Primary chorionepitheliomas of the ovary are of interest both because of their rarity, and also on account of their origin, which is still open to discussion. We have had the opportunity of studying two cases which showed unusual features, the one in its structure and the other in its clinical manifestations.

Case I: Mrs. A. B., aged forty-two years, was admitted to Notre-Dame Hospital on June 28, 1930, for abdominal swelling. She gave a history of continuous uterine bleeding, sometimes quite abundant, from June 1929 to March 1930, with only a few days' interval each month. In March 1930, the hemorrhage ceased, and at that time the patient became aware of the mass in her abdomen.

Menstruation had commenced at the age of fourteen and had been normal and regular until June 1929. The patient had married at the age of twenty-four and had had five pregnancies, the last occurring in 1924. There had been one abortion.

On examination, a mobile, painless mass was found filling the right iliac fossa. The vagina was soft; the cervix hard, mobile, and slightly distended. The uterus was in normal position and painless. The left cul-de-sac was depressible and painless. The left tube was slightly adherent to the tumour, but could be separated from it. The tube was apparently normal.

A diagnosis of pedunculated fibroma of the left horn was made.

The patient was operated on, July 2, 1930 (Dr. A. Magnan). A median laparotomy revealed a large tumour of the left ovary, and a subtotal hysterectomy with bilateral salpingo-oophorectomy was performed. The left tube was slightly adherent to the tumour, but could be separated from it. The tube was apparently normal.

The ovarian tumour weighed 410 grams and measured 16 X 10 X 9 cm. Its surface, somewhat smooth and dark-red in colour, showed greyish streaks of connective tissue. Section revealed rounded areas, variable in size, dark-red and friable, surrounded by an anastomotic network of connective tissue joined to a peripheral capsule.

The histological diagnosis was chorionepithelioma.

A diagnosis of pedunculated fibroma of the left horn was made.

The patient was discharged on July 30, but was re-admitted on August 16. She was bedridden, with shortness of breath, persistent cough, pallor, and marked emaciation. Examination of the lungs revealed a dulness of the right upper part and of the left base, friction sounds, and a blowing sound at the left base. Roentgenograms revealed irregular clear spots scattered throughout the lung. The pulmonary condition became rapidly worse, and death occurred on Sept. 3, 1930.

Autopsy Findings: Autopsy was performed two hours after death. The heart weighed 210 grams; the myocardium was soft and pale. The liver weighed 2000 grams, was pale in colour, with a yellow circle around the central veins. The kidneys (weight of right, 150 grams; of left, 160 grams) showed passive congestion.

The visceral and parietal pleurae were coated with a greyish fibrinous exudate. The right lung weighed 2100 grams, the left 1551 grams. The visceral pleura was pushed upward by a large number of greyish nodules. On section, these nodules were found literally.
to fill the lungs; they were dark grey in colour and varied in size from 5 mm. to 7 cm. in diameter.

The cervix of the uterus was present; there was no evidence of recurrence or of metastasis in the abdomen.

**Histological Study:** The histological findings on the various organs offered nothing of interest. It should be noted, however, that the mucosa of the uterus and of the tubes showed no modification. The pulmonary metastases, being of the same histological structure as the primary tumour, need not be described separately.

The tumour was surrounded by a fibro-connective-tissue capsule having the characteristic structure of ovarian stroma. At one point it contained nerve fibres in which Berger's sympathicotrophic cells were recognized, revealing the site of origin to be in the ovary. The entire center of the tumour was made up of a hemorrhagic mass traversed by necrotic bands or strands, without recognizable structure. On the edges only there appeared wide strands of living cells immersed in blood and here and there implanted on the capsule, which they had invaded.

These living strands are entirely characteristic. They are composed of two types of cells, differing morphologically the one from the other. The first, which form practically of themselves the axial portion of the strands, are distinctly individual; in form they are polygonal due to reciprocal pressure. Their protoplasm is abundant, pale and slightly acidophilic; their nucleus fairly uniform in size, rounded and containing a fine granular chromatin substance.

These cells are separated from the hemorrhagic areas by a continuous layer of large multinucleated plasmodia. The surface of these plasmodia in contact with the blood is sometimes flat, sometimes bulging and covered by a "brush border." Their deep surface is irregular and moulded on the polygonal cells, between which they frequently insert themselves in angular extensions. Their cytoplasm, acidophilic and finely alveolar, frequently contains more or less altered blood cells or iron pigment. At one spot, these plasmodia desquamate; at another, they penetrate, in file, between the polygonal cells, severing the strand, and between them appear fissures into which the red blood cells penetrate. Else-
where there are found transitional forms between plasmodia and polygonal cells, indicating that these two types of cells are of similar origin, responding to different adaptations.

With this construction, the tumour strands are so characteristic as to leave no possible doubt: the polygonal cells are Langhans cells, while their plasmodial covering corresponds in structure and in position to the syncytium of chorionic villi. On the whole, they are the equivalent of monster chorionic villi, devoid of connective vascular axes. The diagnosis of choriocarcinoma is indicated (Fig. 1).

The ovarian tissue bordering on these neoplastic strands is invaded by transparent Langhans cells. Where plasmodia appear in the interstices of the ovarian stroma, they are invariably in contact with the interstitial hemorrhagic areas caused by the invasion of a vessel. These hemorrhagic areas, little by little, dislodge the ovarian tissue and rejoin the central hemorrhagic mass.

One of the fragments is worthy of special mention. It is formed by ovarian stroma which is barely modified by the oedema and is bordered by the invading choriocarcinoma.

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**FIG. 2. CASE I: PERIVASCULAR DECIDUAL CELLS IN THE OVARY; SMALL VESSEL IN THE CENTRE, SURROUNDED BY A MULTISTRATIFIED SHEATH OF TYPICAL DECIDUAL CELLS**

Many vessels of small caliber reveal around their endothelial lining a thick sheath made up of several layers of cells. These cells are large, and are round, oval, or club-shaped. Each cell is sheathed by a delicate collagen lining. Their cytoplasm, which is transparent, clear and acidophilic, contains fine granulations stained blue by phosphotungstic haematoxylin, and black by iron haematoxylin. The nucleus, swollen and lacking in chromatin, is oval and is located in the center of the protoplasm (Fig. 2).

What do these cells signify?

In normal pregnancy, Hubrecht has observed the appearance of decidual cells surrounding the vessels. Pol Gérard found in the myometrium of a small insectivore, *Nasilio brachyrhynchus*, decidual cells, the genesis of which he was able to observe: the connective tissue becomes oedematous and its anastomotic fibroblasts form a loose reticulated tissue. Soon the fibroblasts augment in size, sever their anastomoses, multiply, and form a multistratified
sheath around the vessel. In the meantime, the cytoplasm becomes loaded with fine granulations, which are stained black by iron haematoxylin. The final appearance is as in Fig. 2.

It is thus reasonable to believe that our perivascular cells would have the same significance as decidual cells. The fact is worthy of mention because never, to our knowledge, have such elements been described in relation to a primary ovarian chorionepithelioma. Interest is augmented by the fact that this is likely to throw light on the causality of decidual cells. In normal pregnancy, decidual reaction has been attributed to several hormones: oestrin, folliculin, the placental hormone. In our case, this last hormone seems to play a part since the tumour is formed exclusively of a pure culture of chorioplacental elements.

It would seem, then, that the decidual cells in the ovary, which we have described, are due to the chorionepithelioma, and would follow that the decidual cells in normal pregnancy are determined by a chorioplacental hormone.

Case I

Miss P. C., aged seventeen, was admitted to St. Mary's Hospital on Feb. 26, 1935, with a history of pain in the right lower quadrant for six months, and abdominal swelling.

The girl was born in New Brunswick and had always lived there. She had had the usual diseases of childhood, but no major illness. She had menstruated once only—a profuse flow lasting for three days—December 1934. It was about this time that she noticed a swelling in the lower abdomen. Since the summer of 1934, she had suffered from intermittent attacks of pain in the right lower quadrant. A surgeon was consulted when the swelling was noticed, and an operation was advised. On Feb. 17, 1935, she was operated on at Chatham, N. B., and an inoperable tumour was found. The abdomen was closed, and the wound healed well. The patient was then transferred to St. Mary's Hospital, Montreal, for further investigation.

Physical Examination: The patient was well developed and well nourished, with the normal female appearance and hair distribution. The breasts were normal. The abdomen was full and rounded; the liver and spleen not palpable.

Extending from the pelvis to the umbilicus was a smooth, rounded mass not tender on palpation and not fixed. The hymen was intact, and close interrogation failed to reveal that there had been sexual intercourse.

Roentgenograms taken in the prone position showed gas in the small and large bowels, which were displaced upwards by a mass in the pelvis, apparently on the median line. No detail was apparent in the region of the mass. Otherwise the examination was negative.

Operation was performed on March 1, 1936 (Drs. D. A. Hingston and H. S. Dolan). Attached to the right ovary was a large mass about the size of a baby's head, adherent posteriorly and laterally. It was dissected with great difficulty and with considerable bleeding. The right ovary and tube were removed with it. Because of the oozing from the raw surface a large rubber tube was inserted.

Both the urine and a specimen from the tumour gave a strongly positive Aschheim-Zondek reaction.

Following operation, the patient was given 350 c. c. of blood, and 1500 c. c. of glucose saline. Recovery was uneventful, and she was discharged March 19, 1936. She died four months later, but no details as to the circumstances of her death could be obtained. No autopsy was performed.

Pathological Report: The specimen consisted of a lobulated mass 15 X 10 X 9 cm. The peritoneum was intact, but on one side the mass was shaggy where it had been torn away. Many smaller fragments accompanied the large specimen.

The tumor was composed of very friable greyish tissue throughout which was considerable hemorrhage. In its center, it was soft, mushy and broken down into numerous small cavities which appeared to be due to necrosis.
The histological diagnosis was chorionepithelioma.

Histological Study: Several blocks were taken here and there in the tumour. They all gave the same histological picture, and showed fundamentally the same structure as in Case I (Fig. 3). It is thus unnecessary to describe them at length. Hemorrhage and necroses were, however, much more abundant in this case, and living tumour cells were seen only here and there near the connective tissue of the ovary.

Discussion

The writers who have reported cases of chorionepithelioma of the ovary ascribe different origins to the tumour. We give here, in résumé, the most important observations and the conclusions drawn. At the end of this paper is a bibliography which we have tried to make as complete as possible.

Kleinhans was apparently the first to report a case of chorionepithelioma of the ovary. The tumour, which was the size of a hen's egg, was situated in the ovary and had invaded the wall of the tube. The mucosa was, however, intact. The patient died a short time after operation, and on autopsy several metastases were found disseminated in both lungs. The author believes that an ovarian pregnancy occurred previously.

Fairbairn gives the history of a woman, twenty-five years of age, who after confinement had irregular menstruation, uterine bleeding, and a tumour of the left ovary histologically diagnosed as chorionepithelioma. The woman does not seem to have had any recurrence or metastases, and was well two years after operation. Fairbairn maintains that during pregnancy chorionic-placental elements were carried to the ovary and there gave rise to a chorion-epithelioma.

Pick and Freund have each reported a case of teratoma associated with chorionepithelioma of the ovary. The patients were girls, nine and seven years of age. These two writers are of the opinion that the chorionepithelioma is of teratological origin.

We may thus summarize the various theories which have been suggested in explanation of chorionepithelioma of the ovary:

1. Malignant transformation in the ovary of chorioplacental cells, carried from the uterus or the tube following pregnancy.

2. Malignant transformation in the ovary of trophoblastic elements following ovarian pregnancy.

3. Ovarian metastases of primary chorionepithelioma of the uterus or of the tube.

4. Malignant transformation of the trophoblast in ovarian parthenogenesis, as suggested by L. Loeb in 1911.

(1) The migration, in the human organism, after confinement or abortion, of chorioplacental elements, is a theory that is accepted by many. It happens indeed that, at autopsy of women who have recently been confined, there are found, particularly in the lungs, syncytial elements which present all the characteristics of Van Beneden's syncytium. That some of these elements, arrested in the vessels of different organs, may multiply and give rise to a chorionepithelioma, as they do in the uterus, is not paradoxical.
This migration, followed by malignant transformation, may explain the origin, in women, of certain ectopic chorionepitheliomas.

In the two cases which we have reported, we cannot logically presume a previous pregnancy, either entopic or ectopic. In Case I, the last confinement took place six years prior to the operation, and it is hardly probable that such a remote pregnancy should be the cause of the tumour. The theory of a recent abortion can also be rejected, inasmuch as there is nothing in the history to suggest such a possibility. Moreover, the uterine and tubal mucosae were not altered, and contained none of the elements of pregnancy. The second case was that of a young girl, a virgin. Close investigation and interrogation convinced the attending doctors that this girl had had no sexual intercourse.

(2) Malignant transformation of trophoblastic elements following an ovarian pregnancy is possible in the first case, but is not acceptable in the second.

(3) Ovarian metastases of a chorionepithelioma of the uterus or the tube are not acceptable in either case, as in both the uterus and the tubes were normal.

(4) There remains the last possibility: malignant evolution of trophoblastic elements of parthenogenesis. Without going as far back as Klebs and Schleich, who believed in a cellular fusion as the origin of all cancers, it would seem that Loeb was the first to suggest that teratomas and epitheliomas of the ovary may arise from the parthenogenetic development of the unfertilized ovum.

Henneguy was the first to mention parthenogenesis in the ovary of mammals. Bellonci and Janosik had previously, however, found that maturated
Classification of Dysembryomas Arising from Sex Cells

Female sex cell of the adult
  ↓
Parthenogenesis

Sex cell of the immature
  ↓
Ephebogenesis

Male sex cell of the adult
  ↓
Androgenesis

Teratologic Ovum

Benign tumours (Teratomas)
  ↓
Simple

Epithelium

{dermoid cyst
enteroid cyst
neuro-epithelium

Teratomas with
† - almost all
the tissues of
the adult

Malignant tumours
  ↓
Somatic Tissues

Epithelioma

Embryos with
several tissues, all
neoplastic, but † -
differentiated.

Simple

Sarcoma

Pluritissular

Chorioepithelioma

Trophoblast

Conjunctive tissue

Embryonic (at term) fertility

Neoplastic fertility
ova could show a beginning of true segmentation. Van der Stricht, Branca and Athias are of the opinion that the division of the oocyte, during follicular atresia, is the beginning of the parthenogenetic process. Athias believes that these oocytes often undergo modifications which consist of a nuclear multiplication and a division which suggest either a true segmentation, as if the oocyte were fertilized, or a more irregular, atypical evolution. "Evidemment," he writes, "les phénomènes qui ont lieu dans l'oeuf non fécondé, abstraction faite des mitoses de maturation, peuvent être tenus pour un commencement de développement parthénogénétique."

Hoche and Morlot, considering the question in women, found in the herniated ovary of a young girl, twelve years of age, who had not menstruated, an ovule of a ripened Graafian follicle containing four or five young cells, one of which was in division. They arrived at the conclusion that they were dealing with a ripened ovule, followed by segmentation and nuclear degeneracy. But it is logical to ask if the observations of Hoche and Morlot do not, in reality, represent the beginning of a parthenogenesis.

Newman admits that in armadillos the ovules often present a beginning of parthenogenetic division in the interior of atresic follicles, but that this division does not go beyond the stage of eight blastomeres.

Moreover, Loeb, Courrier, Branca, Courrier and Oberling, and Lelièvre, Peyron and Corsy have published clear figures of parthenogenetic ova with authentic trophoblast in the ovaries of virgin guinea-pigs. Loeb, Courrier and Oberling, and Lelièvre, Peyron and Corsy have drawn attention to the fact that the trophoblastic elements invade the ovarian stroma and the vessels in the manner of a chorionepithelioma.

These observations would seem to prove definitely the reality of the parthenogenetic process in mammals. If in virgin women no chorioplaental elements, such as are present in the guinea-pig, have been described, this is due probably to the greater dimensions of the human ovary, which cannot so easily be divided serially as are the ovaries of small mammals.

If the parthenogenetic origin of the primary chorionepithelioma of the ovary remains doubtful, several facts are, as we have seen, in its favour. On the other hand, it cannot be dissociated from the parthenogenetic origin of ovarian teratomas, which has been suggested by Loeb, Ewing, Peyron and others. The fact that embryonic somatic tissue is not found in chorionepitheliomas which have been developing for several weeks or months does not disprove the coexistence of a teratoma in the early stages of development. The teratoma may well have been attacked and destroyed by the chorionepithelioma, these properties being essential characteristics of the tumour. Moreover, the valuable observations of Pick and Freund prove the coexistence, in tumours that are still small, of teratoma and chorionepithelioma.

This apparently parthenogenetic origin, which is common to the teratoma and the chorionepithelioma, takes us far afield, because it forces us to take into account the teratomas and the chorionepitheliomas of the testicle. An acquired parthenogenetic or rather androgenetic origin has also been suggested for these. This opinion, upheld by Ménétrier and Peyron in France, and by Ewing in the United States, has recently been strongly supported by Limousin, Lemarie and Peyron reporting a case of testicular embryo.
These writers describe a tumour which reproduces a blastogenesis, of varied
and abundant forms, which supplants the process of normal embryology.
They speak of the presence, adjacent to a microscopic nodule of typical
placental tissue, of thousands of small cysts covered with a double layer of
epithelial cells resembling embryonic vesicles, which progress no further than
the bidermic stage of the blastoderm; in a vesicle, a characteristic picture of
a neural groove and special arrangements resembling a primitive trace, a
somite and, possibly, a chordal outline.

This tumour, which so closely imitates normal embryology, obscures, in
so far as its origin is concerned, the hypothesis of a congenital anomaly.
Moreover, the experimental teratomas produced by Michalowsky in the tes-
ticle of the rooster, and the numerous traumatic teratomas of the human
testicle, give still more force to the facts already related.

Thus the theory of the parthenogenetic origin of almost all of the tera-
tomas and the chorioneplitheliomas of the gonads is more and more generally
accepted. It is possible, taking the classification of dysembryomas by Mas-
son, to adapt it to parthenogenesis, and, including in it the chorioneplitheliomas,
draw up the chart reproduced on page 304:

In this way, the teratomas would originate from parthenogenesis in the
adult ovary, from androgenesis in the adult testicle, from ephebogenesis in
the gonads before puberty. And from the ectoderm of these teratologic ova,
in the first stage of their development, would arise the chorioneplitheliomas
independent of normal fertilization.

Evidently, the existence of congenital parasitic teratomas, which are in
some way monozygotic twins, brothers of the host (coccygeal, pharyngo-
cranial, mediastinal, and even gonadal tumours) cannot be denied. However,
the parthenogenetic hypothesis seems to have begun to be demonstrated. It
offers a better explanation of the benign or malignant forms, the mono-
or multi-tissular forms, and the more or less differentiated forms of the majority
of the dysembryomas.

We have thought it to be of interest, while reporting our two cases of
chorioneplithelioma of the ovary, to set forth here the most important argu-
ments in favour of their parthenogenetic origin, to which hypothesis we will-
ingly subscribe.

I desire here to record my sincere thanks to Doctors Harold Dolan and J. Pritchard,
who have permitted me to use the history and the pathological material for Case II.

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