

HYDATIDIFORM MOLE AND CHORIONEPITHELIOMA

BY

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The September number of the American Journal of Gynaecology and Obstetrics contains an original communication styled "An appraisal of chorionepithelioma based on observation in twelve cases" by Samuel L. Siegler, Jacob M. Ravid and Sidney M. Tobin. In the introduction, it has been remarked— "Hydatidiform mole is seldom seen and Chorionepithelioma is rare." Our experience in this part of the world is, however, different. It will be the purpose of this communication to review the many cases of Hydatidiform Moles and Chorionepitheliomata treated in the Eden Hospital, Medical College, Calcutta.

Reports of incidence of Hydatidiform Moles and Chorionepitheliomata are variable not only from place to place but in the same institution from year to year. In the Eden Hospital, for example, in the year 1949, we had nine cases of Hydatidiform Moles and three cases of Chorionepitheliomata, when the total number of Obstetrical cases admitted were 6016. In the same Hospital in the year 1940, there were 19 cases of Hydatidiform Moles and 5 cases of Chorionepitheliomata amongst 5680 cases of pregnant patients admitted.

We record below the case histories

of a few typical cases and comment on them later on.

Case 1. Mrs. S. Age 20 years. Hindu. Primigravida. Period of amenorrhoea fourteen weeks. Height of the uterus well above the umbilicus. Diagnosis:— Hydatidiform Mole. Removal by the abdominal route advised, but this was refused by the relations. Vaginal evacuation was done. There was severe loss of blood. Patient continued to lose moderate amount of blood for the next fortnight, after which there was a severe blood loss. Patient was temporarily resuscitated with blood, plasma and saline transfusions. After an interval of three weeks, there was a severe attack of haemoptysis. She died one month and twenty-one days after the evacuation of the uterus. Growth removed from the uterus was examined histologically. It showed the typical structure of Chorionepithelioma.

Case 2. Mrs. K., Hindu, aged 22. Gravida 3. While in the third month of pregnancy she had an incomplete abortion. The foetus was expelled but the placental tissue was retained. Thirty-six hours after this, the uterine cavity was curetted. Bleeding however, continued. She was curetted again after ten days. Bleeding

stopped for a week. A slight loss continued for the next fortnight. It was decided to explore the uterine cavity for the retention of any products of conception. Under Gas and Oxygen anaesthesia when the cervical canal was being dilated, bright red blood started to pour out of the uterine cavity. Presence of Chorion-epithelioma was apprehended. A Friedman test, done the next day, was positive in 24 hours' time. Blood transfusion was given. Panhysterectomy was done—Typical Chorion-epithelioma was found. Subsequently the patient had a course of deep X ray therapy. She is doing well 5 years after the operation.

Case 3. Mrs. S. First pregnancy ended normally at term with the delivery of a live baby weighing nine pounds. She was admitted to the Hospital fifteen days after the delivery with a temperature of 105° F. Malarial parasites were found in the blood. On being treated with quinine and paludrine the temperature came down to normal. Five days after the remission of the fever, there was severe vaginal flooding with blood. The uterus was found bulky and enlarged to the size of about six weeks' pregnancy. Under anaesthesia the uterine cavity was explored. A good amount of spongy placenta-like tissue was removed. The bleeding stopped, to reappear in ten days' time. The uterus was found enlarged again. Uterus was again explored, a good amount of spongy vascular mass was removed as on the previous occasion. This led to a strong suspicion of Chorionepithelioma. Blood transfusion was given. Laparotomy was done. Typical Chorionepithe-

lioma, perforating the body of the uterus in several places, was removed. The patient had haemoptysis six weeks after the operation. X'ray examination of the lungs showed typical cannon-ball like shadows. Deep X'ray therapy for the lung metastases was started. Patient died after the sixth exposure. Patient was a Phillipino. She was the last surviving of her parents' three daughters. The other two died after the first childbirth in each case on account of "excessive blood loss."

Case 4. Mrs. M. Muslim. Age 15 years. Menarche at 12 years. Periods used to be scanty and painful. She has had prolonged treatment with ovarian and gonadotrophic hormones. She used to complain of frequent periods of amenorrhoea. During such a period of amenorrhoea of about six weeks' duration, she had five injections of Progynon-B Oleosum 50,000 units each. Periods did not appear. On examination the fundus of the uterus was found at the level of the umbilicus. It was diagnosed to be a case of Hydatidiform Mole. She expelled the contents of the uterus spontaneously exactly 70 days after her last menstrual period. A fortnight later she started to bleed. A—Z test was strongly positive. Diagnosis of Chorionepithelioma was made. Total hysterectomy was done. This was followed by deep X'ray therapy. She died three years later after a laparotomy done for an acute abdominal emergency, the details of which are not available.

The above case records will show among other things that Hydatidiform mole is not an essential precursor of Chorionepithelioma. This com-

plication may and does follow even normal pregnancy. Here are our cases for the years 1940 to 1950.

is not always a dependable point. The exact date of the last period is frequently misleading due to the occur-

Chorionepithelioma	Previous Hydatidiform Mole	Previous Abortion	Previous Labour
32	21	7	4

During this period 90 cases of Hydatidiform Moles were treated. As the figures above show only 21 subsequently developed Chorionepithelioma. We have not included in the above list another four cases of Chorionepithelioma whose past history of possible termination of pregnancy was not available. These ninety cases of Hydatidiform Mole were grouped according to age and parity as under:—

<i>Age: Years</i>	
15—25	— 40 cases
26—35	— 50 cases
<i>Parity:</i>	
1st	— 40 cases
2nd	— 20 cases
3rd	— 13 cases
4th	— 10 cases
6th	— 6 cases
9th	— 1 case

From the above figures we find a great preponderance of young mothers. In fact there have been only 30 cases after the second pregnancy. The vast majority of the Chorionepithelioma cases have been in the young. The mortality rate is, unfortunately, also the highest in the young as the figures will show.

We have met with various difficulties in the diagnosis of Hydatidiform moles as also of Chorionepitheliomata. The finding of disproportionate enlargement of the uterus with respect to the period of amenorrhoea

rence of slight blood loss during early pregnancy which is frequently complained of by many young women. The X-ray picture which fails to reveal the existence of foetal skeleton in the early months offers only a negative evidence and has obvious fallacies. Several times I have found a foetus with well developed skeleton in the uterus, when X-ray examination revealed no shadows when screened before the operation. In these cases, one finds massive blood clots in the uterus enveloping the foetus in such a way that the screening gives a negative picture as mentioned above. It is a difficult problem with us here to do an A—Z test. We depend upon the Friedman test. I have found that this test is dependable for the diagnosis of pregnancy. But in higher dilutions of urine as in 1 in 100, the test has been found to be negative in definite cases of Hydatidiform moles. It is accepted that in pregnancy complicated with Hydatidiform moles, nausea and lethargy associated with early pregnancy are very marked. We have not been able to substantiate this observation in at least one third of our cases. We have never observed the passage of individual or discreet vesicles through the vagina in the early stages of the expulsion of a Mole.

The diagnosis of a Chorionepithe-

lioma will depend mainly upon the clinical findings, viz. the persistence of bright red vaginal discharge accompanied by marked and continued enlargement of the body of the uterus after a recent expulsion of the products of conception. Pathological examination of the material obtained by scraping of the uterine cavity has not always been able to detect the existence of a malignant condition. We have never yet done the estimation of the chorionic hormone in the blood. We have found *cyst formation* of both the ovaries in connection with a Hydatidiform mole. Our observations showed the presence of bilateral Lutein Cysts in only 40 per cent of our cases. Another interesting fact which has been noticed is that we have been found in a young girl aged these cysts in persons whose ages are more than 25 years. In fact two-thirds have been found in primigravidae and the other third in second gravidas. The biggest cysts have been found in a young girl aged 18 years and pregnant for the first time within six months after her marriage. We have not been able to trace the total disappearance of these cysts after the complete evacuation of the mole in all cases. The primigravida referred to above with the biggest cyst in our series was examined six months later. The cysts which were of an average size of a "Langra" mango, had dwindled down to the size of a duck's egg. In another case, a cyst which was the size of a tennis ball had dwindled down to the size of ping-pong ball in a month's time. Contrary to the usual observations, such cysts have been infrequently found in associa-

tion with Chorionepitheliomata. The case notes fail to give us any idea of the frequency. From my experience I venture to record that I have not found the presence of these cysts in more than 10 per cent of the cases of Chorionepitheliomata removed by me after abdominal section. In our series we have records of 19 cases of moles actually burrowing into the wall of the uterus. All these cases were accompanied by bilateral cysts. In my earlier cases I had done a panhysterectomy, taking the condition to be malignant. As far as I remember this idea was shared by many of my then colleagues. In fact there is such a specimen in the Madras Maternity Hospital at Egmore. For the last six years, if the patient is young, I have not removed the uterus. No case of subsequent malignancy has so far been reported.

The next point for discussion is the procedure to be adopted in the management of cases with Hydatidiform moles and Chorionepitheliomata. We start with careful preoperative preparations in all cases other than those that come with profuse haemorrhage. In cases with Hydatidiform mole, I am inclined towards vaginal evacuation. The reason for such a bias is the fact that a good 75 per cent of our cases are received in the Hospital when a deliberate abdominal section, with the minimum of preoperative measures, is not feasible. Whereas if vaginal evacuation is undertaken deliberately and steadily, even uteri as big as the size of 30 weeks' pregnancy can be completely and safely evacuated in not more than 15 minutes' time. The essen-

tials for this operation are:—

1. A good anaesthetist, with Gas and Oxygen as the anaesthetic.
2. Blood and/or Plasma transfusion, and,
3. A steady surgeon.

A curette is seldom needed. I have never had to pack an incompletely evacuated uterus. The cervical canal should be dilated without hurry. Each dilator should be in the cervical canal for 30 seconds at least, particularly the bigger ones. The whole hand is introduced into the vagina and only one finger into the uterus. After the finger separates the mole from the uterine wall the hand on the abdomen squeezes the uterus. This way, most of the uterine contents can be expelled. The finger can be re-introduced and as the uterus will now be much smaller, it may not be necessary to introduce the hand into the vagina. When the uterus has thus been emptied, a full ten unit dose of pituitrin will ensure contraction of the uterus. Even if the mole is spontaneously expelled, we always explore the uterine cavity. Such exploration has always revealed substantial portion of retained mole. If the patient is a parous woman beyond the age of 35 years and is in a tolerable condition to stand an abdominal operation, we have deliberately done an abdominal hysterotomy. On at least three occasions it has so happened that patients when being prepared for the abdominal operation have had spontaneous evacuation. My experience of vaginal hysterotomy is far from satisfactory. It is a messy operation with blood and vesicles all over the place. A very respectable

colleague suggested to me the use of a local anaesthetic with Procaine, Penicillin and Ephedrine for this and other vaginal operation.

If after an apparently complete evacuation of a mole the uterus enlarges in size and haemorrhage occurs, the diagnosis would lie between the proliferation of an infiltrating benign mole and a Chorionepithelioma. In view of our bitter experience in respect of at least three of our cases where even biopsy and a Friedman test failed to detect the presence of a Chorionepithelioma, such cases we treat with hysterectomy even in the young. We have lost three patients, all within 25 years of age, for delaying the radical operation. Having done 12 cases of hysterectomy without laboratory support of diagnosis, in ten cases the uterus on section has revealed chorionepithelioma, and in two cases no evidence of malignancy was found. In one of these two, the patient was being curetted for diagnostic purpose by a Senior House Surgeon. He thought he had perforated the uterus. The patient started to lose blood freely. The patient had had three children, the vagina was capacious. A vaginal hysterectomy was rapidly done. The uterus was sent for pathological examination. No evidence of malignancy however was detected.

We have not been able to differentiate between the varieties or various grades of malignancy in our cases of Chorionepitheliomata from a histological point of view. But, from a clinical point of view, we have been convinced that such a differentiation exists. All our cases of chorionepitheliomata after full-term pregnancy

have been rapidly fatal within the maximum period of three months. Some of my colleagues have reported five year cures of cases of definite chorionepitheliomata where only a hysterectomy was done, ovaries or ovary retained and no deep X ray therapy advised. I have removed a Chorionepithelioma in a seventh gravida nine months after the expulsion of a Hydatidiform mole. The uterus was as big as a three months pregnancy. The ovaries were of normal size. I removed them. I have been told about patients recovering even after getting secondaries in the lungs. Two of my patients who had secondaries in the vault of the vagina are still alive today. I have seen only one case of a secondary in the right labium majus. She died six weeks after the operation due to an attack of small-pox.

My conclusions are:—

1. Hydatidiform Moles and Chorionepitheliomata are not rare complications of pregnancy. Chorionepitheliomata are frequently preceded by Hydatidiform Moles. Normal pregnancy ending in abortions and full term labour may also be followed by this malignant condition. The young gravida (between the ages of 15 and 25 years) is more vulnerable to this affection than her older sister.

2. There is no straightforward and characteristic manifestation of these conditions. Diagnosis should be made after full consideration of all

available clinical data.

3. While evacuation by the abdominal route has its special merits and indications, most of the cases could and should be treated by evacuation through the vaginal route, viz. digital evacuation through a dilated cervical canal. Vaginal hysterotomy is not recommended.

4. It is not desirable nor is it safe to wait for confirmation of the diagnosis of the possibility of a Chorionepithelioma from laboratory sources. We venture to opine that in presence of definite clinical findings, radical treatment by hysterectomy is justified.

5. There is probably a gradation in the degree of malignancy in various types of Chorionepitheliomata. Appearance of secondaries in the lungs or anywhere in the body indicate sure death. The only exception, perhaps, is in those cases where secondaries have appeared in the vault of the vagina.

The above is intended to summarize my observations of the cases as they were treated in the Hospital. There are obvious points of criticism and expressions of opinions contrary to those expressed above. The writer will be very grateful to those who will help him in this way. In conclusion, I express my grateful thanks to the Superintendent of the Hospital for allowing me to utilise the records. The Registrar, Dr. Arun Kumar Mitra M.B., has very kindly helped me in going through the notes. I record my sincere thanks to him.