

A CASE OF SYNCYTIOMA MALIGNUM OCCURRING IN A WOMAN WHO DIED THIRTY-ONE YEARS AGO; WITH SOME OBSERVATIONS ON THE MODE OF INVASION OF THESE TUMOURS.

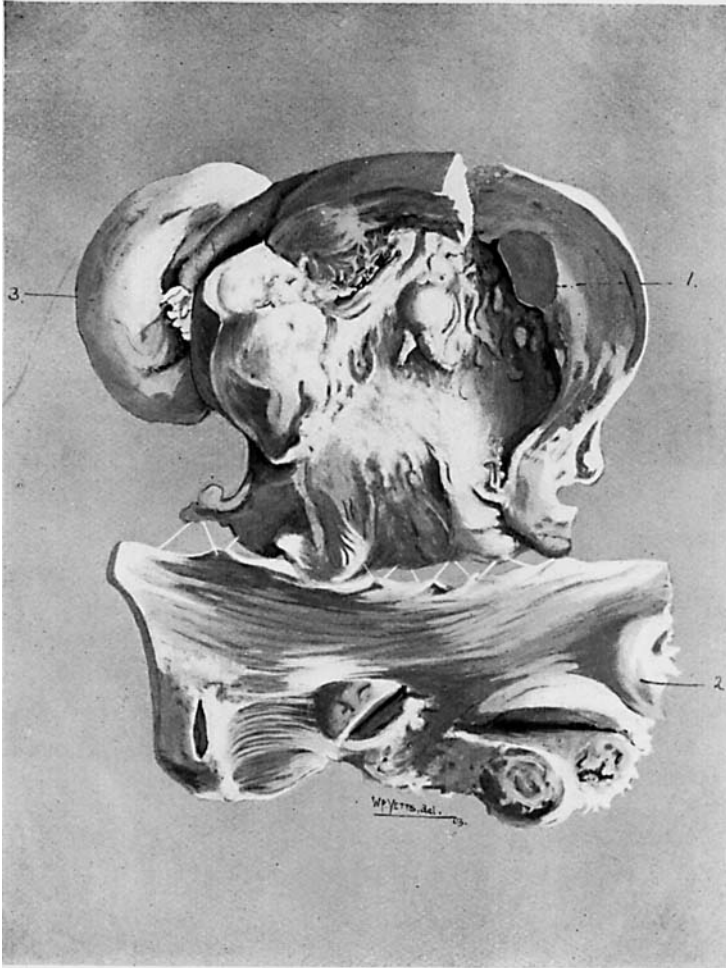
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THERE is in the museum of St. Bartholomew's Hospital a specimen (No. 3014) which was removed from the body of a woman aged 23, 31 years ago (October 3rd, 1872). It is thus described in the catalogue:—"Malignant ulceration of the interior of the uterus with tumours of the vaginal wall. The vaginal wall contains tumours of all sizes up to that of a walnut. The tumours are situated chiefly in the orifice and anterior wall of the vagina. The uterus, which is three or four times its natural size, is, on its inner surface, covered with black detritus deeply ulcerated in places, and sloughy. The tissue of the organ is pale and soft. Both ovaries are highly cystic. There was no peri-uterine hæmatocele. The patient had miliary tuberculosis of the lungs and pyæmia." The naked-eye appearances of this specimen suggested that it was probably of the nature of a malignant syncytioma, and I therefore obtained permission to re-examine it. Fortunately records of both the clinical history of the case and the post-mortem appearances have been preserved. This is probably the earliest case of this form of malignant disease of which we have so complete a record, and as such I venture to publish it.

The clinical history:—

"H. L., aged 23, was admitted into Martha Ward on August 26th, 1872, suffering from hæmorrhage and from some tumour occupying the anterior vaginal wall. The patient has been married for five years, and has had three children, the youngest of whom is 2½ years old. She has had one miscarriage—a vesicular mole—fifteen months ago. Since then she has never been well, nearly always losing blood from the vagina. For the last five months she has noticed a swelling in the vagina, which has been gradually growing larger, and causing pain and discomfort; she has also suffered from dysuria; now she can only void an ounce or two of urine at a time. For the last ten days her breathing has been very short, and she has suffered from cough and expectoration." On admission her complexion was sallow and jaundiced, the eyes dull and heavy, the tongue furred but moist. The pulse-rate was 142 beats per minute, the temperature 102·2, and the respirations 30 per minute. On examination of the chest impaired resonance, amounting to actual dulness in each axilla, was discovered, and

FIG. A.



1. Growth in uterus.
2. Growth in vagina.
3. Cystic ovary.

numerous râles and crepitations were heard. On palpation the abdomen was tender; in the right iliac fossa a distinct tumour was felt, about the size of a large egg, elastic and very tender to the touch. After admission she lived for nearly six weeks; the temperature remained high, respiration grew more and more difficult, the vaginal discharge became very offensive, and on October 3rd she died with the symptoms of septic infection.

Post-mortem Examination. This was made on October 4th; the notes are headed:—

“Hæmatomata vaginæ, ulcerous metritis, pyæmia, cystic ovaries, pulmonary tuberculosis.”

There is slight jaundice. Old scrofulous scars are present underneath the left ramus of the inferior maxilla. The peritoneal cavity is full of pus, and the organs matted together by soft lymph. The right pleural cavity contains about one pint of pus, also soft lymph. The peri-cardium is natural. The vaginal wall is full of hæmatomata of all sizes up to a walnut, the blood is some of it quite recent, some decolourised. There are also smaller hæmatomata, obviously contained in blood-vessels, situated chiefly about the ostium vaginæ in the anterior wall. The uterus is three or four times its natural size, its tissues pale and soft. Its anterior surface is covered with black detritus, and deeply ulcerated in places, the whole surface being sloughy. Both ovaries are highly cystic, and the left adherent to the left side of the vagina. There is no perimetric hæmatocele. The stomach and intestines are natural. The liver shows extreme parenchymatous degeneration. The heart is natural. The kidneys show parenchymatous degeneration. The right lung is full of pyæmial nodules, the left contains only a few; both are studded with hard nodules, no doubt tubercular. The spleen is large and soft, it shows many disintegrating pyæmic infarcts.

It is easy, in the light of recent research, to recognise in this history and autopsy a typical case of syncytioma malignum. The cystic ovaries, the hydatid mole, the uterine tumour, the vaginal hæmatomata “obviously contained in blood-vessels,” the lungs “studded with hard nodules, no doubt tubercular,” all fall into their place like the pieces of a puzzle to which we hold the key; but thirty-one years ago the very careful and competent observer who wrote these notes must have wondered much what was the explanation of the varied lesions.

The specimen preserved (Fig. A) consists of two portions:—(1) An upper part, comprising the uterus and ovaries; (2) a lower part, the vaginal wall. The two have been united by sutures. The uterus is much enlarged, measuring 6 inches in length and $6\frac{1}{4}$ inches from side to side at its widest part. It has been laid open on its anterior aspect. The walls are much thickened, measuring $1\frac{1}{2}$ inches; for the most part they are pale in colour and firm in consistence, but near the mucosa they are irregular and ulcerated, and a recent section shows that this part is of a reddish-brown colour. The mucosa on the

posterior uterine wall is covered with sloughy detritus, but near its centre a definite rounded tumour, the size of a marble, can be seen. Near the upper extremity of the cavity on the right side is a deeply ulcerated portion; the margins of this crater-like depression show the presence of new-growth, but the centre is entirely converted into a sloughy mass, in which very little of the original structure can be detected. The ulceration and new-growth are limited to the body of the uterus, the cervix being apparently free from disease. Both ovaries are enlarged and cystic, their size resembling that of a goose's egg. Their peritoneal aspect is covered with shaggy adhesions. The vaginal wall contains several tumours, varying in size from a hazel nut to a pigeon's egg, they project into the lumen of the vagina, and the larger tumours also project markedly from the deeper aspect of the vaginal walls. Their surface is ulcerated and necrosed, and on section their structure resembles very closely that of an old laminated blood-clot.

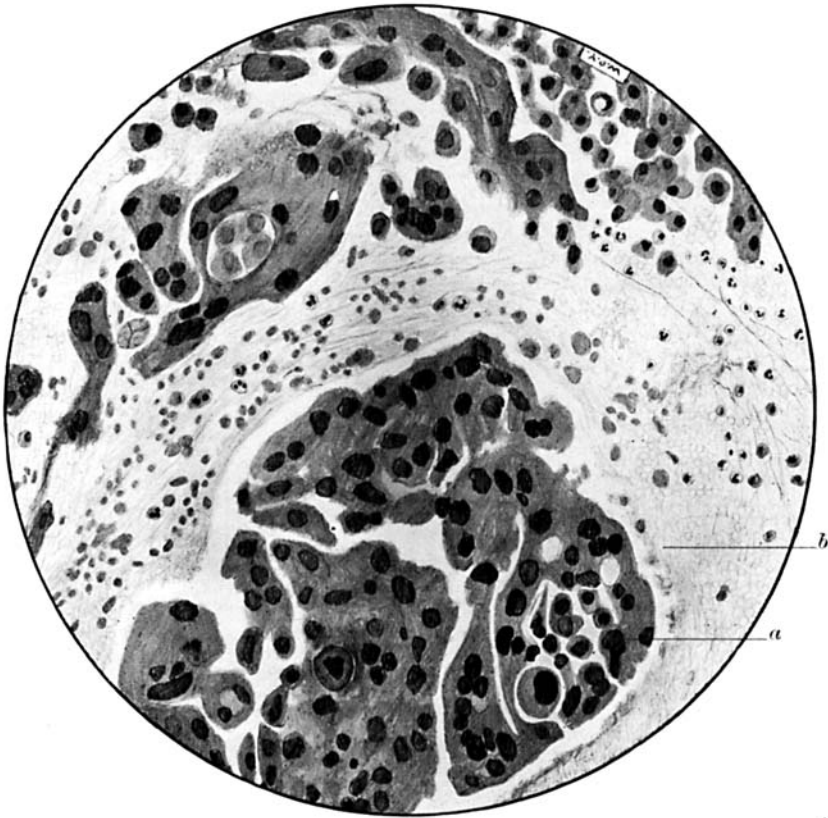
A section (1) through the uterine wall at the base of one of the secondary nodules shows a large number of dilated blood-spaces, some with definite vessel walls, some with a mere lining of flattened endothelium, whilst others show no lining wall, but look as though they might have been formed by the separation and pushing aside of muscle bundles. They, however, much more probably have their origin in the phagocytic action of the tissues of which the growth is composed. Their lumen is occupied by red blood corpuscles and an unusually large number of leucocytes; in some of them, too, cells resembling those of the growth are seen, whilst others are definitely lined by syncytial masses. The tissue in which these spaces are embedded consists partly of unstriped muscle fibres, but chiefly of cells, some with a relatively large vesicular nucleus showing a well-rounded chromatin network and karyokinetic figures surrounded by varying amounts of somewhat granular protoplasm (Langhans' cells), others are small round cells, probably of inflammatory origin. Apart from the presence of occasional muscle fibres and strands of fibrous tissue, no stroma can be distinguished. The cells have an irregular distribution, but are grouped mainly around the blood-spaces. Towards the surface tongue-shaped processes of syncytial tissue are seen; they possess deeply and evenly staining nuclei, their protoplasm stains readily with eosin. These processes partly infiltrate the deeper tissues and partly line and project into the blood-spaces. Further in portions of the syncytial masses cell-outlines can be distinguished. In this section the actively invading elements appear to be the Langhan's cells rather than the syncytial masses.

SECTION 1.



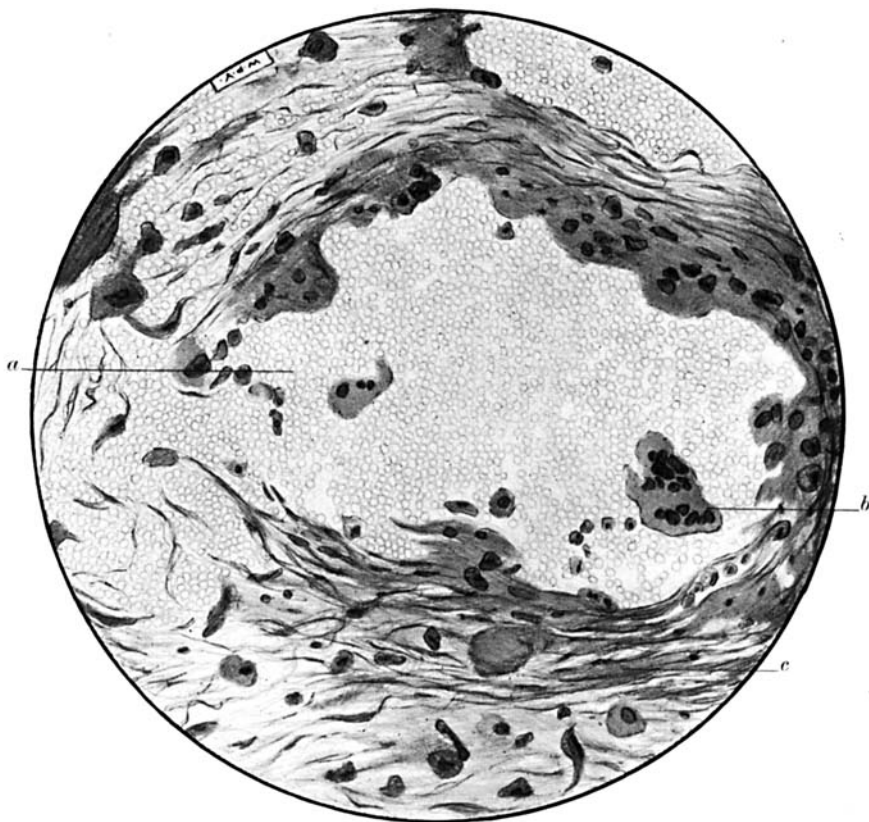
- (a) Blood-spaces.
- (b) Invading cells.
- (c) Uterine muscle.

SECTION 2.



- (a) Syncytial masses.
- (b) Blood-space.

SECTION 3.



- (a) Blood-space almost completely lined by syncytial tissue.
- (b) Detached portion of syncytial tissue lying in blood-space.
- (c) Muscle fibres of vaginal wall.

Sections 2 and 3, through one of the secondary tumours in the vagina, shows abundant syncytial tissue and fewer cellular elements. The syncytium is deeply stained, the nuclei distinct and uniform for the most part, but sometimes showing a vesicular form with chromatin figures. It has a roughly aveolar arrangement, sometimes in irregular masses, sometimes in bands. The protoplasm is in places vacuolated, and in some of the larger vacuoles red blood corpuscles can be seen; in some of the masses distinct cell-outlines are visible. Of the cellular elements some resemble very closely the cells of Langhans' layer, and many modifications can be found between these and the syncytial masses. There are present also large numbers of the so-called "giant cells," some containing as many as eight or ten nuclei. Neither the nuclei nor the protoplasm of these "cells" show any features which serve to differentiate them from the syncytial masses. The relation of the growth to the blood-spaces is very clearly demonstrated, some of the spaces are almost completely lined by vacuolated syncytium, and detached portions can be seen lying in the blood-stream.

Chipman,¹ in a very valuable paper which he has lately published upon the placenta of the rabbit, has clearly shown that this curious relation between the maternal blood-vessels and the foetal invading tissues has a physiological prototype in that animal. In considering the invasion of the maternal by the foetal tissues, he writes:—"This general advance (*i.e.*, of the ectoderm) is, as it were, led by deeper ingrowths, which penetrate along the course of the maternal vessels. Where the vessel is cut longitudinally we can see the process. The ectoderm surrounds the distal end of the vessel, and then advances along its walls, gradually replacing its endothelium, which disappears. The foetal tissue *swallows*, as it were, the maternal capillary space. The ectodermal ingrowths which at the eighth day invaded the blocked gland mouths have now no further glandular track; for the solid gland channels have disappeared. Their further direction is determined by the blood-vessels. The more superficial of the ectodermal cells—those nearest to the maternal tissues—begin to show a plasmodial change. The maternal capillaries, which appear completely surrounded by the foetal ectoderm, have entirely lost their endothelium, and lie as maternal blood-spaces in the midst of this ectoderm. The advancing ectodermal lamina surrounds and includes—*swallows*—not only maternal vessels, but also irregular hæmorrhagic cavities in the intermediary region, for the endothelium of the maternal capillaries swollen and degenerated in front of the ectoderm ruptures here and there, and especially at the junction of the two

tissues—fœtal and maternal, and there result hæmorrhagic cavities with ragged cellular wall and containing maternal blood; and these blood-cavities it is which are in their turn surrounded and included—swallowed—by the advancing ectoderm.”

This process then, in the placenta of the rabbit, has been followed in full detail, and Chipman has illustrated his work with many beautiful micro-photographs showing the various stages which he has described. Though not yet fully demonstrated, the knowledge we possess of the development of the human placenta points to a similar connection between fœtal and maternal tissues; and the mode of invasion of this tumour, so well illustrated in the sections I have described, follows closely the physiological process by which in a normal pregnancy the parasitic ovum grafts itself on to the maternal host.

Section i. shows a portion of the uterine wall which lies immediately beneath the tumour; it is traversed by a network of blood-spaces, some are vessels with well-marked walls, some are lined merely by endothelium, and in others no definite lining wall can be distinguished; some, however, have a syncytial lining. It is around these blood-spaces that the cells which form the outposts of the tumour are grouped, as though these spaces formed a scaffolding upon which the invading tumour is built up. It is a matter of great difficulty to distinguish between these cells and decidual cells. Kühne,² Andrews,³ Teacher⁴ and others have described histological characters by which the Langhans' cells may be distinguished from the decidual cells, but the descriptions of these observers do not agree, and the method recommended of tracing doubtful cells to their ultimate source through intermediate forms is a very fallacious one. A careful study of this point (using material derived in the one case from uterine casts of patients the subjects of tubal gestation, and in the other from an ovum still in situ in the tube, and then comparing these sections with those obtained from early abortions) has convinced me that in many instances it is impossible to say whether cells are of decidual origin or belong to the “haft zotten” or cell-knots.

Section 3 shows one of these blood-spaces lined with syncytium, and there can be seen lying free in the blood-stream a detached portion of this tissue. It is difficult to resist the conclusion that it is in this fashion that dissemination occurs, and the process is strictly analogous to the deportation of villi which there is good reason to believe occurs in normal pregnancies, and which has been demonstrated in certain pathological conditions. There is then in the mode

of invasion and dissemination additional evidence in favour of the theory that these tumours are of foetal origin.

That tissues taken from the body of a woman who died thirty-one years ago should be used to show how closely a tumour which at that time was unknown, follows in its invasion a physiological prototype revealed only by the latest research, is an apt commentary on the motto of the Pathological Society, "Nec Silet Mors."

REFERENCES.

- ¹ "Observations on the Placenta of the Rabbit, with special reference to the presence of Glycogen, Fat and Iron." *Studies from the Royal Victoria Hospital, Montreal.* Vol. i., No. 4.
- ² *Beitrag. zur Anatomie Tubenschwangerschaft.*
- ³ *Journal of Obstetrics and Gynæcol.* Vol. iii., No. 5, p. 427.
- ⁴ *Journal of Obstetrics and Gynæcol.* Vol. iv., No. 1, p. 46-47.