

INVASIVE HYDATIDIFORM MOLE

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ACCORDING to DeLee, hydatidiform mole occurs in one in 2,000 pregnancies. Greenhill states that 4% of pregnancies which result in spontaneous abortions are hydatid moles and are unrecognized as such. In the Boston-Lying-In Hospital, from January 1932 to January 1942, there were 14 cases of hydatidiform mole, which ran about one in 2,051.

The three cases which will be described were gathered from a total of over 4,000 confinements, from 1935 to 1948, and it is probably unique that all three cases occurred within a few months of each other in the latter part of 1947 and early part of 1948, and that we have had no case prior to this time or since.

The etiology of hydatidiform mole is unknown. It is a cystic degeneration of the chorionic villi. Grossly, the mole resembles a bunch of grapes, varied in size, from a pinhead to a hen's egg. In practically all cases there was no sign of a fetus, although in a twin or multiple pregnancy, a fully developed fetus may be found. Matthieu reported three cases in which a fetus occurred. DeLee and Greenhill state that 2% of hydatidiform moles develop into chorioepitheliomas and that 50% of chorioepitheliomas are derived from the hydatidiform moles. DeLee states that hydatidiform moles occur more frequently in multipara aged over 35 years.

The diagnostic pointers in these moles may be summed up as follows: (1) Irregular vaginal bleeding. (2) Fulminating onset of toxic states. (3) Enlargement of uterus, disproportionate to the number of months of pregnancy. (4) The passage of vesicular material from the vagina. (As will be noted in one case described, the diagnosis was made when the patient passed some typical vesicular material.) In the other two cases, the diagnosis was made because of the unduly great enlargement of the uterus, out of all proportion to the stated number of months of pregnancy.

Careful studies of pathology may give us accurate information on the malignant potentialities of these tumours. The Aschheim Zondek test is of value in eliminating the possibility of chorioepithelioma, because the test usually becomes negative after ten days and if it persists it can indicate either that a piece of the mole

still exists or that malignant changes have taken place.

Hertig and Sheldon in their excellent paper, attempted to show correlation between the histologic appearance of the hydatidiform mole and the subsequent clinical course of the patient with respect to the development of chorionic malignancy, and they were able to evaluate malignant potentialities of a mole much more accurately. In their grading of these potentially malignant tumours, two general histologic principles were kept in mind: (1) the degree to which the trophoblast resembled or differed from that of the normal placental tissue in the first trimester of pregnancy and (2) the absolute degree to which it appears to be undifferentiated, using the criteria employed in grading any tumour. Comparison in the first trimester trophoblast was used as a criterion, since it is from pathologic chorion of this developmental age that hydatidiform moles arise.

They found that the more malignant the mole, the more its trophoblast resembled the differentiating trophoblast of the early human ovum during its first week after implantation.

"It is evident from a study of placental development and growth that a tumour derived from trophoblast differs from any other tumour in two respects, (1) it is derived from structures that are not an integral part of the host, and (2) its benign prototype is normally invasive, opens and permeates blood vessels, and thereby often metastasizes to the lungs.

"Because of the first fundamental difference, namely, the tumour host relationship, it is theoretically possible that no matter how malignant a mole appears microscopically, any particular area of trophoblast may not have been in juxta-position to the uterine wall, and hence could not have invaded it. . . . The second fundamental difference, namely the semimalignant attributes of all trophoblast, makes it clear that, since most pregnant patients have trophoblastic metastases, but rarely die from chorioepithelioma, there must be some factor other than its pure morphologic appearance which allows one metastasis to persist and kill the patient while the other disappears. The lytic substance postulated by Fraenkel is possibly the explanation for this phenomenon."

In the 200 cases which Gertug and Sheldon studied, they were able to establish classification on a histologic basis as follows:

1. *Benign hydatidiform moles*: showing none to slight hyperplasia of the trophoblast.
 2. *Probable benign hydatidiform moles*, showing slight to moderate hyperplasia of the trophoblast.
 3. *Possible benign hyperplasia with slight anaplasia*.
 4. *Possible malignant hydatidiform moles*, variable hyperplasia and moderate anaplasia of trophoblast.
 5. *Probable malignant hydatidiform moles*, marked anaplasia of trophoblast.
 6. *Malignant hydatidiform moles*, marked anaplasia of trophoblast, (exuberant hyperplasia), and often evidence of endometrium invasion.
- Chronic malignancies*: (1) Chorionepithelioma. (2) Syncytial endometritis. (3) Chorioadenoma destruens and (4) Chorioncarcinoma.

The three cases herewith concerned, from the gross and microscopic appearance, would come under the classification of chorioadenoma destruens and "this is the designation used to cover the group of chorionic malignancies which are characterized pathologically by persistent invasion of the myometrium by low-grade malignant trophoblast, usually attached to its parent-villus. These tumours rarely, if ever, give rise to clinical evidence of metastases, and therefore the prognosis is excellent providing the uterus is removed. This group is characterized clinically by variable amounts of uterine subinvolution, post-molar vaginal bleeding and usually a persistently positive test for chorionic gonadotrophic hormone."

The only serious, though rare, complication of this type is perforation of the uterus, with its resultant sepsis and hæmorrhage and except for this complication, it has been shown that following hysterectomy one can be assured of an almost 100% cure.

Hertig feels that "conservatism should be used in treatment of these cases so that many uteri that might be needlessly sacrificed, would be spared". In only one of the 32 cases he referred to was the uterus removed solely because of a persistently positive Friedman test. Since the test for chorionic gonadotrophic hormone may remain positive for as long as 16 weeks following the expulsion of the benign mole, the average being three months, with variations of 6 days to 10 months according to Pyane, it is obvious that it is of little help in diagnosing chorionadenoma destruens. However, post-molar vaginal bleeding and sub-involution of the uterus are almost invariably present and indicate the need for at least a uterine curettage, with the probability of the subsequent hysterectomy.

The probability that none of the chorioadenomata destruens is subject to metastases appears to be of clinical significance, since this group can be benefited by proper therapy (hysterectomy). Therefore it behooves the clinician to be on the watch for evidence of that condition.

CASE 1

White female, age 32. Past history, non-contributory. Had one child, age 2 years. Patient had three months' amenorrhœa and suddenly began to spot. She was admitted to hospital, examination revealed a uterus about the size of 5 to 6 month pregnancy, soft and spongy on palpation. There were no fetal heart sounds and x-rays of the pelvis did not reveal any fetal skeleton.

Shortly after admission the patient went into labour and passed a profuse amount of vesicles. The uterus con-

tracted down to the size of a two-months' pregnancy and about 7 days after admission she was discharged in good health and no bleeding *per vaginam*. An x-ray of the chest taken prior to dismissal did not reveal any disease. A follow-up showed a definite sub-involution of the uterus and some persistent bleeding.

She was admitted to hospital a month later and a diagnostic curettage was done. Pathological report did not reveal any evidence of malignancy. In spite of this the patient continued to bleed and it was felt advisable to recommend hysterectomy. Finally, two months after the original expulsion of the mole, a total hysterectomy was performed and the following is the pathologists report:

The gross examination reveals a body of uterus showing a marked adenomatous polyposis of the endometrium and what looks like the remnants of a hydatidiform mole. The ovary shows one plum- and one cherry-sized simple follicular cyst containing straw-coloured fluid.

Histological examination reveals some chorionic villi superficially with Langhans and syncytial cells but the latter cells are also invading the superficial and relatively deep sinusoids in the uterine wall. However, there has been no infiltration into the muscle nor are there mitotic figures in the Langhans cells seen. It presents a difficult problem in diagnosis but seems to me to belong to the invasive mole or chorio-adenoma destruens class rather than a true choriocarcinoma.

CASE 2

White female, age 46. Patient had amenorrhœa for four months and because she felt that she was near the menopause, did not deem it necessary to consult the doctor, but when she noticed that her abdomen was reaching large proportions and also because of some spotting, we were consulted and found her abdomen to be the size of a 6 month pregnancy. She was admitted to hospital and x-ray of chest and pelvis were taken: there were changes in the right lung suggestive of low grade chronic inflammation, but no definite diagnosis was made.

A day after admission she began to bleed and had contractions and expelled a large amount of hydatidiform cysts. Uterus contracted down to practically normal size. Her bleeding at the time was quite profuse and required supportive treatment by blood transfusions. She was discharged but continued to bleed for almost two months and on examination of the uterus, it was found to be sub-involutated and large, and hysterectomy was advised. Pan-hysterectomy was performed. The following is the pathological report:

The gross and histological appearances reveal a body and cervix of uterus showing a hydatidiform mole which is involving the inner aspect of the cavity, but there does not appear to be any undue proliferation and infiltration of the Langhans cells, which one would expect if choriocarcinomatous transformation had taken place. Such a condition, of course, is potentially malignant and the patient should be kept under observation.

CASE 3

White female, age 23. Past history non-contributory. History of amenorrhœa for three months. Prenatal care revealed uterus size of 4 to 5 month pregnancy. X-ray did not reveal any evidence of fetal skeleton. Admitted to hospital and two days after admission began to have crampy pains and bleeding and on the 3rd day expelled an hydatidiform mole. Patient was discharged 10 days after admittance and advised to return for routine check-up. X-ray of chest was negative.

After a lapse of only two weeks patient began to bleed profusely. She was admitted for D. & C. Shortly after her second admission began to bleed again. Examination revealed a large uterus and she was advised hysterectomy. This was carried out successfully. Following is the pathological report:

The gross and histological appearance reveal a large uterus containing a lemon sized necrotic mass, the remains of a hydatidiform mole, with cedematous chorionic

villi, which has destroyed the whole thickness of the uterine wall almost to the serous coat. There is no proliferation of the Langhan's or syncytial cells and hence I feel that the condition is thus still benign although it has been locally invasive.

These three patients have been followed very carefully since their operations. Their A.Z. tests have been negative on two occasions. The follow-up of x-ray of lungs have been persistently negative and patients are enjoying good health.

The striking thing about these three cases was the similarity in their symptoms and their course; all three came to hysterectomy because of persistent sub-involution, and persistent bleeding. The only dissimilarity was that one was ap-

proaching the menopause and one was a multipara, one had but one child and one was childless. The three have no evidence of metastases to the lungs, their A.Z. tests are negative and they have been diagnosed pathologically as belonging to the group of invasive moles without metastases, or chorioadenoma destruens.

BIBLIOGRAPHY

1. HERTIG, A. T. AND SHELDON, W. H.: *Am. J. Obst. & Gynec.*, 53: 1, 1947.
2. GASTINEAU, C. F. *et al.*: *J. Clin. Endocrinol.*, 9: 615, 1949.
3. GOHSTAND, L.: *M. J. Australia*, 1: 434, 1947.
4. PAYNE, F. L.: *Surg., Gynec. & Obst.*, 73: 8, 1941.
5. MATHIEU, A.: *Surg., Gynec. & Obst.*, 68: 844, 1939.
6. KRETCHMAR, L. H.: *Marquette M. Rev.*, p. 1, November, 1948.
7. HENNESSY, J. P.: *Am. J. Obst. & Gynec.*, 57: 779, 1949.