Clinicopathological study of Gestational Trophoblastic Disease

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ABSTRACT

Several potential etiologic risk factors have been evaluated for the development of complete hydatidiform mole. The two established risk factors that have emerged are extremes of maternal age and prior molar pregnancy. Advanced or very young maternal age has consistently correlated with higher rates of complete hydatidiform mole. Compared to women aged 21-35 years, the risk of a complete mole is 1.9 times higher for women both more than 35 years and less than 21 years as well as 7.5 times higher for women more than 40 years. (49, 50) The risk of repeat molar pregnancy after 1 mole is about 1% or about 10-20 times the risk for the general population. The present study on the gestational trophoblastic disease (GTD) was carried out as it is one of the fascinating gynaecological tumours. Hence a clinicopathological study of gestational trophoblastic disease was undertaken with relevance to the histopathological study of GTD and clinical correlation.

INTRODUCTION

GTD is a heterogeneous group after abnormal fertilisation of entangled damages triggered by Trophoblastic placenta epithelia. It is a placental disease triggered by the exuberant growth of placenta trophoblastic cells. The disease is an unusual trophoblast (Deep et al., 2013), it includes a variety of maternity disorders, including both premalignant and malignant anomalies. Malignant lesions tumours may include a complete mole, partial mole and hydatiform, whereby malignant anomalies involve the invasive mole, choriocarcinoma, the tumour trophoblast placental region, tumour trophoblast epithelioid, etc. (Seckl et al., 2010; Saraf and Ghodke, 2016; Tse et al., 2012).

The word gestational neoplasm (GTN), which may grow, metastasise, and death when left untreated, was commonly extended to intrusive moles (CCM and PSTT). A part of human placenta is trophoblast. It aims to implant an embryo; it also provides the development of fetus with blood and nutrients and disposes of wastes (Rozina et al., 2011; Yakasai, 2015). It also produces essential hormones for parenting.

Aims and Objectives

1. To study histopathology of different forms of gestational trophoblastic disease.

2. To study histopathology of different forms of gestational trophoblastic disease as per standard classification (WHO & FIGO) and correlate with clinical presentation.

3. To study the correlation between gestational trophoblastic disease and blood group of the patient.
LITERATURE REVIEW

Aetius, a doctor from Mesopotamia (Modern day Iraq) in 1600 AD noted resemblance of the vesicles in hydatidiform mole to large drops of water. They developed the term “Hydatide” from the Greek language for “drop hydatid” (Ivy et al., 2010; Lurain, 2011; Blay et al., 2012). This is followed by the story of the countess of Henneberg, who was so cursed that she brought forth 365 stillborn children (each a molar vesicle) on Good Friday in 1276 (Yakasai et al., 2012). Several studies have shown that the history of prior spontaneous or induced abortion is more common in patients with hydatidiform mole and choriocarcinoma. Women who had one hydatidiform mole are more significant risk of having another (Agrawal et al., 2015). In another study in India by Shrivastava and Gandhewar (2014) had a majority of GTD patients in the age group of 20-25 years, comprising 66%. Another study performed by Sunkesula et al. (2014) the incidence of GTD was very high with 77.78% found between 21-29 years age group and least after 30 years with 13.33%. This study also showed a peak incidence of GTD in 20-25 years age group with 64%.

MATERIALS AND METHODS

Data collection

The two-year data from was retrieved from archives of the department of pathology. Cases of GTD were studied prospectively. All women who were diagnosed with GTD from our hospital and specimens or slide blocks from outside the hospital were included in the present study. The total number of deliveries was taken from hospital registries. During the study period, the material consisted of 3 hysterec- tomy specimens and 986 specimens of products of conception from the uterus, uterine curetting or suction evacuation.

Sample Size

The gestational trophoblastic disease was diagnosed in 77 cases, were included in the study.

Study plan

All specimens from our hospital and specimens or slide blocks from outside were included in the present study. Histopathological (Gross & Microscopic) examinations of all specimens were done at the department of pathology as per the standard procedure. Clinical history of the patients including age, chief complaints, menstrual history, gestational age, history of previous pregnancy; was noted. Serum Beta hCG levels were noted. Blood groups of all the patients were noted. USG reports, if done, were noted. The study was conducted as per the proforma of the present study. All the data collected was then studied and analysed.

OBSERVATIONS AND DISCUSSION

Data Collection

The present study deals with gestational trophoblastic diseases (GTD). GTDs are a group of captivating diseases. It is a placental disease, arising from abnormal proliferation of trophoblastic cells in the placenta. The present work was an observational, descriptive and analytical type of study. This study consisted of 77 cases of GTD, diagnosed and classified histopathologically in the department of pathology at tertiary care hospital, carried out for two years. Therefore, GTD cases from the hospital were taken under consideration prospectively. All the collected data then correlated clinically and analysed.

During the study period, we received 986 specimens of products of conception. All the specimens were fixed, gроссed and processed as per the standard procedure. Then microscopic evaluation was done under a light microscope which revealed a diagnosis of GTD and mimickers of GTD. In our study, we got 74 (7.51%) GTD cases, 507 (51.42%) cases of hydropic abortus, 224 (22.72%) cases of retained products of conception, infected products of conception were 168 (17.03%), and only blood clots in 13 (1.32%) cases were observed (Table 1).

Figure 1: Histopathological classification of GTD

We also received hysterectomy specimens, of which three were diagnosed as GTD. Three of them were diagnosed as invasive mole, choriocarcinoma and PSTT. Seventy-four moles and 01 cases of each invasive mole, choriocarcinoma and PSTT; collectively, we got 77 cases for the present study.

The following table (Table 2) shows all GTD cases classified according to histopathological diagnosis. Out of the 77 cases of GTD, the majority were hydatidiform mole (Complete mole and Partial mole)
Table 1: Histomorphological distribution of products of conception

| Different specimens        | No. of cases | Percentage (%) |
|---------------------------|--------------|----------------|
| Molar pregnancies         | 74           | 7.51%          |
| Hydropic abortus          | 507          | 51.42%         |
| Retained POC*             | 224          | 22.72%         |
| Infected POC*             | 168          | 17.03%         |
| Blood clots               | 13           | 1.32%          |
| Total                     | 986          | 100%           |

* (POC= Products of conception)

Table 2: Histopathological diagnosis of all GTD

| Type of GTD                             | No. | Percentage |
|-----------------------------------------|-----|------------|
| Hydatidiform mole                       | 74  | 96.10%     |
| Invasive mole                           | 01  | 1.30%      |
| Choriocarcinoma                         | 01  | 1.30%      |
| Placental site trophoblastic tumour     | 01  | 1.30%      |
| Total                                   | 77  | 100%       |

Table 3: Clinical presentation of GTD

| Clinical presentation                  | No. of cases | Percentage |
|----------------------------------------|--------------|------------|
| Bleeding per vagina                    | 73           | 94.80%     |
| Amenorrhea                             | 71           | 92.20%     |
| Pain                                   | 48           | 62.35%     |
| Hyperemesis gravida                    | 08           | 10.40%     |
| Passing grape-like vesicles            | 05           | 6.50%      |
| Hyperthyroidism                        | 02           | 2.60%      |

Table 4: ABO Blood grouping and GTD

| Diagnosis                        | Blood group (ABO type) |   |   |   |
|----------------------------------|------------------------|---|---|---|
|                                  | A | B | AB | O |
| Complete mole                    | 29| 2 | 2  | 12|
| Partial mole                     | 8 | 3 | 6  | 12|
| Invasive mole                    | 1 | 0 | 0  | 0 |
| PSTT                             | 0 | 0 | 0  | 1 |
| Choriocarcinoma                  | 0 | 0 | 0  | 1 |
| Total                            | 38| 05| 08 | 26|
| Percentage                       | 49.35% | 6.50% | 10.40% | 33.75% |

Table 5: Histopathological diagnosis of mole

| Histopathological diagnosis       | No. of patients | Percentage |
|-----------------------------------|-----------------|------------|
| Complete mole                     | 43              | 57.34%     |
| Partial mole                      | 31              | 41.33%     |
| Invasive mole                     | 01              | 1.33%      |
| Total of 75                       | 100%            |            |
Majority of the patients belonged to the age group 20-25 years, with 44 (57.14%) cases, followed by 25 (32.47%) cases in the age group of 25-30 (Figure 2). Least 03 (3.90%) cases were found in the age group less than 20 years. The youngest case encountered were two 19-year-old females whereas the oldest was 38 years.

In our study, majority of GTD was seen in primigravida comprising of 34 (44.16%) cases, followed by 22 (28.57%) cases in G2, 15 (19.48%) cases in G3, 04 (5.9%) cases in G4 and 02 (2.60%) in more...
than G4. There was a single case of G9 noted in the present study (Figure 3).

**GTD and clinical presentation**

In our study, out of 77 cases of the GTD, the majority were 73 (94.80%) patients, presented with PV bleeding and 71 (92.20%) patients presented with amenorrhoea. 48 (62.35%) cases presented with lower abdominal pain. Hyperemesis gravid arum reported in 08 (10.14%) cases, 05 (6.50%) cases gave a history of passing grape-like vesicles while 02 (2.60%) patients had hyperthyroidism that came with complaints of sweating, palpitation and tachycardia (Table 3, Figure 4).

ABO Blood grouping and GTD: Blood groups were noted in all cases of GTD (Table 4).

**Beta hCG levels and GTD**

Following table showing beta hCG level among all cases. It ranged from 65340 to 6114780 mIU/ml with mean being 267837.40 mIU/ml. Out of 77 cases, majority 41 (53.25%) cases, had pre-evacuation Beta hCG levels between 50000-1,00,000 mIU/ml, followed by 34 (44.15%) cases having Beta hCG levels between 1,00,000-5,00,000 mIU/ml. 02 (2.60%) cases showed Beta hCG levels more than 5,00,000 and below 10,00,000 mIU/ml (Figure 5 and Figure 6).

**Histopathological diagnosis and molar pregnancy**

All cases were diagnosed with microscopically and classified. Following table is showing the classification of molar pregnancies (Table 5).

In our study, the diagnosis of gestational trophoblastic disease was made based on clinical presentations, serum Beta hCG levels and the diagnosis was confirmed by histomorphology. Out of 75 cases of hydatidiform mole, 43 (57.34%) showed histomorphological features of complete hydatidiform mole. 31 (41.33%) were partial hydatidiform mole, and 1 case of invasive mole (1.33%) was observed in the present study (Table 5).

In complete mole, villi were of various sizes, but all showed oedematous changes. The proliferating cytotrophoblast and syncytiotrophoblast showed circumferential growth from the villous surface. Mild to moderate degree of trophoblastic proliferation was noted. Out of 43 cases of complete hydatidiform mole, 41 (95.34%) cases demonstrated diffuse hydropic swelling of villi and circumferential trophoblastic proliferation. All 43 cases showed round smooth villous outline. 02 (4.65%) cases of early complete hydatidiform mole demonstrated focal trophoblastic proliferation without hydropic changes in villi.

Around 23 (53.48%) cases showed central cistern formation characterised by prominent central space that is an entirely acellular fluid-filled space within the centre of the villi. 36 (83.72%) cases out of 43 had myxoid intervillous stroma, 02 (4.56%) had hydropic intervillous stroma, and 05 (11.62%) cases showed both myxoids as well as the hydropic stroma. Only 13 (30.23%) cases showed intermediate trophoblasts. Only 08 (18.60%) cases showed trophoblastic inclusion.

Focal proliferations of cytotrophoblast and syncytiotrophoblast cells were seen in all 31 cases of partial mole. Trophoblastic hyperplasia is less marked, focal and consists of small tufts of trophoblast. All 31 cases of the partial mole had scalloped outline of the enlarged villi invaginations into the villous stroma. 27 (87.09%) cases showed trophoblastic inclusions. Central cisterns are less conspicuous and present in 04 (12.90%) cases out of 31 of partial mole.

In the present study, an invasive mole was diagnosed in a 28 year, multipara. Her pre-operative Beta hCG levels were 128000mIU/ml. Her blood group was positive. This was seen in a total hysterectomy specimen measuring 10.5cm x 8cm x 4.5cm in a multiparous woman, Small grape-like vesicles measuring 4cm x 3.5cm seen within the endometrial cavity. It was seen invading up to serosa, but uterus was non-ruptured. Many small vesicles were adhering to the endometrial cavity.

Hysterectomy specimen was measuring 10cm x 5.5cm x 4.5cm. The tumour was well-circumscribed, polypoidal, projecting into the uterine cavity. Cut a section of the tumour was soft, tan-grey-brown. Focal areas of haemorrhages and necrosis were noted (Figure 7).

Microscopically it showed proliferation of intermediate trophoblastic cells. The monomorphic population of polypoidal intermediate cells arranged in sheets having hyperchromatic nuclei and eosinophilic to pale cytoplasm (Figure 8). No infiltration of muscle fibres by chorionic villi. Vascular invasion was also noted.

**CONCLUSION**

Prevalence of hydatidiform mole was higher among all entities of gestational trophoblastic disease. Primigravida presenting with abnormal vaginal bleeding must be evaluated for GTD. Histomorphological features of complete hydatidiform mole differ from partial mole according to trophoblastic proliferation, villous contours, scalloping borders and central cisterns. Multi-centred studies are required.
in India to determine the true incidence and overall outcome of gestational trophoblastic diseases that will help in understanding the burden of disease. Follow-up of such patients is a challenging task. But the diagnosis and follow-up of these patients is essential for early detection of malignant trophoblastic diseases and to reduce the mortality rate.

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**Conflict of Interest**
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