative patient did not require narcotics for relief of pain in tumor sites and by 3-15-55 there was definite regression of breast lesion. On 3-28-55 patient became suddenly comatose and died. An autopsy was refused by relatives.

Case Number 2---M. M.

Patient was a 52 year old white female who had a left radical mastectomy four years previously for an anaplastic type carcinoma and received post operative irradiation. At the time of surgery she had back and left leg pain.

She was first seen by U. N. Orthopedic Department for a pathologic fracture of the left leg. Fracture was treated by an intramedullary nail and tumor tissue was recovered from area at time of surgery. Left axillary mass was biopsied and reported as carcinoma.

Patient was received by Surgical Department and they felt that some palliation might be offered by adrenalectomy and oophorectomy. This was completed on 10-16-54. Following surgery

there was some relief of bone pain, but no decrease in size of axillary mass. Patient did not return to Out-Patient department for follow-up and continued down hill and died 5-9-1955.

Case 3- A. S.

Patient is a 72 year old white female who five years previously had had an inoperable mass in right breast and received X-Ray radiation to that area.

Patient was first seen by U. N. Surgical department in September 1955. At that time the right breast was markedly indurated, fixed, and the surface was ulcerated over anterior and lateral aspects extending into the axilla with marked edema of the right arm. Adrenalectomy and oophorectomy was completed on 9-11-55. Following this procedure there was complete subsidence of edema of arm and absence of pain in this area. This was associated with gain in weight and a feeling of well-being by the patient.

The ulcerated area continued to decrease in size but by 8-3-56 edema of arm had started to return and X-Ray of the chest revealed basilar effusion. Patient seemed to be in cardiac decompensation and was treated for it by medical department.

On 8-17-56 patient had sudden onset of shortness of breath and died shortly afterwards.

An autopsy revealed metastatic, wide spread of tumor to bones, liver, lungs, and chest wall. There were multiple thrombi

in pulmonary vessels and large embolus occluding the right pulmonary artery. The cause of death was considered to be carcinomatosis, primary in breast, with pulmonary embolus.

Study of the primary tissue at the time of the autopsy revealed a rather poorly differentiated adenocarcinoma.

E. C.

Patient was a 54 year old white female who was first admitted to Immanuel D. Hospital June 28, 1955 complaining of partial paralysis of her face and ptosis of her left eye lid. She had severe pain in cervical, dorsal, and lumbo-sacral spine. She had had a left radical mastectomy in 1950 and a right radical mastectomy in 1954 both for carcinoma of the breast. She had received radiation to supraclavicular and back for metastasis in 1951. She had received testosterone therapy.

When first seen there was hirsutism of the face and brownish pigmentation of the entire body. Metastatic bone survey showed tumor infiltration of the skull, cervical, dorsal, and lumbo-sacral spine. Oophorectomy and adrenalectomy was completed July 8, 1955. Following surgery there was complete disappearance of bone pain in areas of metastases. Tumor was demonstrated in the right ovary, both adrenals, and section of the twelfth rib. There was marked improvement in the clinical picture, she gained weight, facial paralysis and ptosis disappeared, and was able to take an extended trip with her husband.

She was readmitted to the hospital October 13, 1955 for recurrence of pain in cervical spine which had begun one week prior to admission. Patient grew rapidly worse and died October 18, 1955.

The autopsy revealed metastatic spread of tumor to bone, liver, lung, chest wall, and soft tissues. Careful and extensive examination of the brain did not reveal any tumor tissue. No primary tissue was available for study; however histological picture of the tumor in skin incision, and liver revealed a rather poorly differentiated adenocarcinoma.

L. H.

Patient is a 51 year old white female who had had an excisional biopsy of mass in the right breast four years prior to admission. Histological picture is that of a poorly differentiated adenocarcinoma. She had received radiation to the breast. On admission to the hospital there was a large right supraclavicular mass and an axillary mass. There was partial paralysis of the right arm, probably from brachial plexis infiltration, and edema of the right arm. Oophorectomy and adrenalectomy was completed on 8-19-56. Within two days there was absence of bone pain in the right shoulder and she had increased muscle power. Edema of the arm decreased. Patient continued to improve and by 10-1-56 the supraclavicular and axillary metastases had decreased to one-half their size. Remission continued

until approximately 2-25-57 by which time she had developed blurring of vision, headache, and cough presumably from tumor infiltration. The patient is living at the present time, though expectation of life is short.

M. D.

Patient was a 45 year old white female who had a radical left and a simple right mastectomy for carcinoma of the breast in 1952 whose histological pattern was that of a poorly differentiated adenocarcinoma. She had received radiation therapy and testosterone therapy. When admitted to the hospital she had an extensive involvement of the bone, pleura, and supraclavicular areas. Adrenalectomy and oophorectomy were completed on 5-23-55. Within seven days there was marked subjective improvement. Bone pain which had been present had completely disappeared, patient was able to sit comfortably for the first time in several months. Patient continued to improve and then grew rapidly worse and died 1-1-56.

E. H.

Patient was a 51 year old white female who had a small papillary mass removed from the left chest wall. Histological examination revealed an undifferentiated carcinoma. No mass was demonstrated in either breast, but the histological pattern seemed most likely to be that of primary in the breast. The patient developed bone metastases and pain in these areas and was subjected to adrenalectomy and oophorectomy.

The patient died 5-8-56 having shown no response to therapy. X-Ray metastatic bone survey just prior to the time of death revealed wide-spread involvement of tumor which would be compatible with that of a carcinoma of the breast.

E. S.

The patient was a 50 year old white female who had noticed a mass in the right breast approximately one year prior to admission. She had noticed some scaling of the nipple. On admission she had a large mass occupying most of the right breast. The breast was fixed, very firm and over-lying skin had orange-peel appearance. The nipple was ulcerated and retracted. There were two supraclavicular subcutaneous masses. A node biopsy revealed histological pattern of an undifferentiated carcinoma. Oophorectomy and adrenalectomy was completed on 2-28-56. There was no response to therapy and the patient died 5-6-56.

S. L.

Patient is a 45 year old white female who had a right radical mastectomy done in 1951 for carcinoma of the breast. Five months prior to admission she had onset of pain in left leg and received x-ray treatment to that area and x-ray sterilization with improvement of symptoms. On admission there was involvement of pleura, cervical and dorsal spine with pain in these areas. There was flaccid paralysis of the left side extremities with loss of reflexes. Surgery

was completed 9-12-55. No primary tissue was available for study; however tumor in adrenal glands was that of a duct cell carcinoma. There was no response to therapy.

R. M.

Patient was a 43 year old white female who had a radical right mastectomy 8 years previous for a tumor whose histological pattern was that of a poorly differentiated adenocarcinoma. When the patient was first seen by Dr. Herbert Davis there were metastases to both supraclavicular regions, to bone, and lung requiring thoracentesis. A hysterectomy and oophorectomy had been preformed two months prior and at this time tumor was demonstrated in the liver.

A bilateral adrenalectomy was preformed May 5, 1954 and tumor was demonstrated in the right adrenal gland. A course of nitrogen mustard was given the patient before she left the hospital. There was marked subjective improvement and she required thoracentesis much less frequently for relief of dyspnea. Patient died April 17, 1955.

CONCLUSIONS

There were 12 cases which had been subjected to adrenalectomy and oophorectomy for management of carcinoma of the breast at the University of Nebraska Hospital and Immanuel Hospital. In one case there was no tumor tissue available for study and this case had to be excluded from the series. Of the remaining 11 cases, primary tissue was available for study in only 6 cases; however, of the remaining 5 cases primary tissue could not be obtained for study and in these cases tumor in adrenal glands, skin, or from a node biopsy was studied for histological pattern. In one case (E. H.) a breast mass was never identified and tumor from skin was used for diagnosis. The clinical course in this case was that of a primary breast carcinoma.

In this series of 11 cases there were no cases which could be classified as a well differentiated adenocarcinoma. The 5 cases which were classified as poorly differentiated adenocarcinoma all responded to a marked degree to this therapy. The single case of duct cell carcinoma demonstrated no response to this therapy. The five cases of undifferentiated carcinoma demonstrated slight response in three cases. The degree of palliation offered in these cases was of slight degree. It is interesting that one of the cases of undifferentiated carcinoma who had a marked response to hypophysectomy and had become refractory, gained a slight degree of response following adrenalectomy and oophorectomy. The patient died

approximately three weeks following surgery and adequate evaluation was not possible.

In an attempt to make this paper as complete as possible a statistical analysis was attempted, however please bare in mind that a total of only 70 cases could be extracted from the literature and statistics based on only 81 cases are not necessarily valid.

In reviewing Chart 3 it is noted that none of the cases of undifferentiated or duct cell carcinoma responded to a marked degree to this type of therapy. It is interesting to note that the two cases of inflammatory carcinoma responded to a marked degree to this type of therapy. One perhaps would not suspect that such a marked degree of palliation could be offered to a patient when examining the histological picture of this type tumor.

The best prognosis as to a marked degree of response to this therapy seems to be those tumors having a histological picture of an adeno or papillary carcinoma.

In Chart number 4 all of the cases of each histological pattern were grouped together and percentages of response were determined. It is noted that of the total of 81 cases only 47% responded even to a slight degree and 53% failed to respond even to a slight degree. When combining the total cases of adeno and papillary carcinoma it is noted that 88.9% of these cases responded to therapy. In combining all of the cases of duct cell and undifferentiated carcinoma it is noted

that only 11.1% of these responded and when a response was obtained that it was of a slight degree.

SUMMARY

A series of 11 unreported cases of carcinoma of the breast which were managed by bilateral adrenalectomy and oophorectomy were presented. The clinical response to this type of therapy was correlated with the histological pattern of the tumor. It was found that 3 of the 5 cases of undifferentiated carcinoma responded to a slight degree to this therapy. A total of 8 (72.7%) of the 11 cases responded to therapy.

A series of 70 cases were taken from the literature where the histological pattern of the tumor was known and combined with the 11 cases presented. It was found that 47% of the total cases responded to therapy and 53% failed to respond to therapy.

It was concluded that:

1. Adenocarcinoma and Papillary carcinoma respond in a high percentage of cases (88.9%) and that when a remission was induced that it was of a much greater degree than that of duct-cell or undifferentiated carcinoma.
2. Undifferentiated and duct-cell carcinoma respond in a low percentage (11.1%) and when a remission was induced that it was of only a slight degree.
3. Perhaps, that inflammatory carcinoma, responds in a good percentage of cases--(100%) in this series of two cases.

4. Histological study of the primary tissue may be used as index of response to therapy management by bilateral adrenalectomy and oophorectomy.

Chart No. 1

Patient	Age	Histological Pattern	Response
L. H.	51	Poorly differentiated Adenocarcinoma	Marked--living 6 Mo. P. O.
M. D.	45	Poorly differentiated Adenocarcinoma	Marked--lived 7 Mo. P. O.
E. L.		Undifferentiated	None
A. S.	72	Poorly differentiated Adenocarcinoma	Marked--lived 13 Mo. P. O.
K. P.	62	Undifferentiated	Slight Duration 1 Mo.
M. M.	52	Undifferentiated	Slight lived 7 Mo. P. O.
Total 6 Cases			% Response 83.33%

Chart No. 2

Primary Tissue Not Available			
Patient	Age	Histological Pattern	Response
E. C.	54	Poorly differentiated Adenocarcinoma	Marked lived 4 Mo. P. O.
R. M.		Poorly differentiated Adenocarcinoma	Marked
E. S.	50	Undifferentiated	None lived 3 Mo. P. O.
S. L.	45	Duct Cell	None
E. H.	51	Undifferentiated	Slight
Total 5 Cases			% Response 60.0%
Total Cases 11		Total % Response 72.7%	

Chart No. 3

Cases Taken From Literature					
Source	No. Cases	Histological Type	No. Resp.	No. NOT Resp.	Degree
(21)	2	Duct Cell	2	0	Slight
	2	Adenocarcinoma	2	0	Marked
	1	Papillary	1	0	Marked
(12)	1	Adenocarcinoma	1	0	Marked
(10)	19	Adeno & Papillary	16	3	Marked
	8	Duct Cell	1	7	Slight
	16	Undifferentiated	0	16	
(15)	12	Undifferentiated	3	9	Slight
	2	Inflammiatry	2	0	Marked
	7	Adenocarcinoma	6	1	Sl-Marked
Totals	70		34	36	

<u>Chart No. 4</u>		Total Cases			
<u>Tumor Type</u>	<u>Total No. Cases</u>	<u>Resp. %</u>		<u>No Resp. %</u>	
Duct Cell	11	1	9.09%	10	90.91%
Inflammiatory	2	2	100.00%	0	
Adenocarcinoma	34	30	88.2%	4	11.8%
Papillary	1	1	100.0%	0	
Undifferentiated	33	4	12.1%	29	87.9%
Total Cases	81	38	<u>47%</u>	43	<u>53%</u>

Chart No. 5 The Incidence of Metastases in 25 Cases
and Their Response to Adrenalectomy &

<u>Tissue Involved</u>	<u>Oophorectomy</u>	
	<u>Incidence</u>	<u>Regression</u>
Bone	20	10
Lung & Fleura	7	3
Chest Wall	5	2
Producing Edema of Arm	6	1
Lymph Nodes	4	2
Intracranial	4	2
Liver	1	1

Reproduced from Ruggins & Dao (10)

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