

## HISTOPATHOLOGICAL REVIEW OF PARTIAL AND COMPLETE HYDATIDIFORM MOLES IN A TERTIARY CARE HOSPITAL, LAHORE – PAKISTAN

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### ABSTRACT

*Background:* Hydatidiform mole is an abnormal gestation characterized by trophoblastic hyperplasia and overgrowth of placental villi. Hydatidiform mole is classified as complete (CHM) and partial hydatidiform mole (PHM). The diagnosis is based on histopathology and genetic origin. The incidence of molar pregnancy varies in different parts of the world. The malignant potential of this disease is higher in South East Asia as compared to western countries. Objective of the present study was to determine the frequency, clinical presentation and morphological features of hydatidiform mole. This retrospective, descriptive case series was conducted in the Department of Pathology Postgraduate Medical Institute and Lahore General Hospital, from 1st Jan 2009 to 31st Dec 2010.

*Methods:* The case records of all the molar pregnancy specimens during the study period were analysed regarding patient's history, clinical examination, morphological features and laboratory investigations. The main outcomes were measured in terms of duration, gestational age, morphological features and investigations.

*Results:* A total of 60 cases were examined during the study period, which included 40 cases of complete hydatidiform mole and 20 cases of partial hydatidiform mole.

*Conclusion:* Frequency of CHM was higher as compared to PHM. The disease was common at extremes of ages. Morphological findings of CHM differ from PHM on the basis of degree of trophoblastic hyperplasia, villous contours and scalloping, presence of distinct cisterns and nucleated Red Blood Cells (RBC) in fetal vessels. We concluded that there is no single criterion for the differentiate CHM and PHM. *P57<sup>kip2</sup>* expression can be used in association with the histological findings for a definitive diagnosis.

*Keywords:* Hydatidiform mole, Trophoblastic hyperplasia, Cisterns.

### INTRODUCTION

Hydatidiform mole is an abnormal gestation characterized by trophoblastic hyperplasia and overgrowth of placental villi. Hydatidiform mole is classified as complete and partial hydatidiform mole. The diagnosis is based on histopathology and genetic origin.<sup>1</sup> Accurate diagnosis and classification of hydatidiform mole is important as the risk of persistent gestational trophoblastic disease, including the choriocarcinoma, is significantly high. The risk of choriocarcinoma in CHM is 10% – 30% and in PHM is 0.5% – 5%.<sup>2</sup> There is no reliable report for prevalence and incidence of molar pregnancy in Pakistan. However in the United States, hydatidiform mole complicates approximately 1 in 1,500 pregnancies, with much higher rates in Asia (e.g. up to one in 100 pregnancies in Indonesia). According to one study in Tehran, the incidence of disease is 6.7 / 1,000 live deliveries.<sup>3</sup>

Histological examination is the main tool in the diagnosis of molar pregnancy including the degree of trophoblastic hyperplasia, villous contours and

scalloping, presence of distinct cisterns, trophoblastic inclusions, and presence or absence of nucleated RBC in fetal vessels.<sup>4,5</sup> However there is considerable overlap in the histological features between CHM and PHM, resulting in significant interobserver variability in the diagnosis. Moreover, molar pregnancies are being evacuated early in gestation, before the development of well established classical morphological features, thus adding to the difficulty in diagnosis.<sup>3</sup>

### PATIENTS AND METHODS

This retrospective, descriptive case review was conducted at the Department of Pathology Postgraduate Medical Institute / Lahore General Hospital from 1st Jan 2009 to 31<sup>st</sup> Dec 2010. The case records of all these patients with molar pregnancy were analysed regarding the age of patients, gestational age, signs and symptoms, histopathology and other investigations. All patients having molar pregnancy with elevated  $\beta$ -HCG (human chorionic gonadotropin), ultrasonic or histopathological evidence of the

disease were included in the study. The criteria for diagnosis of CHM and PHM were those of Szulman and Surti<sup>6,7</sup> and a histological diagnosis was attempted in all cases, even when material was scanty.

The following features were graded:

- (a) Hyperplasia of trophoblasts; diffuse (perivillous circumferential); focal (perivillous multifocal); absent.
- (b) Cistern: present; absent.
- (c) Pseudoinclusions of trophoblasts: present; absent.
- (d) Fetal vessels in villous stroma: present; absent.

Patients having incomplete history and without  $\beta$ -HCG levels were excluded. Socioeconomic status of patient was labelled as poor if monthly income was up to rupees 7,000 per months, middle if income was up to 20,000 per month and upper class if monthly income was more than 50000 rupees per months. Data was analysed using SPSS version 16 and 18.

**RESULTS**

There were a total of 60 specimens of molar pregnancy in the department of Pathology they included

Table 1: Socio-demographic data in 60 cases.

| Parameters                  | No. of Patients (%) |
|-----------------------------|---------------------|
| <i>Age (years)</i>          |                     |
| < 20                        | 23 (38.3)           |
| 21 – 35                     | 9 (15)              |
| > 35                        | 28 (46.6)           |
| <i>Parity</i>               |                     |
| 0 – 1                       | 26 (43.3)           |
| 2 – 4                       | 17 (28.3)           |
| > 4                         | 19 (31.6)           |
| <i>Socioeconomic Status</i> |                     |
| Low                         | 33 (55)             |
| Middle                      | 26 (43.3)           |
| High                        | 4 (6.6)             |

Table 3: Morphological Features in complete and partial moles.

| Type of mole  | Trophoblastic hyperplasia |         | Pseudo inclusion |        | Cisterns |        | Vessels in the villous stroma |        | Foetal parts |        |
|---------------|---------------------------|---------|------------------|--------|----------|--------|-------------------------------|--------|--------------|--------|
|               | Focal                     | Diffuse | Present          | Absent | Present  | Absent | Present                       | Absent | Present      | Absent |
| Complete mole | 9                         | 31      | 37               | 3      | 38       | 2      | 0                             | 40     | 0            | 40     |
| Partial mole  | 17                        | 3       | 4                | 16     | 5        | 15     | 13                            | 7      | 5            | 15     |

40 cases of complete hydatidiform mole and 20 cases of partial mole. The study period was from 1<sup>st</sup> Jan 2009 to 31<sup>st</sup> Dec 2010. Majority of the patients aged more than 35 years. In 23 (38.3%) patients, the disease presented in < 20 years and in 9 (15%) between 21 – 35 years (Table 1). The most common presenting symptom was bleeding per vaginum followed by pain in lower abdomen. The gestational period in 19 (31.6%) patients was between 1 – 2 months, in 34 (46.6%) patients between 2 – 5 month and only 7 (21.6%) patients presented after 5 months of gestation (Table 2).

Table 3 shows the morphological features of all cases with their diagnoses. Diffuse trophoblastic hyperplasia was seen in most cases of CHM. Complete hydatidiform mole was diagnosed in 40 Patients and partial in 20 (Table 4).

Table 2: Gestational age in 60 cases.

| Gestational Age | No of Patients (%) |
|-----------------|--------------------|
| 1 – 2 month     | 19 (31.6)          |
| 2 – 5 month     | 34 (46.6)          |
| >5 month        | 7 (21.6)           |

Table 4: Types of hydatidiform moles.

| Type                       | No of patients (%) |
|----------------------------|--------------------|
| Complete hydatidiform mole | 40 (66.6)          |
| Partial hydatidiform mole  | 20 (33.3)          |

**DISCUSSION**

A hydatidiform mole is a pregnancy / conceptus in which the placenta contains grapelike vesicles that are visible to the naked eye. The vesicles arise by the hydropic change within the chorionic villi. When inspected under the microscope, hyperplasia of the trophoblastic tissue is noted. The diagnosis of hydatidiform mole is clinically important because of its potential to give rise to persistent gestational trophoblastic disease including invasive mole, choriocarcinoma and placental site trophoblastic tumors. Furthermore, the distinction between complete and partial mole is also significant.<sup>8</sup>

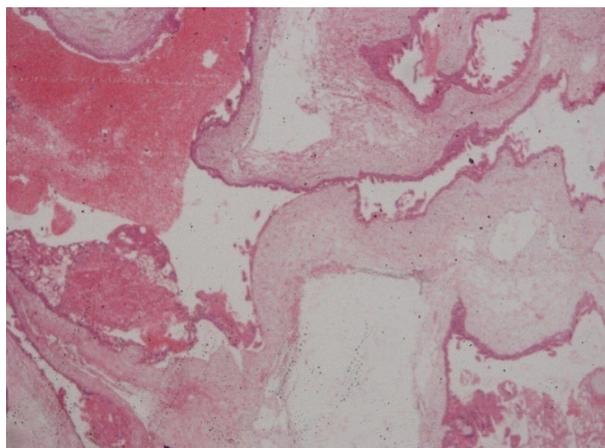


Fig. 1: Complete mole at 40x (H&E) magnification.

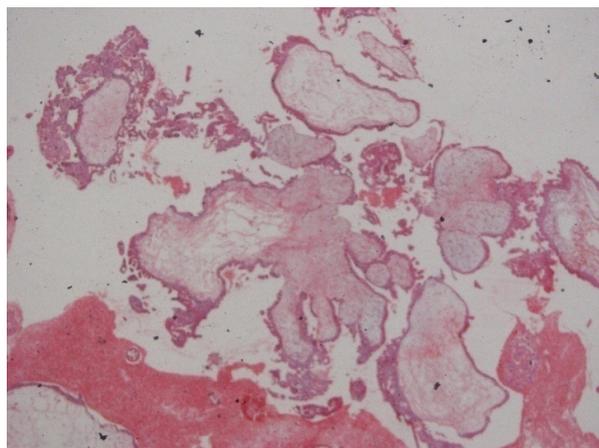


Fig. 3: Partial mole at 40x (H&E) magnification.

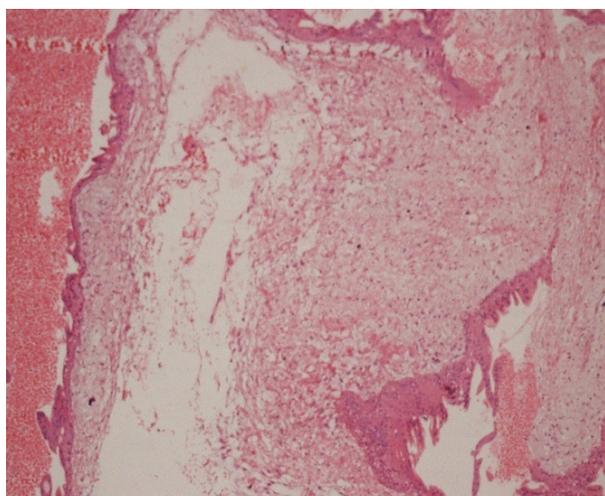


Fig. 2: Complete mole at 400x (H&E) magnification.

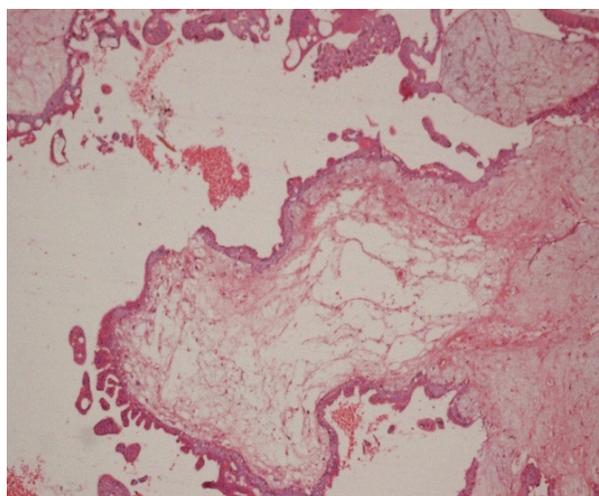


Fig. 4: Partial mole at 400x (H&E) magnification.

The typical clinical presentation of complete molar pregnancies has changed with the advent of high – resolution ultrasonography. Most moles are now diagnosed in the first trimester before the onset of the classical signs and symptoms.<sup>2</sup> The most common classical symptom of a complete mole is vaginal bleeding due to early separation of molar tissue from the decidua. The uterus may become distended by large amount of blood, and dark fluid may leak into the vagina. This symptom occurs in 50% of cases. Patients may also report severe nausea and vomiting. This is due to extremely high levels of HCG.

Mainly two risk factors increase the likelihood for the development of molar pregnancy: The woman being either too young or too old for a pregnancy (under 20 yrs, or over 35 yrs), and with previous history of molar pregnancy.<sup>9</sup> The aetiology of this condition is not completely understood. Potential risk factors may include defects in the ova, ab-

normalities within the uterus, or nutritional deficiencies such as diet low in protein, folic acid and carotene. Another reason is that our patients had low socioeconomic status (Table 1). A study conducted by Tham stated that the high incidence in Asia is generally attributed to low socioeconomic status and malnutrition.<sup>10</sup> Maternal reproductive age is the most consistent risk factor for hydatidiform mole in every region and ethnic group. In this study, disease was more common at extremes of reproductive ages. It is consistent with the findings of studies from Singapore, Karachi and Nawabshah.<sup>10</sup> The available evidence suggests that hydatidiform mole arises as a consequence of defective ova. It is premature in young and post mature in old ages.<sup>10</sup>

Histological examination forms the main tool in the diagnosis of molar pregnancy including the degree of trophoblastic hyperplasia, villous contours and scalloping, presence of distinct cisterns, trophoblastic inclusions, and the presence or absence of

nucleated RBC's in fetal vessels.<sup>2,4</sup> However there is considerable overlap in the histological features between complete and partial hydatidiform mole, resulting in significant interobserver variability in the diagnosis. Moreover, molar pregnancies are being evacuated early in gestation, before the development of well established classical morphological features, thus adding to the difficulty in diagnosis.<sup>2</sup>

It is well known that CHM and PHM represent two independent conditions. Biological variability and scarcity of available tissue, however, will sometimes impose difficulties in the differential diagnosis, mainly between CHM and PHM.<sup>11</sup> The present study aimed to evaluate what parameters commonly used are helpful in the differential diagnosis of the two conditions. Abnormal trophoblastic hyperplasia is a requirement for the diagnosis of molar pregnancy. In all cases of CHM, the degree of hyperplasia was more marked than in PHM, and it exhibited a circumferential pattern. Villous oedema was a constant feature in both conditions but cistern formation was mainly seen in CHM.

In the previous literature, villous hydrops was the most striking feature of products of conception affected by molar disease. The degree of villous hydrops may be much less marked and patchy in both CHM and PHM. Enlarged hydropic villi in molar pregnancies are usually more circular in cross section with hypocellular villous cores and trophoblast attenuation.<sup>12</sup> Whether a hydatidiform mole is complete or partial, requires deoxyribonucleic acid (DNA) flow cytometry for karyotyping but this technique is relatively expensive, time consuming and requires the resources that may not be available in a routine histopathological settings.<sup>5</sup>

The P57<sup>kip2</sup> protein is a cyclin – dependent kinase – inhibitor (CDKN1C) and tumour suppressor encoded by a paternally imprinted gene, located on chromosome 11p<sup>15.5</sup> and predominantly expressed from the maternal allele in most cases. Lack of p57<sup>kip2</sup> activity leads to loss of cell cycle control and contributes to trophoblastic hyperplasia.<sup>14</sup> Thus p57<sup>kip2</sup> is a valuable diagnostic tool that could be used to differentiate complete and partial hydatidiform mole. It was shown to be a highly specific and sensitive marker.<sup>15</sup>

We conclude that there is no single criterion for the distinction of CHM and PHM. The disease was common in extremes of ages. Frequency of complete hydatidiform mole was higher as compared to partial hydatidiform mole. Morphological findings of complete hydatidiform mole differ from partial hydatidiform mole but with some overlap. P57<sup>kip2</sup> expression can be used in association with the histological findings for the definitive diagnosis.

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