

THE  
GLASGOW MEDICAL JOURNAL.

No. II. AUGUST, 1911.



ORIGINAL ARTICLES.

THE TREATMENT OF INOPERABLE CARCINOMA  
OF THE FEMALE MAMMA.

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IN a communication I made to the Medico-Chirurgical Society of Glasgow on 6th May, 1910, on the treatment of inoperable carcinoma of the female mamma, I showed Mrs. E., aged 46, as an illustration in support of the treatment of such cases by oöphorectomy. This patient had her left breast removed in February, 1907, but recurrence took place locally within twelve months. An attempt was made by me to remove the recurrence in June, 1908, but without any satisfactory result. In December, 1908, her condition was as follows:—

At the anterior border of the axilla was a firm hard mass, about the size of a walnut, and in the infra-clavicular fossa there was an indefinite hardness suggestive of infiltration, while in the supra-clavicular space enlarged glands could be felt, and seemed to extend downwards under and behind the clavicle. In the skin on either side of the scar there was a

whitish nodule presenting the usual appearance of a secondary cancerous nodule in the skin. As no further local treatment seemed advisable I removed both ovaries on 28th January, 1909. She made a good recovery, and was then put on small doses of thyroid extract. Her progress was very satisfactory. She gained rapidly in weight and strength, and there was a marked improvement in the conditions around the scar.

Examined on 30th March, the hard mass above mentioned could not be felt, and the scar tissue had become more pliant and freely movable over the subjacent structures. The sense of hardness and resistance in the infra-clavicular area had gone and no glandular enlargement could be made out in the supra-clavicular fossa or axilla.

When shown on 6th May, 1910, at the Society there was an absence of any apparent disease, and her general health was good, but, as was stated then, she had obscure pains in the back and limbs which might be indicative of fresh manifestations of the disease. Unfortunately this proved to be the case. While away in the country for a change, symptoms of loss of power in her legs came on, and she was later on readmitted to the Glasgow Cancer Hospital, where she died on 12th December, 1910, with all the indications of a secondary cancerous growth in the vertebral column and with other reappearances of the disease.

Permission was given for an examination of the body, which was done by Drs. Dunn and Whittingham, to both of whom I am much indebted for the microscopic sections and drawings in the case. The following is the report:—

“*External.*—Body is that of an emaciated woman. Left breast has been removed. Both hips are flexed and turned over to the right side with contracture of the muscles. There is marked œdema of the feet. There is a large scar over area of left breast,  $4\frac{1}{2}$  inches long, and extending obliquely upwards and outwards towards the left axilla. At the upper end of this scar there is a slightly prominent mass under the skin, about the size of a walnut. Some small cervical glands can be felt through the skin on both sides. There is a scar between umbilicus and symphysis, about 3 inches long. A few prominent glands are felt in the left groin.

“*Internal.*—Pericardial sac contains clear fluid. The heart muscle is atrophied, of a brown colour, and dry in section. The valves are normal. No tumour nodules are found. The right pleural cavity contains several ounces of clear fluid.

The visceral pleura, particularly over the lower lobe, is dotted with miliary tumours. The lower lobe is semi-consolidated, contracted in size, and on section shows presence of diffuse infiltration by carcinoma, which shows a tendency to spread along the bronchi. The left visceral pleura shows a less abundant distribution of miliary tumours, and carcinoma cannot be definitely seen in the lung itself. The connective tissues in the posterior mediastinum are firmer and more adherent than normal. Definite cancer nodes are not found.

“*Abdomen.*—The liver is atrophic, and about a dozen small miliary tumours are found on the surface. Section shows slight evidence of venous congestion. The spleen is of moderate size; lymphoid tissue present shows no tumours.

“Kidneys are atrophic and pale. The medulla of right suprarenal is more opaque than normal, possibly carcinomatous. Both ovaries have been removed by operation. Uterus is about normal in size. Erosion is seen on the right side and posterior part of os internum.

“The outer end of the pectoral scar and the prominent nodule in the upper part of it near the anterior fold of left axilla is found to consist chiefly of carcinoma, and additional nodules are found in the underlying pectoralis muscle.

“The vertebral bodies are removed in one strip in front by cutting the pedicles. The bodies are split after removal. Carcinoma is found to exist in most of them. The eleventh has given way and collapsed anteriorly so as to cause an oblique kinking of the column. There is very slight projection of tumour backwards from these bodies (tenth to twelfth) at this level, but there is more prominent projection of the laminae from the same vertebræ.”

Several microscopic sections were made of the various secondary growths found, and they reveal some points of interest. Of a section across the situation of the operation scar, and including an underlying nodule, Dr. Dunn reports as follows:—“The whole of the tissue, skin, subcutaneous tissue, scar tissue, muscle, and deep fascia are invaded by scirrhus carcinoma, the epithelial cells being in very small groups and strands. Here and there are seen several areas of much degenerated fibrous tissue, which may possibly represent the remains of former tumour tissue, as the appearances represented by these areas are not usually seen.”

Of a section made from another large portion of skin and subcutaneous tissue removed from the neighbourhood of the scar, Dr. Dunn says that it shows a condition of extreme

fibrosis in the subcutaneous tissue, which, however, exhibits a slight but diffuse permeation of cancer cells. A section of the pectoral muscle reveals a single large mass of actively-growing carcinoma. Microscopical examination of the suprarenal showed invasion of the medulla by cancer cells; and other structures, as, for instance, the pleura, which appeared to be fibrous, were found to be in reality permeated with cancer.

Dr. Whittingham examined the glands removed from the left groin. In their cortex there was marked cancerous infiltration, less of it in their medulla, but no cancer cells were seen in the efferent lymphatic vessels. The fibrous tissue of the gland was much increased, and here and there it was noted that scattered through it were masses of cartilaginous structure—an interesting point in view of the fact pointed out by other pathologists that in bone metastases in cancer ossification may occur in the lymphatic glands (see Fig. 1). In the mass removed from the vertebral column there was present a good deal of fibrous tissue stroma, invaded with the plump carcinomatous cells in small groups, and marked cartilaginous transformation was seen similar to that in the inguinal glands (Fig. 2).

In the liver nodules Dr. Whittingham found that there were carcinomatous cells, not of hepatic origin, scattered through a loose matrix, and that the liver lobules were somewhat displaced at the edge of the growth which was infiltrating them. There was present here, too, some leucocytic infiltration, and, generally, some venous congestion.

Examination of the lung revealed masses of round cancer cells in the perivascular and peribronchial lymphatics, while here and there were seen small collections of growths in the alveoli. There was present a distinct broncho-pneumonia, and some of the alveoli (more distant from the bronchioles) showed a catarrhal condition, and were somewhat emphysematous.

Apart from the fact, that, as this case was shown so recently at the Medico-Chirurgical Society, it is only fair to give its after-history, I also feel that its publication is useful in that the full *post-mortem* report upon it permits me to draw attention to the effects of oöphorectomy and the present position of the operation as a means of treatment in inoperable carcinoma of the female mamma. Introduced in 1896 to the notice of the profession, and based on the close relationship that exists between the ovary and mamma in the matter of

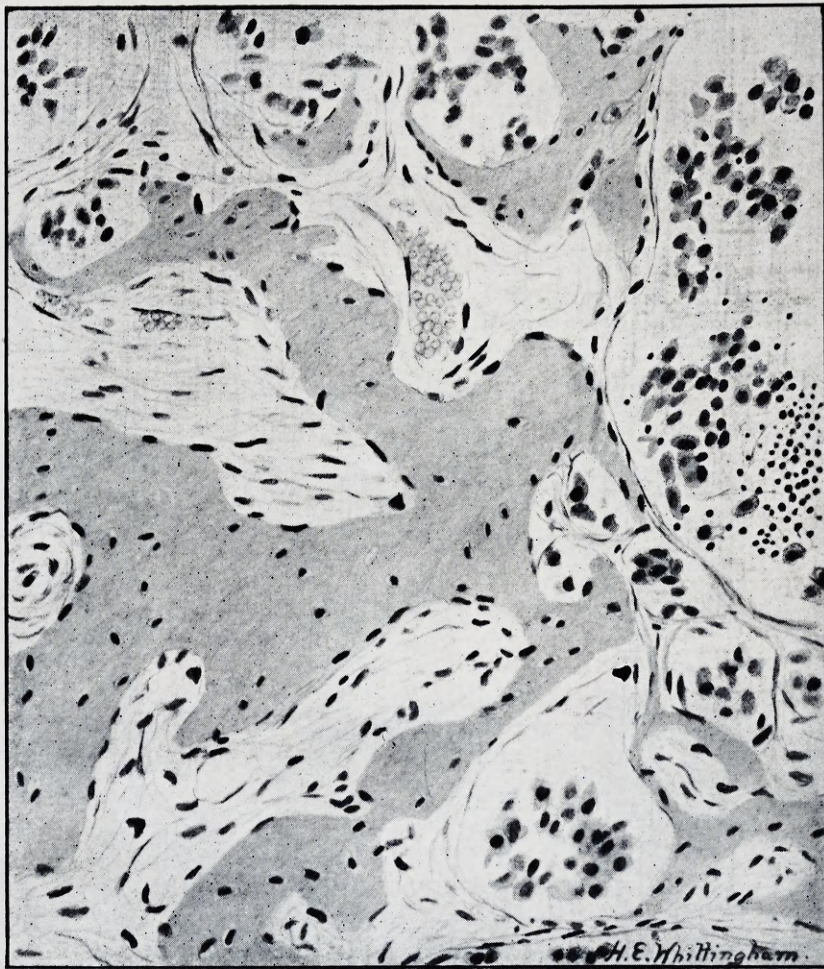


FIG. 1.  
Cancer in inguinal glands; fibrous stroma showing cartilage formation.

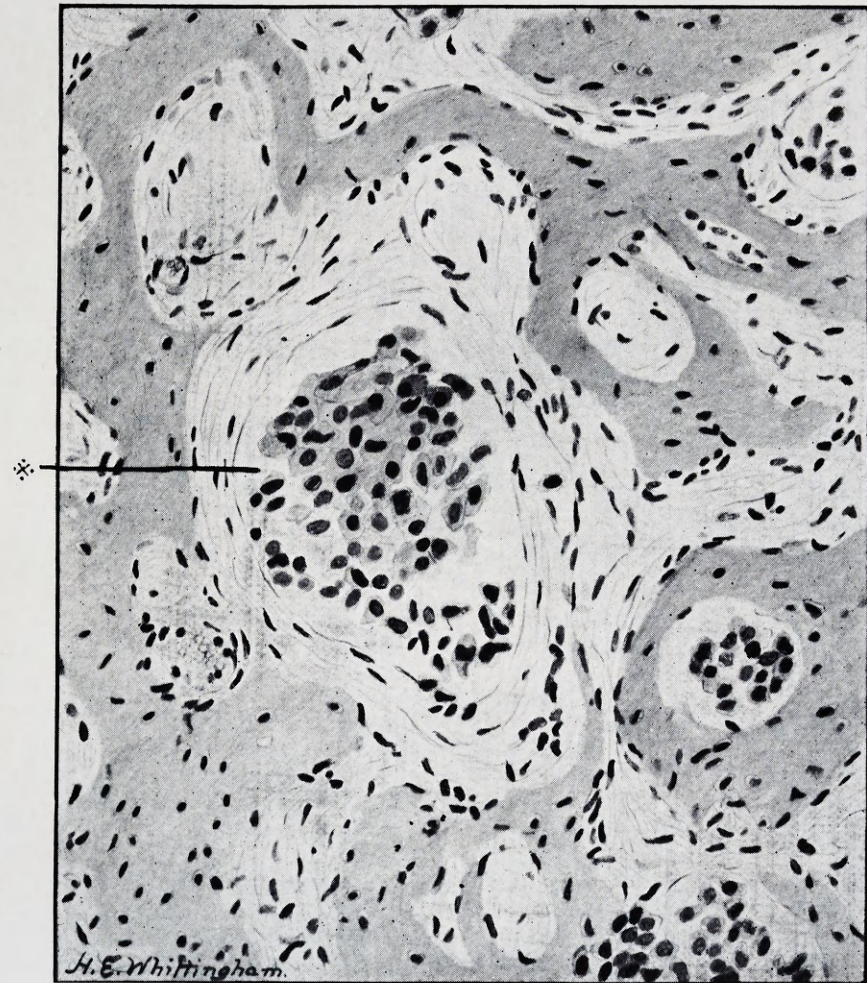


FIG. 2.  
Growth in vertebral column. \* Group of cancer cells in fibrous stroma.

lactation, I can only repeat here what I stated to Sir Henry Morris when he kindly asked me in March, 1908, for a short account of my opinion on the effect of oöphorectomy and thyroid extract in inoperable mammary cancer to embody in the paper he was reading at the International Medical Congress at Brussels on the "Treatment of Inoperable Cancer." In my reply I told Sir Henry Morris that I had no great change of opinion to announce since 1902, when the subject was up for discussion in Manchester at the British Medical Association. At that time I had satisfied myself that cases of carcinoma mammæ of an acute type of carcinoma or that were the subject of metastatic visceral growths were in no way benefited by the operation of oöphorectomy, with the result that the cases suitable for the procedure became more limited. I also in July, 1902, had realised that in many of the cases the effects of oöphorectomy on the local manifestations of the disease were transient, and that fresh nodules did appear coincidentally with the disappearance of the older ones. At the same time there was a certain limited number of cases of inoperable mammary cancer in which the beneficial effects of the operation had been more permanent, and in whom there had been for some years a period of apparent cure. Lastly, there was a large body of evidence from outside and independent sources that showed conclusively that in a very considerable proportion of cases the operation had been followed by an improvement in the general health, by relief of pain, and by a disappearance of uncomfortable sensations generally. Further, at that time, while not regarding the administration of thyroid extract as essential to the success of oöphorectomy, I had a strong belief in its therapeutic action, and that its power as a lymphatic stimulant was beneficial in its effects upon cancer cells in the lymphatic spaces. As a result of the above experience gained in my earlier work it follows that the cases in which I have performed oöphorectomy since 1902 have become much more limited, and I have tried it only in picked cases. I have not had with them any marked permanent success, but I have had no reason to change the opinions that I held in 1902, and I consider that the following conclusions fairly represent the position of the procedure as a therapeutic measure in *inoperable* mammary cancer:—

1. That there has been a complete disappearance of the outward manifestations of the disease in some few cases.
2. That there has been an improvement in the general health and the progress of the malady in a larger number.

3. That in only a very limited number was the disappearance of the growths for any considerable time. One or two have had freedom from outward manifestations of the disease for five to six years, and several for two years, but in the larger number the disease manifested itself within twelve months.

4. That as yet no permanent cure has been effected by oöphorectomy, and the operation can only claim to confer a certain amount of immunity for a period that varies with different cases.

5. That there is reliable evidence that the operation influences the course of carcinoma mammæ, but it is uncertain in its action and seems to some extent independent of age.

6. The most favourable cases seem to be those in which the carcinoma is not of an acute type, and in persons before the climateric, although some benefit after the menopause.

7. Cases with visceral deposits, or where the manifestations of the disease are of a rapid and active character, are not influenced by oöphorectomy in the slightest degree.

8. The operation makes itself felt chiefly on cutaneous and subcutaneous nodules, and to a less extent on glandular enlargements. It apparently does so by inducing a fibrous change in the affected tissues. It has apparently no effect on visceral and bony metastases.

9. In my opinion the operation has been narrowed down to a comparatively small group of cases, and even in these no results of a permanent nature can be looked for; but in view of the very small mortality of the operation *per se*, it is a procedure that can be fairly put before the patient as having possible palliative effects that may carry with them improved health.

10. Further experience of the use of thyroid extract confirms my opinion of its usefulness if employed in small doses and carefully watched. Even after ordinary operations for removal of cancer I administer it for long periods, and, I think, with advantage.

11. Mr. Stanley Boyd gave a list of 54 cases of oöphorectomy in the *British Medical Journal* for October, 1900, and of these 19 (35 per cent) were more or less markedly benefited, 34 were not benefited or were only doubtfully benefited, and 1 died of exhaustion.

12. In July, 1902, in the *British Medical Journal*, Mr. Alexis Thomson published an analysis of 80 cases, grouped in three tables under the following headings:—

*Table I.*—Cases in which decided improvement followed

oöphorectomy, and in which life was prolonged for more than twelve months after the operation—18 cases.

*Table II.*—Cases in which decided improvement followed oöphorectomy, in which life was prolonged for less than twelve months after the operation, or which have been under observation for less than twelve months since the operation—11 cases.

*Table III.*—Cases which were not appreciably influenced by oöphorectomy—51 cases.

Since then the only other contribution to the subject has been a study by Dr. Hugh Lett of about 100 collected cases treated by oöphorectomy, to which reference is made by Thomson and Miles in their *Manual of Surgery*. They say "that nearly one half of the patients under 50 years of age derived marked benefit in the form of relief from pain, improvement in the general health, diminution or even temporary disappearance of the growth, and healing of the ulcers."

Mrs. E.'s case certainly manifested for a time all the above favourable conditions, and for six months she enjoyed excellent health. The improvement, however, did not last, no doubt in consequence of the vertebral lesion, a state of matters that even her improved general health could not meet. The microscopic sections showed that the arrest of the growth and its disappearance were probably due to an increase of the fibrous stroma of the tumour at the expense of the cellular elements. Of great interest, too, is the appearance of cartilaginous masses in the inguinal glands, the preliminary stage of that glandular ossification that has been recorded in cases of bony metastases in cancer. What exactly is the interpretation of this fact it is not easy to say, but it is a feature of malignant disease that might be of service had we the explanation of it. Disappointing as is the result in Mrs. E.'s case, it supports the view I hold strongly that in women over 40, with no visceral or bony lesions, whose general health is fair, and who are still menstruating, oöphorectomy should be offered in inoperable mammary cancer.

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