

DOUBLE CARCINOMA OF THE UTERUS, WITH METASTASES.¹

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(PLATE III.)

THE material for the following study was obtained post-mortem at the Middlesex Hospital, and a short description of the case was included in an article on "Multiple Primary Malignant Growths," by R. A. Young, in the Third Cancer Report of the Middlesex Hospital Cancer Research Laboratories.

S. S. C., æt. 50, was admitted to the Cancer Wards with a recurrence in the pelvis two years after having undergone vaginal hysterectomy at another hospital. The condition before operation was diagnosed as malignant ulceration of the cervix, but no details of the pathological examination of the parts then removed can now be obtained, and there is no note in the clinical records as to whether the ovaries were removed or not at the operation. On admission to the Middlesex Hospital she was found to have extensive induration of the pelvic floor with ulceration of the vaginal vault. She died a month after admission. At the autopsy nodules of growth were found in the lower lobe of the right lung near its base posteriorly; the liver was riddled with them, especially in the right lobe; the spleen had a few small deposits underneath its capsule; the left kidney contained one or two small masses; the left suprarenal was infiltrated with new growth; the lumbar glands were extensively affected; the thoracic duct right up to its junction with the left internal jugular and subclavian veins was a solid rod of growth, and from it a small mass projected into the left innominate vein. The pelvis was occupied by a large mass of new growth, soft and friable on pressure, adhering all round to the pelvic wall. No trace of ovaries could be found. There was nothing to suggest that the case differed in any way from the ordinary advanced cancer of the cervix, but, following the usual routine, portions from the various deposits were taken for histological examination.

Owing to the different appearances found on microscopic examination it was at first thought that the sections from two different cases had been accidentally mixed, but this was found improbable. For a time it was considered that one had to deal with two separate kinds of carcinoma which had metastasised separately, and, as a matter of fact, the case was thus described, but subsequent examination showed that the two types of growth were present together in one section, and the whole case became the subject of more minute investigation.

¹ Demonstrated at meeting of Pathological Society of Great Britain and Ireland, January 1908. [Received for publication, May 13, 1909.]

Pelvic mass.—Three pieces of tissue from the recurrent mass in the pelvis had been preserved. Two of these, although some hundreds of sections were cut from them, showed only one type of growth—abundance of loose connective tissue with many small round cells and irregular acini composed of columnar cells usually one layer in thickness. The third piece was likewise mostly adeno-carcinoma, but in addition there was found a small nodule of squamous epithelial cells with keratohyalin formation and central disintegration of the mass (Plate III. Fig. 1).

Lumbar lymph gland.—In some sections one type predominated or was exclusively represented, but many sections showed both kinds—squamous-cell and columnar-cell epithelium—in about equal proportions side by side (Plate III. Fig. 2).

Thoracic duct.—Two pieces of tissue had been taken for examination from different parts. One of these showed only dense fibrous tissue with acini of columnar cells; the other showed both squamous epithelium and adeno-carcinoma (Plate III. Fig. 3).

Left kidney.—Both types were found represented (Plate III. Fig. 4). The illustration is of interest as showing, in addition to the separate structures, the interposition of a few squamous cells in the columnar-celled wall of the acinus.

Left suprarenal.—The two kinds of growth are found side by side. Plate III. Fig. 5, chosen like the others from a microscopic field containing both, does not show the columnar cells as typical as they are elsewhere in the section, but there is no difficulty in differentiating the two forms at any part.

Spleen.—Only one piece of tissue was available for examination, and though carefully examined it failed to show more than the one type. Columnar-celled acini were found underneath the capsule set in dense fibrous tissue.

Liver.—Here again only one piece of tissue was preserved, and though a fairly large piece it showed nowhere more than one kind—squamous-cell carcinoma. Acinous structures observed at one part were proved not to be portions of the growth by the fact that they had intact elastic tissue around them; they were changed bile ductules. In this case, as well as in the last, it might be that the two kinds of growth were “plated out”—squamous epithelioma existing pure in the liver, and adeno-carcinoma in the spleen, but it is more probable, judging from what was found to be the case in the other deposits, that if more pieces from the two organs had been taken for examination we should have found both types coexistent.

Lung.—Epithelioma and adeno-carcinoma existed side by side in the nodule examined. Plate III. Fig. 6 shows the alternate arrangement of squamous and columnar cell areas around a free space. They are quite distinct, though together. In this section there are two kinds of columnar epithelium, one belonging to the new growth and the other proper to the lung, as shown by the presence of cilia and an elastic tissue sheath.

It is unfortunate that no pathological report on the original growth removed at operation can now be obtained, and conjecture can ill supply this defect. One thing is certain from the clinical examination, an ulcer of malignant character existed in the cervix uteri. It may have been the sole primary growth, or only one of two such, and to this locality we may safely attribute the origin of the squamous-cell portions of the metastases, though it is quite within the bounds of possibility that it may have originated within the cavity of the uterus. Cases have been reported where areas of squamous epithelium, instead

of columnar, were found within the uterus; squamous epitheliomata confined to the body of the uterus, though rare, are not unknown; and it is common to find squamous epithelium covering a portion, at least, of a polypus growing from inside the cavity of the uterus. But after giving due consideration to the probabilities, one is more justified in attributing the origin of the squamous epithelioma to its common site in the cervix than to the body of the uterus, especially in view of the clinical findings. It would seem most natural to attribute the adeno-carcinoma to an original focus inside the uterus. Cases of two independent cancers of the uterus, squamous epithelioma of the cervix and adeno-carcinoma of the body, have been reported from time to time, but as far as my reading of the literature goes there has been no subsequent examination of the body to show whether the growths metastasized separately or blended. In a collection of cases of multiple growths given by Lubarsch and Oestartag there is no record of any double carcinoma so blending in its metastases. If the two probable conditions coexisted—epithelioma in the cervix and adeno-carcinoma in the body—they might well have permeated the collecting lymphatics of the uterus together, for the usual anatomical separation of corporeal and cervical collecting lymphatics is only an artificial one, and post-mortem observation has demonstrated that cancers originating in the cervix may affect those lumbar lymphatic glands considered by anatomists to be supplied from the corpus uteri more frequently than the glands of the external and internal iliac groups. In point of fact, the lymphatic collecting trunks from the whole internal genital organs of the female are so intimately connected that cancers starting from any two points, as, for example, in the cervix and in the ovary, might join and blend with each other before the lymphatic glands are reached. Though it is probable that the two growths were synchronous in their dissemination, yet one may have started in front of the other; all the afferent channels to a lymphatic gland are not blocked when the latter becomes the seat of a cancerous deposit. This can be demonstrated experimentally. If we accept this origin from two separate foci of growth we are called upon to explain the admixture of the two types in the various metastases. In the liver and in the spleen where we found a single type we might attribute these to emboli, vascular or lymphatic, of single cells or small masses; but in the other organs, where the two are found together, mixed emboli are not so probable, and the most natural explanation is that the two growths blended not far from their origin, and that the metastatic deposits were the result of a continuous lymphatic permeation.

An adeno-carcinoma might have been, and probably was, present in the body of the uterus at the same time as the epithelioma of the cervix, for the presence of the latter might have diverted an examination of the interior, or the two might have been continuous. In view,

however, of this uncertainty, it may be that the adeno-carcinomatous portion was derived from the epithelium of the ovaries or of the Fallopian tubes, and we cannot obtain any information from the clinical notes as to whether these structures were removed or examined, nor does the post-mortem examination help us much, though no trace of these structures could be found in the pelvic mass.

It is necessary to consider whether the double tumour may have originated from a single focus: (a) where two types of cells are close together; (b) where the cells might be relegated to one or other type, *i.e.* indifferent; (c) where the cells normally are of one type only.

(a) At the os uteri in the normal uterus the squamous cells of the cervix meet the columnar cells of the uterus, so that within a microscopic area there may be the two types present, and a carcinoma arising from such an area might have two component parts corresponding to the squamous and columnar characters of the parent tissue. In most multiparæ, as in this case, there is a slight extroversion of the endocervix, so that outside of the os uteri there is a ring of tissue covered by squamous epithelium which has replaced the original cubical or columnar epithelium, or which is the result of conversion of the one into the other (*cf.* uterine polypi), and which contains columnar cell-lined glands. Here we have cells of two different types close together, one which has been always columnar, and the other, now squamous, which may have been originally columnar.

(b) Closely associated with the latter is the fact that wherever there is a change from one epithelium to another of a different kind in continuity with it, as, for example, squamous epithelium of the skin and glandular epithelium of the mamma, there is always an area of cells between the two definite types where it is impossible to say to which kind they belong. They have some of the characters of both, they have not all the characters of either, and it is very likely that in processes of proliferation and repair they become one or other. They are normally indifferent. If such an area was the starting-point of a malignant process these cells might breed true and be always indifferent, or they might give us cells, now of one kind, now of another.

(c) The cancer may have started from an epithelium of one kind only where the cells in normal extrauterine life were definite. It must be remembered that the epithelium of the cervix and that of the body were derived from a single structure—the Wolffian duct and the cells in their proliferation have shown their histogenetic characters, now one kind, now another.

We should in these latter cases explain the appearance of distinct types as "growth forms," and say they were biassed towards the one or the other by the surrounding tissues. It is difficult to see how we could have the two types together as shown in the sections of the nodules from the lung and kidney under identical conditions of environment. But the strongest argument against an origin from a

focus where the cells are normally indifferent, embryologically indifferent, or pathologically changed from one type to another, is the fact that in all our sections there is no evidence of any transitional forms between the two types of cells: each stands out distinct—the columnar cells with their cylindrical shape and darkly staining oval basal nucleus and the epithelial cells with their polygonal shape, intercellular bridges, and their large round vesicular nucleus, so that the great probability is we are dealing with a double tumour, the component parts of which have originated from two foci not far separated from each other, of normally distinct types of epithelium.

DESCRIPTION OF PLATE III.

FIG. 1.—Section of recurrent mass in pelvis. ($\times 70$.)

FIG. 2.—Section from a lumbar lymph gland. ($\times 70$.)

FIG. 3.—Section from thoracic duct. ($\times 70$.)

FIG. 4.—Section from nodule in left kidney. ($\times 55$.)

FIG. 5.—Section from nodule in left suprarenal gland. ($\times 100$.)

FIG. 6.—Section of nodule in lung. ($\times 120$.)

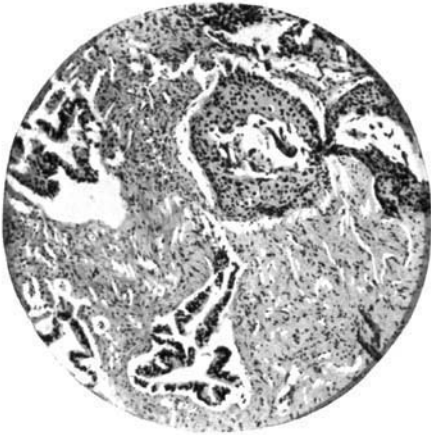


Fig. 1.

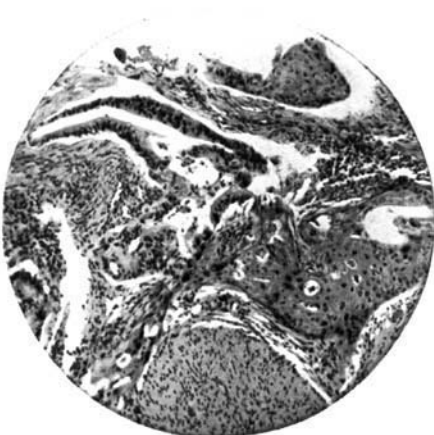


Fig. 2.

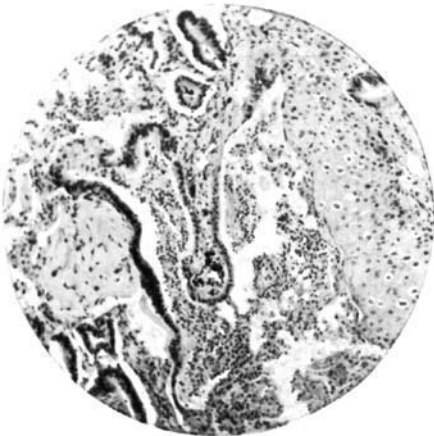


Fig. 3.

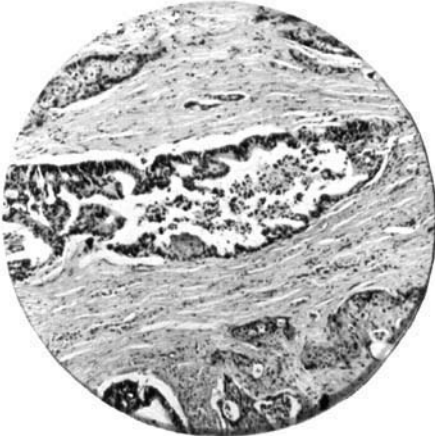


Fig. 4.

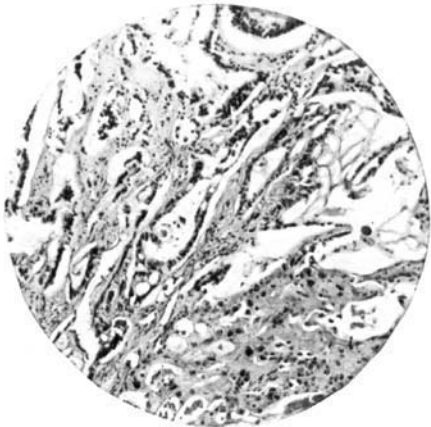


Fig. 5.

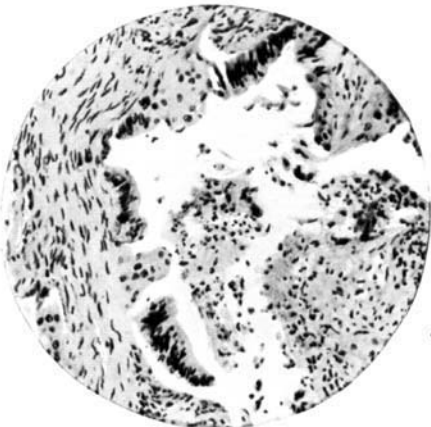


Fig. 6.