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CANCER OF THE BREAST TREATED BY OOPHORECTOMY

BY

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The treatment of advanced cancer remains an important problem, and any encouragement we gain in an endeavour to help these patients should be made known so that others may benefit. The case record is therefore presented of a patient with advanced cancer of the breast who was treated solely by bilateral oophorectomy; the disease disappeared entirely during the six months following the operation, and she was free from demonstrable disease 22 months later. This patient called attention to the fact that the various lumps increased in size immediately before menstruation, and it was this observation which made me decide to perform the operation. The experience of others has been sought in the literature and is presented to enable an assessment to be made of the present position in order to plan for a further step forward.

Case Report

A married woman, aged 50, with two children, was seen on April 13, 1948, with multiple lumps.

History.—Two years previously she noticed a swelling of the right side of the face in the region of the parotid salivary gland and pre-auricular lymph nodes. In July, 1947, a small painless lump, which increased in size, appeared above the inner end of the left clavicle. In December, 1947, she noticed a large lump in the left breast and a small lump on the outer aspect of the left arm. Other similar nodules developed in the skin over the right shoulder, chest wall, and right loin. These lumps varied in size with the menstrual cycle, being largest just before menstruation began. Her general health was good; there was no loss of weight.

Menstrual History.—Menstruation started at the age of 16; the cycle varied from 21 to 26 days; the duration of period was 7 to 8 days. During the past two years she has lost clots.

Examination.—Her general condition was good and no abnormality was detected. A nodular lump 3.4 by 2.2 cm. was seen in the right parotid region. In the left supraclavicular region a hard irregular swelling 5 by 2.5 cm. was found. There was no abnormality in the right breast. A hard irregular lump 3.5 cm. in diameter was found in the upper and inner quadrant of the left breast, attached to overlying skin and somewhat tethered to underlying structures. Hard fixed lymph nodes were present in the left axilla. In the right axilla there were no enlarged lymph nodes. Multiple nodules were seen in the skin over the right shoulder, left arm, chest wall, and right loin. The abdomen was normal. Radiological examination of the chest, dorsal and lumbar spine, and pelvic bones revealed no metastases. A blood count showed: red cells, 4,080,000 per c.mm.; white cells, 6,400 per c.mm.; Hb, 78%; C.I., 0.98;

anisocytosis was rather marked; leucocytes appeared normal (Figs. 1A to 2B illustrate the case.)

Operation.—On July 7, 1948, a bilateral oophorectomy was performed and the skin nodule from the right shoulder region was excised.

Pathologist's Report on Specimens.—“(a) Both ovaries:—There is an enlargement of one ovary by a cyst with water contents (2.5 by 2 cm.); the other ovary appears normal. Microscopy shows that the ovarian cyst has a thin lining of luteal cells. In the other ovary there is a wide, ill-defined zone of theca-cell formation; otherwise there is no abnormality. (b) An elliptical piece of non-ulcerated skin (2.2 by 1 cm.) with underlying fat (1.2 cm. deep) in which there is a firm white growth merging into the dermis and projecting on one part of the cut surface. Microscopy reveals a secondary spheroidal-cell carcinoma arranged as compact groups, narrow cords, and isolated cells in the subcutis and deep layers of the dermis.”



FIG. 1A.—Tumour in right pre-auricular region. Before bilateral oophorectomy.



FIG. 1B.—Tumour in right pre-auricular region has disappeared after bilateral oophorectomy.

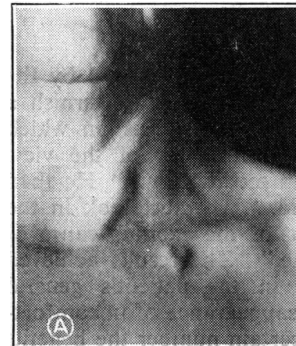


FIG. 2A.—Skin nodule below left clavicle. Before bilateral oophorectomy.

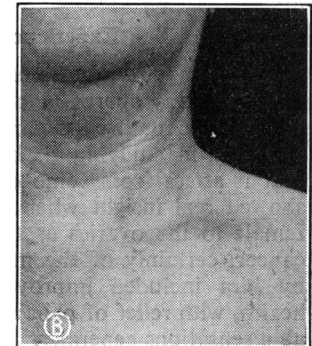


FIG. 2B.—Skin nodule below left clavicle has disappeared after bilateral oophorectomy.

Subsequent Progress.—On August 17 the lumps were smaller; and some skin nodules had disappeared. On October 26 the swelling in the right parotid region had practically disappeared; the lump in the left breast was very soft, 2.5 cm. in diameter. On January 25, 1949, there was a residual area of slight thickening at the site of the original tumour in the left breast, a small lymph node in the left axilla, and an area of thickening in skin of the left arm. On February 22 all lumps had disappeared; the tissues of the left breast were soft and pliable and resembled a normal breast; there were no enlarged lymph nodes in the left axilla; the face was normal; and all the skin nodules had disappeared. On May 23, 1950, the patient was well, with no sign of carcinoma.

Historical Basis

As long ago as 1896 a new treatment was introduced for advanced cancer of the breast by G. T. Beatson, of Glasgow. The patient was referred to him by Dr. J. W.

Wallace, who described her condition in a letter and considered that nothing could be done except "something in the way of a dressing—this latter will be accepted by her as a great deal." In 1889 Schinzinger conceived the idea that the prognosis of breast cancer in young women might be improved by oophorectomy, but it seems that he never carried it out. Thus Beatson's case is the first on record, and is now quoted not only for the historic interest but for its practical importance.

Beatson's First Case.—A woman aged 33 had noticed a tumour in her left breast when nursing her first child three years previous to coming under observation, but it did not increase until her second lactation 20 months later. After a delay of 10 months she applied for relief from a breast tumour 5 by 3½ in. (12.7 by 8.9 cm.) with nodules and an ulcer in the skin over it. An extensive operation was done and was followed by immediate and inoperable recurrence. Shortly afterwards she was referred to Beatson with a large mass 3½ by 2½ in. (8.9 by 6.4 cm.) in the scar adherent to the chest wall and with surrounding skin nodules. The viscera and bones appeared normal and her general condition was fair. Thyroid extract was given for a month without result; then bilateral oophorectomy was performed, and was followed by thyroid extract, 15–20 gr. (1–1.3 g.) daily. The diagnosis of carcinoma of the breast was confirmed by microscopy. Eight months after this operation all trace of disease had gone, and this was certified by many of the best surgeons in Edinburgh when she was shown at a clinical meeting there.

In 1902 a discussion was held in London on the treatment of inoperable cancer, and Henry Morris spoke of this new treatment, stating that "it has been tested by Dr. Beatson in a scientific manner, and has been placed before the profession in a thoroughly temperate and scientific spirit. It has also been defended by him without animus and with great ability."

The Experience of Early Workers

Beatson (1902) confessed that he was fascinated by the effects of this operation because "they seem to furnish a clue to the nature of cancer and to the lines on which to work in studying it, being confirmatory of the view that it arises from some error in metabolism." He then showed real insight when he said, "We must look in the female to the ovaries as the seat of the exciting cause of cancer, certainly of the mammae." The results achieved by him included improvement in the patient's general health, with relief of pain and disappearance of uncomfortable sensations generally. In a certain number the benefits were more permanent: some patients with inoperable cancer remained well some years later and the disease disappeared.

Boyd (1900) was impressed with this new conception and said: "This case of Beatson's altered my whole feeling with regard to cancer. Previously my only hope of curing it lay in earlier and wider operation, but now it was clear that the relation between a cancer and the body could be so altered that the latter could prevail over the former." He reviewed a series of 54 cases: 19 (35%) received marked benefit, 34 (63%) received doubtful or no benefit, and one died of exhaustion. Life was prolonged in these patients by at least six months, and he noticed that in the majority the growth reappeared or began to enlarge in six to twelve months after operation.

Snow (1902) had not seen useful results in a series of 12 cases. Thomson (1902) analysed the results in a series of 80 cases which he had collected and found that decided improvement had occurred in 18 (22%). He was of the opinion that the value of the operation was established.

Lett (1905) presented the results of an analysis of 99 cases with inoperable breast cancer treated by oophorectomy. There was much improvement in 23.2%, and distinct though less improvement in 13.1%. One patient was well five years later. The benefits included relief from pain, marked diminution and even disappearance of the growth, healing of ulcers, and prolongation of life. The most favourable age group was between 45 and 50 years; in relatively young patients he thought the method was worthy of further trial; after 50 years of age the operation was rarely worth doing.

Bruce Clarke (1905) reported that in all cases he had operated on there was some improvement, and one patient was alive five years after oophorectomy for a recurrent carcinoma, the growth having shrivelled and remained stationary in size.

McAdam Eccles (1905) described a case in which oophorectomy had been performed for extensive cancer in which all the nodules atrophied except at one or two small points.

Torek (1914) reported improvement in a series of seven cases, and in one the growth disappeared almost completely. The tumours began to grow again after six to seven months, sometimes sooner, in every case except one. In the latter case the tumour, which had been firmly fixed to the chest wall, became mobile and a radical mastectomy was performed 10 weeks after oophorectomy.

Waring (1928) stated that he had practised this operation for a number of years and considered that in from 20 to 30% of patients the primary growth diminished and might almost disappear, and secondary growths became much smaller, but the results seemed to be temporary; the disease recommenced its active growth after two to four years.

Recent Experience

Regarding this operation Beatson (1902) reflected, "If after a fair trial it is found wanting, then I hope it will be abandoned and forgotten." Interest has, however, continued in the method, either used alone or in conjunction with other treatment. Thus Horsley (1944) performs radical mastectomy and bilateral oophorectomy for all patients in the premenopausal state, and states that only two patients developed recurrence in a series of 25 in all stages of the disease; one of these patients had gelatinous carcinoma and the other had bilateral carcinoma with probable internal metastases. Adair and co-workers (1945) reviewed the results in a series of 31 cases and found improvement in 4 (12.9%); these patients were in the premenopausal state. An interesting report was made by Herrell (1937) concerning a series of 1,906 women treated for cancer of the breast and a series of 1,011 women of a similar age group without this disease. In the first group bilateral oophorectomy had been performed in 1.5% before the breast condition was diagnosed; in the second group 15.4% had undergone this operation. From this evidence it seems that interruption of ovarian function may protect a number of women from cancer of the breast.

An interesting study was made by Dargent concerning carcinoma of the breast in castrated women. In a series of 2,000 cases of carcinoma of the breast at the Centre Anticancéreux, Lyons, he found 32 (1.6%) occurring in castrated women. Thus, although the disease is rare in these patients, it does occur. It is of interest to note in this series that the number of patients over the age of 60 is high, and when castration was performed between the ages of 40 and 50 the disease appeared late. Further, in

all cases the development of the carcinoma was slow even in cases of early onset.

X-Irradiation of the Ovaries

Interruption of ovarian function by x-irradiation in cancer of the breast was first used by de Courmelles in 1904. In this country Wintz (1926) was one of the pioneers in this treatment. Dresser (1936) reviewed the results in a series of 59 patients with metastases who received ovarian x-irradiation; 30 were premenopausal and 43% of these obtained benefit. Relief of pain and improvement in general health occurred, and a number showed regression of bone metastases; this benefit extended over periods up to three years. In the post-menopausal group no regression of metastases occurred, but symptomatic improvement was seen in 48.2%. Ritvo and Peterson (1944) state that the most satisfactory results are found in patients with osseous metastases; these lesions partially regress, and in some cases re-ossification occurs, with complete disappearance of the disease. The treatment does not prevent new metastases from appearing. Halberstaedter and Hochman found improvement in 56% of a series of 60 cases in all stages of the disease; bone metastases responded particularly well; cutaneous recurrences were affected to a less degree, and lymph-node deposits showed little response. Taylor (1939) concluded that an artificial menopause may be expected to result in temporary regressions or improvement in about one-third of the cases with recurrent and advanced cancer of the breast. Hunt (1940) reported regression of pulmonary metastases after ovarian irradiation.

Improvement after ovarian irradiation seems to be temporary and lasts for a period up to two years. It is known that some patients continue to menstruate and become pregnant afterwards; a case of twin pregnancy was reported by Kaplan (1927). When complete cessation of ovarian function is required bilateral oophorectomy must be performed.

Vicarious Secretion of Oestrogen.—There is evidence that ovarian irradiation and bilateral oophorectomy do not suppress oestrogen formation in the body. Significant amounts of oestrogen have been demonstrated in the urine of women who are over the accepted age of the menopause. Frank and co-workers (1934) demonstrated an oestrogenic cycle in the blood of a woman whose uterus and ovaries were removed, and Laroche and co-workers (1933) found oestrogen in the urine of 26 women after bilateral oophorectomy. The suggestion has been made that the vicarious secretion of oestrogen occurs from the adrenal and pituitary glands. Patients with advanced cancer of the breast treated by bilateral oophorectomy must be kept under periodic review and any oestrogen excretion in the urine is measured. If it is shown that oestrogenic function has restarted it can be combated by the administration of androgen.

Summary

The case record of a woman with advanced cancer of the breast is presented; the disease completely disappeared after bilateral oophorectomy. It was observed that the lumps increased in size immediately before menstruation began.

A survey of the literature on the subject is made and the value of the treatment shown.

Bilateral oophorectomy is better than x-irradiation of the ovaries.

Patients must be kept under periodic review and oestrogen excretion estimations made, so that if excretion occurs androgen can be given.

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NOCTURNAL ENURESIS: A SPECIAL APPROACH TO TREATMENT

BY

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In a large home for deprived children the problem of enuresis is of great importance and practical interest. After reading much of the literature on this subject one is left rather bewildered at the number of different methods that are claimed as effective and yet are in fact unreliable and unconfirmed by further workers. Mowrer and Mowrer (1938) claim that all of 30 cases treated became dry. We therefore decided to try their method, using the device which wakens the child as soon as the act of micturition begins. This device has proved very helpful indeed, not only as an effective remedy but also as an aid in the study of the child's reaction to treatment. By this method we have treated 20 cases; 15 are now dry and 5 greatly improved. It is strange that this work and its claim have scant recognition. Deacon (1939), using the same method on a small number of mental defectives, claimed a successful therapeutic result in six out of seven cases. Later, Seiger (1946) described his own modification of the apparatus, which is now marketed in America, particularly for habit-training in young children, but we are doubtful of the desirability of using the apparatus for this purpose.

Although the present study is confined mainly to the assessment of our success with this form of treatment, in no way do we wish to minimize the effect of an adequate physical and psychological investigation of each case and the importance of proper treatment of the child's personality difficulties; but in seeking some further aid to break its well-established habit and restore lack of confidence this method has a common-sense appeal.

The Apparatus

The device used is a modification of that described by Mowrer (1938). Their original pad, on which the child slept, consisted of two layers of bronze gauze, approxi-