HYDATIDIFORM MOLE

A review of 240 cases with special reference to prophylactic management

by

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Introduction

The description of hydatidiform mole dates back to very ancient times. Aetius of Amide in Greece, 6th century was one of the oldest known authors to have described and named it "Hydatid" Smellie (1759) defined hydatidiform mole as a conceptus usually devoid of an intact foetus in which all or many of the chorionic villi shows gross nodular swelling culminating in cyst formation with disintegration of blood vessels and variable proliferation of trophoblasts. Velpeau (1827) was the first person to describe hydatidiform mole as a result of hydropic degeneration of chorionic villi.

The incidence of hydatidiform mole varies in different parts of the world. A higher incidence has been reported in Asian countries. Reports from various centres in India show a uniformly high incidence (Das 1938, Bhaskar Rao 1961 Mathur and Shah 1964, Sreenivasa Rao 1969, Kalyanikutty and Nalini 1970). The incidence is high in Kerala also. This paper presents a review of 240 cases of hydatidiform mole at S.A.T. Hospital, Trivandrum during the six year period from 1966 to 1971.

Material and Methods

During this period, the hospital recorded a total number of 49730 pregnancies and 35071 deliveries. The total number of hydatidiform mole cases was 240. All the cases admitted to the hospital during this period were included in the study. Detailed analysis is made as to the incidence according to age, parity and presenting complaints. In the management of patients, particular importance was given to the prophylactic method, either by subjecting the patients to total hysterectomy in cases of multiparous women or to prophylactic methotrexate administration in cases of primigravid patients or women with one or two children in the younger age group.

Chorionic gonadotrophin assay was carried out using different techniques during the course of study. To start with we used the frog test, later switched on to the DAP test and towards the end of present study, pregnosticon test was utilised. Methotrexate was given prophylactically to 132 patients. Both injections

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and tablets were used according to the availability.

Two regimens were adopted, an intensive regimen and an intermittent regimen. Most of the patients received an intensive regimen of methotrexate. One week after evacuation these patients were subjected to D and C with the concomitant use of methotrexate.

Intensive regimen: Methotrexate was given as 0.4 mg/Kg for four successive days. No single dose exceeded 25 mg. The first dose of methotrexate was given 1-2 hour before the curettage. If it is given orally, the dose is given over a period of five days to reduce the toxicity. If a second course is to be given, an interval of 2 weeks was allowed in between.

Intermittent regimen: Methotrexate was given 0.6 mg/Kg body weight, twice weekly for 3 weeks. If toxic manifestations occurred, a single dose was omitted. Only a few patients were given this, as the dose of methotrexate required is greater and the hospital stay prolonged. Before administration of methotrexate, total leucocyte count, differential count, platelet counts and haemoglobin were estimated. In addition liver function tests, blood urea and serum creatinine were done in all cases receiving methotrexate. Patients were not given methotrexate when the total leucocyte count was below 3000, or platelet count below 100,000 or when the liver function tests were abnormal or when there was renal dysfunction as indicated by raised blood urea and serum creatinine. Haemograms were done just prior to the initiation of treatment, on the third day of methotrexate therapy and after completing the course. Prophylactic antibiotics and blood transfusions were given in doubtful cases.

In the absence of toxicity the patients were discharged 2-3 days after methotrexate therapy and they were followed-up for a variable period of time from 1 year to 4 years.

Results

The age and parity distribution are given in Tables I and II, respectively. The

TABLE I

Age Distribution in 240 Cases of Hydatidiform Mole

Age groups	No.	Percentage
15-19	38	15.83
20-24	81	33.75
25-29	48	20 00
30-34	36	15.00
35-39	10	4.17
40-44	17	7.08
45-50	9	3.75
Above 50	1	0.42
Total	240	100.00

TABLE II

Parity in 240 Cases of Hydatidiform Mole

Parity	No.	Percentage
0	54	22.50
1	56	23 33
2	34	14.17
3	25	10.42
4	17	7.08
5	19	7.92
6	5	2.08
7	8	3.33
8	10	4.17
9	2	0.83
10	5	2.08
Above 10	1	0.42
Unknown	4	1.67
Total	240	100.00

maximum number of cases were seen in the younger age group (15-34 years) with highest peak between the age of 20-24 years. Only 15.4 per cent of total cases

were seen above the age of 35 years. 60% of the cases occurred in 0-2 parity group. 12.9 per cent were seen above 5th parity.

Bleeding per vaginam after a period of amenorrhoea, inability to appreciate foetal movements, mass in the abdomen, pain in the abdomen, excessive vomiting and oedema, were the common presenting complaints. 93 per cent of cases in our series complained of bleeding per vaginam and 75 per cent could not appreciate foetal movements. 77.5 per cent showed size of uterus larger than the period of amenorrhoea, 52.5 per cent showed gross anaemia and 17.5 per cent pre-eclamptic toxaemia. The size of uterus varied, but 28.75 per cent of cases were between 21 to 24 weeks' size. (Table III).

TABLE III

Size of Uterus in 240 Cases of Hydatidiform Mole

Size of uterus	Number	Percentage
Up to 8 weeks	23	9.58
8-12 weeks	28	11.87
13-16 weeks	24	10.00
17-20 weeks	40	16.67
21-24 weeks	69	28.75
25-28 weeks	34	14.17
29-32 weeks	16	6.67
33-36 weeks	2	0.83
Unknown	4	1.66
TOTAL	240	100.00

TABLE IV

Duration of Molar Pregnancy in 240 Cases

Duration	No. of cases	Percentage
1-2 months	36	15
3-4 months	144	60
5-6 months	48	20
Not known	12	5

Table IV shows the duration of molar pregnancy. In 60 per cent of the cases the duration was 12 to 16 weeks with a maximum period upto 24 weeks.

TABLE V

Blood Group Distribution in 120 Cases of Hydatidifom mole Compared With a Control Group

Blood Group	Hydatidiform mole patients	Control
A	39	33
B	30	30
O	43	49
AB	8	8

Table V shows the distribution of blood groups in 120 cases in which the blood groups were known, compared with a control group. There is no significant variation in the pattern in blood group distribution in hydatidiform mole patients from the control group.

TABLE VI

Method of Treatment given in 240 Cases of Hydatidiform Mole

Type of treatment	No. of cases	Percentage
Evacuation alone	22	9.16
Evacuation + D and C	42	17.05
Evacuation, D and C and Methotrexate	128	53.33
Hysterectomy	43	17.92
Hysterectomy + Methotrexate	4	1.67
Discharged against medical advice	1	0.42
Total	240	100.00

Table VI shows methods of treatment adopted in the cases. In 22 patients only evacuation was done, whereas in 42 cases a second D and C was alone done. Most of these patients were referred from other hospitals after evacuation. One hundred and twenty-eight patients were given pro-

phylactic methotrexate, mostly one course of methotrexate only was given when the chorionic gonadotrophin test became normal. The dose of methotrexate used is given in Table VII. Abdominal pain, lip ulceration, vomiting skin rashes, fever, alopecia, leucopoenia and bleeding tendencies were the toxic manifestations encountered. Two patients had severe drug toxicity and expired (Table VIII).

TABLE VII

Dose of Methotrexate Used in 132 Patients With Hydatidiform Mole

Dose	No. of cases	Percentage
Upto 75 mg.	94	71.21
75-100	29	21.96
100-150	4	3.03
151-200	2	1.52
201-250	2	1.52
Above 250	1	0.76
Total	132	100.00

TABLE VIII

Methotrexate Toxicity in 132 Cases of Hydatidiform Mole

Toxicity	No. of cases	Percentage
Diarrhoea	24	18.18
Abdominal pain	15	12.12
Lip ulceration	15	12.12
Vomiting	8	6.61
Skin rashes	6	4 55
Leucopoenia	4	3.30
Fever	3	2.27
Alopecia	3	2.27
Bleeding tendencies	2	1.67
Death due to toxicity	2	1.67
No toxicity	5	37.84

One had a superadded amoebic hepatitis also. These cases were at the initial stage of study when we were inexperienced with the use of methotrexate. Thereafter we showed no hesitation in the use of blood transfusions and antibiotics in treating toxic symptoms. None of the patients received folinic acid.

Forty-three patients had prophylactic hysterectomy. They were in the age group above 35 with 3 or more children. Four of these cases received methotrexate following hysterectomy, because the immunological test remained positive after 2 weeks of operation. The test became promptly negative after a course of methotrexate. In none of these cases there were any evidence of choriocarcinoma, either clinically or histopathologically.

78 per cent of patients had regular check-up. Two patients from the prophylactic Methotrexate group developed choriocarcinoma after 1½ years.

Case I.

This was a 20 year old second para. She had negative biological test at the time of discharge. Never turned up for check-up. She reported after 1½ years with irregular bleeding per vaginam. On examination there was no evidence of choriocarcinoma. X'ray chest was normal. D & C was done, and histopathology showed choriocarcinoma. Meanwhile the patient had gone home and returned three weeks after with profuse bleeding. On examination there was a friable growth protruding through the cervical canal. Uterus was enlarged. Immediately panhysterectomy was done and methotrexate started. She died of choriocarcinoma.

Case II.

A 18-year old primigravida, immunological test was negative at the time of discharge. Had no check-up, and after 14 months presented with a bleeding suburethral nodule. X'ray chest showed multiple secondaries. Died in spite of treatment with methotrexate.

One patient from the hysterectomy group subsequently developed choriocarcinoma.

Case III.

35 year old multipara had panhysterectomy for vesicular mole 2 years back. His-

topathology report was syncytial endometritis. Had one check-up in the first three months. She presented with cough and haemoptysis. On examination there were multiple secondary deposits in the chest, the immunological test was positive, but there was no evidence of recurrence in the pelvis. Methrotrexate was out of stock at that time and we tried with a course of mitomycin, apparently with no effect on the metastases. She was taken home in a moribund condition.

Discussion

The incidence of 1 in 207 pregnancies seen in these series is comparable to the reported incidence from various centres in India and Asian countries as shown in Table IX. The joint project for the study of choriocarcinoma and hydatidiform mole have found that maximum number of trophoblastic tumours they have registered are from Asian countries. The increased incidence in Asian countries have been attributed to earlier marriage, high fertility rate, low socioeconomic conditions, malnutrition, anaemia, etc. (Acosta-Sison 1964, Poen 1965). The higher rate seen in this part of the country may be partly due to the higher density of population along with malnutrition. An association with tuberculosis has been shown by Sison.

TABLE IX

Comparative Frequency of Hydatidiform Mole

Author	Year	Country	Incidence in relation to pregnancy
Novak	1947	U.S.A.	1:2500
Hertig & Sheldon	1947	U.S.A.	1:2062
Hasegawa	1957	Japan	1:232
Acosta-Sison	1964	Philippines	1:200
Wei & Ouyang	1963	Taiwan	1:125
Ian Donald	1959	U.K.	1:2000
Das, P. C.	1956	Calcutta	1:447
Bhaskar Rao	1961	Madras	1:361
Mathur & Shah	1964	Ahmedabad	1:200
Sreenivasa Rao	1969	Visakapattanam	1:191
Kalyanikutty & Nalini	1970	Trivandrum	1:480
Present Study	1972	Trivandrum	1:207

Maximum number of cases were seen between the ages of 20 to 28 years (53.75%). This is in conformity with the findings of other workers. (Bhaskar Rao 1961, Mathur and Shah 1964). The maximum incidence was seen in the highest fertility period. The average age in our series was found to be 25.86 years.

There has been some discussion as to whether molar pregnancy tends to become more frequent as parity increases or whether this factor has no influence whatsoever. 60% of our cases occurred below the 3rd parity group and only 12.9% were seen above the 5th parity group. Hence, multiparity cannot be considered a determining factor in the frequency of molar pregnancies.

Average duration of molar pregnancies ranged from 12-16 weeks. The size of uterus in 77.5% cases was more than the period of amenorrhoea. Pre-eclamptic toxaemia is usually an associated finding in molar pregnancies, but the present study shows only 17.5 per cent incidence

of pre-eclamptic toxaemia.

Diagnosis of the condition is usually made from the history, clinical findings and plain X'ray of abdomen in cases where the uterus is more than 16 weeks' of gestation. Clinical findings included enlargement of uterus out of proportion to the period of amenorrhoea, doughy feel of the uterus, absence of external and internal ballotment and signs of toxaemia. Estimation of chorionic gonadotrophin is of limited value in the diagnosis, especially in the early stages. But persistently higher levels after 100 days of the last menstrual period, when usually there is a rapid decline of chorionic gonadotrophins in normal pregnancy, is indicative of an abnormal growth of trophoblast. However, the confirmatory sign is the passage of the vesicles.

Because of the malignant potentiality of hydatidiform mole prophylactic chemotherapy has been tried by many workers. In Acosta-Sison's series (1964) prophylactic methotrexate was given to 18 patients and prophylactic hysterectomy was done for 13 patients between the ages of 35-50. None of them developed choriocarcinoma, whereas in 164 cases who did not have prophylactic treatment, 17% developed chorionic malignancy. In Tow's series (1966) in which 52 patients received prophylactic methotrexate, 3 courses of 50 mg. each, one developed choriocarcinoma (1.92%). Koga and Maeda 1968 from Japan give an incidence of 7.1% choriocarcinoma developing when no prophylaxis was given, whereas none of 107 patients who received prophylactic methotrexate developed choriocarcinoma.

In our series, out of 43 cases who were subjected to prophylactic hysterectomy, all remained symptoms free till date except one who had died of widespread secondary deposits in lung 2 years after panhysterectomy for a vesicular mole (Case III). Four of these had a positive biological test after hysterectomy, and, therefore, a course of methotrexate was given. The test became negative and remained so thereafter.

Out of 128 patients who were given prophylactic methotrexate two died of toxicity. Two patients subsequently developed choriocarcinoma and died (Case I and II). Thus the mortality in this group is 3.13%.

There were 64 patients who received no active treatment. The follow-up was very irregular in this group and no one is known to have developed choriocarcinoma.

Pregnancy Following Vesicular Mole

Ten patients had normal deliveries following prophylactic chemotherapy. All the patients were advised to adopt some form of contraceptive measures after chemotherapy. This was discontinued after 1-2 years and out of the 10 patients who conceived later, in none of them there was any evidence of congenital malformations of the foetus.

Summary and Conclusions

The incidence of hydatidiform mole in the present study was 1:207 pregnancies.

53.75 per cent cases were seen between the ages of 20-29 years. The average age was found to be 25.86 years.

Multiparity cannot be considered as a determining factor in the development of hydatidiform mole.

Pre-eclamptic toxaemia was associated with only 17.5% cases, unlike the usually reported higher percentage.

Prophylactic chemotherapy appeared to be definitely beneficial in patients of younger age groups and prophylactic

hysterectomy in multiparous women of older age groups.

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