SARCOMA-DECIDUO-CELLULARE, OR DECIDUOMA MALIGNUM.

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ON the 16th July, 1888, at a meeting of the Leipzig Obstetrical Society, Professor Sänger made a communication upon "two uncommon cases of abortion," one of which was the first recorded example of the disease which we have now to consider. Since then nearly one hundred cases have been recorded, and a considerable literature has accumulated, from which we have learned that this disease differs sufficiently from all others hitherto described to justify its separate consideration. Observers are almost unanimous as to its connection with pregnancy, its clinical features, pathological appearances, and appropriate treatment; and they differ only in their views as to its origin.

The case reported by Sänger was so typical of the entire group of recorded cases that I think a *résumé* of it will serve as an introduction better than any mere definition.

The patient was a young married woman, aged twenty-three, who aborted at the eighth week in consequence of a fall from a railway carriage. The abortion was incomplete, and hæmorrhage continued for three weeks. In the fourth week the discharge became fœtid, and Sänger was called in. He found the patient very anæmic, with symptoms of septic absorption and putrefaction of the uterine contents. The uterus was thoroughly cleared out, hæmorrhage and discharge ceased, and the temperature became normal; the pulse, however, continued to be over 100°, and recovery was so slow

that she did not leave her bed for five months. Her protracted convalescence was attributed to a small exudation in the left parametrium. An enlargement of the uterus was also observed, but was supposed to be due to subinvolution. She had not long left her bed when she was obliged to return to it again in consequence of fever and pains in the right hypogastrium, where a tumour as large as a goose-egg had formed in the neighbourhood of the iliac crest. It was soft and tender, and, being supposed to be an abscess, was incised but no pus escaped. It consisted of a soft, spongy substance, of which about a handful was removed, leaving a cavity, at the bottom of which lay the bare and roughened bone. On microscopic examination this tissue showed large multinucleated round cells, with spindle cells and numerous apoplexies. Soon after this operation pulmonary symptoms set in, with cough and dyspnoea, and she died seven months from the commencement of her illness.

On *post-mortem* examination the uterus was found to be infested with dark purple-red, spongy nodules, varying in size from that of a walnut to that of a large apple. The mucous membrane was smooth and nowhere perforated by the growths. Metastases were found in the iliac fossa, lungs, diaphragm, and ribs. The left lung was compressed by a hæmatothorax. Microscopic examination of the uterine tumour showed numerous apoplexies, large nucleated round cells, and cells resembling decidual giant cells, suggesting the idea that here was a new growth of the decidua belonging to the group sarcomata which had never before been described.

Clinical Features.—The clinical features of this disease are thus summed up by Süniger :—

1. A birth, abortion, or hydatidiform mole, followed by
2. Constant or repeated hæmorrhages ;
3. After this, and generally following an examination or intrauterine manipulation, putrid discharges with fever ;

4. Increasing size and irregular shape of the uterus ;
5. Rapidly progressing and towards the close, intensely marked anæmia ;
6. Recognisable metastases, especially in the vagina ;
7. Cough, dyspnœa, bloody expectoration, and other symptoms of pulmonary metastases and hæmatothorax ;
8. Rapid course of the disease, which usually proves fatal within six to seven months.

The first point of importance is the connection of this disease with pregnancy. In all recorded cases it has come on after an abortion, hydatidiform mole, or, very rarely, after delivery at term. In about half the cases it has followed the expulsion of a hydatidiform mole—a remarkable fact of much importance with regard to its etiology. The second point is hæmorrhage, which either continues after the expulsion of the ovum or commences shortly afterwards. In a few cases it did not occur for a considerable time, and in one recorded by Whitridge Williams it was altogether absent, the first evidence of the disease being metastatic deposits in the vagina and lungs. In the majority of cases, however, it is the most prominent symptom, so that the patient soon becomes profoundly anæmic. The surface is pale and in places slightly œdematous, the face especially assumes a pallid ichteric cachectic appearance.

When the tumour sloughs the discharge becomes offensive, and septic fever sets in. It is, therefore, of the utmost importance to observe the strictest antiseptic precautions in dealing with these cases.

On physical examination the uterus is found enlarged, often irregular in shape, and in some cases the os is sufficiently dilated to admit a finger, in which case the growth may be directly felt.

The course of the disease is one of marked malignancy ; in fact it is the most rapidly fatal of all malignant uterine

growths, death occurring from hæmorrhage, septic infection, or pulmonary complications within a few weeks, rarely months, after the first symptoms have been observed.

Pathological Anatomy.—The uterus is usually found infested with new growths, varying in size and colour, but generally of a dark purple-red. They involve the muscular tissue of the uterus, so the peripheral margin is ill defined, and after removal the uterine wall appears thinned. The growth is soft and, where not coloured with blood, of a greyish-red hue; it closely resembles placental tissue in its irregular fissured surface, its fibrous appearance on section, extreme vascularity, and numerous apoplexies. It is, however, much softer and more friable, and its uterine surface shows a remarkable tendency to slough.

Microscopically these growths are composed of a fibrous reticulum presenting an alveolar and cavernous structure, containing numerous apoplexies, two varieties of cellular elements, and sometimes chorionic villi, but no glands, blood-vessels, or lymphatics. The two varieties of cells contrast remarkably. The one are large individual cells varying from round or polygonal to spindle shape, the nuclei are large, and the outline of their cell protoplasm is clearly defined—they resemble Langhan's cells. The others are protoplasmic masses of various shape, which contain a number of irregularly shaped nuclei, rich in chromatin, but with no line of separation between the cells, and resemble the syncytial layer which forms the superficial covering of the chorionic villi. Both varieties of elements show a marked tendency to retraction of their protoplasm and vacuolation. Mitotic figures are frequently observed in the cells, but nowhere in the protoplasmic masses.

Diagnosis.—As an early diagnosis is of vital importance, we cannot wait for symptoms to develop themselves, and fortunately it is not difficult, provided careful clinical and micro-

scopic attention be devoted to it. When hæmorrhage occurs after an abortion or molar pregnancy the uterus should always be thoroughly evacuated by the finger and curette, so that one may be certain that everything has been removed and a smooth surface left. If after this hæmorrhage recurs, and a second evacuation reveals a quantity of soft, friable tissue, the case is certainly not one of simple abortion, and is in all probability one of deciduoma. One must, however, be certain that the first curetting was thorough and complete. The size and shape of the uterus varies, but is never below the normal, and enlargement of the organ after discharge of the ovum is of much diagnostic value. The os is often sufficiently open to admit the finger, but may require artificial dilatation. Soft masses of friable material resembling placenta are then discovered, and portions removed by the curette should always be submitted to microscopic examination.

Treatment.—Total extirpation of the uterus is the only method of treatment which has hitherto yielded any benefit, and it is of the utmost importance that this operation should be performed at the earliest possible time before the patient has become exhausted by hæmorrhage, and before putrefaction sets in or metastases have occurred. It must not, however, be regarded as hopeless even under such unfavourable conditions, for cases have been reported by Crobak and Von Franke where, in spite of evidence of pulmonary embolism, as shown by bloody expectoration and other symptoms, recovery has followed operation. Lönnberg-Mannheimer saw numerous metastases in the cervix, introitus vaginæ and vagina; yet the patient had no return for eighteen months after operation. Cazin found a metastasis in the ovary. Three years after the operation she was well. Schauta extirpated a metastatic growth from the vagina along with the uterus. At the time of publication there had been no return.

Histogenesis.—According to most observers this disease is always connected with and is probably due to pregnancy. The only dissentients from this view were Drs. Eden and Kanthack, who stated at the meeting of the London Obstetrical Society, in the discussion on Dr. Herbert Spencer's case, that the microscopic appearances were in no way peculiar, but similar to those found in sarcomata in other places, and that in some of the cases pregnancy was doubtful. In the discussion which followed Dr. Haultain's communication to the British Gynæcological Society, however, Dr. Eden stated that he was personally in full agreement with the views of J. Veit, in the "*Handbuch der Gynækologie*," that the disease was a sarcoma modified by the occurrence of pregnancy. We may, therefore, assume as generally accepted that the disease is in some way due to pregnancy. In order to understand the conflicting views as to its origin we must briefly recall the normal condition of the tissues which it affects. The placental villi consist of a stroma covered by two layers of epithelium—an inner called Langhan's layer, composed of individual cells with a distinct cell wall, and an outer formed of protoplasmic masses without any line of demarcation, termed the syncytium. These villi penetrate the decidua serotina and maternal blood-vessels forming the placenta.

Now, the disease which we are considering has been supposed by different observers to originate from each of these structures, and hence the varying nomenclature. Thus, Säger believes that it originated in the decidua, and he gave it at first the name of *deciduoma malignum*, but subsequently he preferred to call it *sarcoma-deciduo-cellulare* because he believed that it originated in the cellular layer of that membrane after it had been altered by pregnancy. Gotschalk believed that it originated, in a case described by him, in the stroma of the villi. Marchand, Gebhard, and Haultain attributed its origin to the epithelium covering the villi,

and Whitridge Williams to the outer layer or syncytium only, and termed it carcinoma syncytiale, chorion epithelioma, or blastoma-deciduo-chorion-cellulare.

These authorities may, therefore, be divided into those who hold that the disease is a sarcoma, and those who regard it as a carcinoma. Sanger regarded it as a sarcoma of the cellular layer of the decidua because of the similarity of structure in both the size and shape of the cells, and the presence of a reticulum, the only difference being that in the pathological cells the nuclei were larger and the surrounding protoplasmic ring narrower. He rejected Veit's theory that the disease was due to the modification of a pre-existing sarcoma, because no case has been recorded of the implantation of an ovum upon a sarcomatous or carcinomatous endometrium, and he believed that his claim to the growth being different from all others hitherto described stood or fell with its origin during pregnancy. Veit, however, in the newly-published "*Handbuch der Gynekologie*" still maintains that the sarcoma precedes the pregnancy and is modified by it. He admits that no case has been recorded of the implantation of an ovum upon a carcinomatous endometrium; but in nodular sarcoma the membrane resembles that in myomatous uteri, and that as pregnancy occurs in the one so it may also in the other. He considers that it is impossible to regard all the protoplasmic masses as true syncytium derived from the outer layer of the villi, but rather, as it has been shown, that in normal pregnancy other cells, such as the epithelium of the lining membrane of the uterus, and especially of its glands, often take on a syncytial form, and therefore syncytium in the wider sense cannot be regarded as a distinct tissue, but as a stage in the development of certain cells. So a sarcoma may, under the influence of pregnancy, come to resemble syncytium; and since fetal elements are not always found in these cases they cannot be regarded as

the chief characteristic, but, as masses resembling syncytium are the rule, the disease should be regarded as a process in which, under the influence of pregnancy, certain cells take on a syncytial character. Hydatidiform moles, so frequently associated with deciduoma, are not the cause but the result of uterine disease, and, regarding deciduoma in a similar manner, the primary disease is to be sought for in the uterus.

In fibro-sarcomata the uterine mucous membrane is in a condition resembling that in myomata, in which pregnancy often occurs, and so it may in sarcomata, but under the influence of pregnancy the growth undergoes changes, and its cells assume a syncytial character. Under the influence of the growth pregnancy may be disturbed or ended, a hydatidiform mole develop, or it may go to term. At the birth the entire ovum may be expelled or a villous or villous epithelium retained, grow into the veins, and be carried into the circulation, causing metastases. In either case the tumour goes on growing and leads to a fatal termination. The disease remains the same whether it does or does not contain foetal elements, the latter being accidental. The essentials are the original uterine disease and the occurrence of pregnancy, under the influence of which the syncytial changes in the growth occur.

Gotschalk, in 1892, described a case in which the stroma of the villi was changed into a structure formed entirely of large polymorphous cells, whose epithelial covering showed a remarkable proliferation. He regarded the disease as a sarcoma, and believed that it originated in the stroma of the villi. This case was the first in which the disease was diagnosed and the uterus extirpated during the patient's life.

A number of pathologists regard this disease as of epithelial origin, and therefore a carcinoma. Foremost amongst these is Marchand, whose writings have done much to elucidate its pathology, and especially its connection with

hydatidiform mole. In an elaborate paper, beautifully illustrated, which he read before the British Gynæcological Society in June, 1899, Dr. Haultain warmly advocated Marchand's views, and stated that the chain of evidence in favour of this new growth being of epithelial origin had to his mind no weak link. The structural appearances, the physiological prototype of the young villi, and the interesting association with myxoma of the chorion, which it closely resembles anatomically, physiologically, and pathologically, all serve to prove that it is of epithelial origin.

It would be impossible in the present state of our knowledge to say which of these views is the correct one, but personally I am inclined to believe that Veit's views are the least fanciful and most probably correct.

I shall now report the case which I had the misfortune to meet with:—

Mrs. G., aged thirty-three, mother of four children, had suffered for some years from retroversion and metritis. The pregnancy which ended so unfortunately commenced in February, 1897, and threatened to end in abortion in April. This was, however, averted, and the uterus continued to enlarge until August, when it ceased to do so. I, therefore, came to the conclusion that the fœtus was dead, but as there were no urgent symptoms, and as the patient was averse to operative interference, I awaited its natural expulsion. But when a month after full term there was no sign of this taking place I determined to interfere, and accordingly on the 18th of December introduced sea-tangle tents, and the following day, having completed the dilatation with Hegar's dilators, I evacuated a hydatidiform mole. The uterus was completely emptied and scraped with Rheinstädter's spoon. She made a good convalescence, but her periods soon returned and were profuse. In March, 1898, when staying with some friends at Monkstown, I was informed that she had severe hæmorrhage, and I advised her to call in a local practitioner; but as she did not do so I concluded that the account I had received was exaggerated. Shortly after this she called upon me at my house, and upon examination I found a swelling in Douglas's pouch which felt like a retroverted fundus; but upon

Section from DR. SMYLY's case of Sarcoma-deciduo-cellulare.

a Langhan's Cells.

b Syncytium.

further examination I found the fundus in its normal position. I then supposed that the tumour at the back was an enlarged tube, and considered it to be a contra-indication to intra-uterine interference. She continued to have hæmorrhages after this, and at 10 o'clock p.m. on May 10th her husband called upon me and told me that she had violent pains and hæmorrhage. I at once went out and found her in a condition of intense anæmia; her bed and a night-chair beside it contained an enormous quantity of blood and clots. She was almost pulseless, cold, and very restless. I immediately washed out her vagina and uterus with very hot creolin lotion and plugged the vagina with iodoform gauze and cotton wadding moistened with creolin lotion. The Master of the Rotunda Hospital, who had been summoned in the meantime, arrived about midnight, and remained with me about three hours. During this time she had been steadily improving, and as no blood came through the plug we agreed to give her $\frac{1}{2}$ grain of morphia hypodermically and postpone further measures until daylight. At six o'clock, however, violent and agonising expulsive pains set in, which were not relieved by a grain of opium administered by the mouth and $\frac{1}{3}$ grain morphia hypodermically. The plug soon became saturated with blood, and a brisk hæmorrhage came through it. The patient became faint, then restless, calling out for air, and refusing local interference. Dr. Purefoy was again summoned, and also Dr. Piel, and in spite of her alarming condition she was ætherised and the plug removed. I now found the os sufficiently dilated to admit two fingers, which at once detected and removed a large quantity of placenta-like tissue. The uterus was thoroughly cleared out by Rheinstädter's flushing curette, but the wall was so thin that during the process I was in constant fear of perforating it. Plugging being for this reason out of the question, and the prevention of further hæmorrhage a matter of vital importance, I washed out the cavity with a dilute solution of perchloride of iron; the patient was by this time in a very collapsed condition, her limbs cold, and brow bathed with clammy sweat. Having used all ordinary means with little apparent benefit we resolved to infuse saline solution, but by the time the necessary apparatus had been procured she had so far recovered that we considered it unnecessary. During the next few days she improved slowly, but on the third morning the discharge became offensive, and the uterus was washed out with creolin lotion, and as the temperature continued to rise this was repeated daily until the sixth day when I found the organ completely fixed

by parametric inflammation; she complained of intense pelvic pain and vesical irritation. On the tenth day the base of the right lung became solid, with much cough and dyspnoea; an empyema formed on the same side, from which a quantity of stinking pus was subsequently evacuated. The septic fever continued for about two months, when she died. There was no *post-mortem* examination.

It was only at the time of operation that the possibility of the case being one of deciduoma malignum occurred to us, and the diagnosis was confirmed by Dr. Earl's examination of the tissues removed.

The microscopic appearances are well shown in the accompanying photographs which were taken for me by Professor Scott from Dr. Earl's preparations. I showed these specimens at the meeting of the British Medical Association in Edinburgh, and Dr Sanger declared the case to be a typical example of the disease which he had described.

DR. PUREFOY said he had never felt the tissue of the uterine wall in such a condition of utter degradation and softening as it was in this case. It felt like brown paper. The mole structure removed on the first occasion was of a nature not commonly seen in these cases. He thought it was mixed fleshy and hydatidiform mole. Scattered through it were distinct vesicles, evidence of vesicular degeneration being also present.

DR. SMITH said he was inclined to regard it as an ordinary sarcoma influenced by pregnancy. He knew some eminent pathologists who thought it an ordinary sarcoma. The whole literature of the subject was embodied in Dr. Smyly's excellent paper.

DR. A. V. MACAN said there was one case not mentioned by Dr. Smyly—i.e., Pick's case—in which he found the metastasis of the ordinary hydatid mole not to be malignant. Pick considers that the fœtal structures are only accidental, and they may even form embolisms without being malignant. Opposed to Veit's opinion (with which most people would agree) was that which regarded it as carcinoma of the outer layers of the epithelium covering the villi.

DR. SMYLY, replying, said the point about metastasis in cases

of hydatidiform mole was one of extreme practical importance, because anyone who had not learned otherwise would think that when metastasis occurred the case was hopeless. But the metastasis might not be malignant; a woman might have benign metastasis in her lungs and recover after operation. Of course, if there were malignant metastases the case would be perfectly hopeless.