Research Article

Gestational trophoblastic diseases: An institutional experience

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Abstract

Objective: To determine the frequency, pathological aspects, clinical presentation and management outcomes of Gestational trophoblastic diseases **Study Design**: Descriptive case series **Place and Duration**: Department of Pathology, NRI Medical college, Chinakakani, Mangalgiri. **Patients and Methods**: The case records of all the gestational trophoblastic diseases during one year study period were analysed regarding the clinical illness, history, pathological findings, clinical examination, investigations, treatment and the follow up. The main outcomes were measured in terms of duration, antecedent pregnancy, investigations, treatment and follow up. **Results**: There were a total of 100 patients presenting with different female genital tract neoplasia at NRI hospital during one year study period, including 27 (27%) cases of GTD. Hydatidiform mole was seen in 23(85.18%) patients of which Complete mole in 12 (52.17%) and partial mole in 11 (47.8%) patients, invasive mole in1 (3.703%) patient, epithelioid trophoblastic tumour in 1(3.703%), placental site trophoblastic 1(3.703%) and choriocarcinoma in 1(3.703%) patients. The mean age of the patients was 22 years. The highest incidence was found in para 1. Twenty four patients (86.9%) had suction evacuation and three patients (13.04%) underwent hysterectomy. Patients received chemotherapy, 17(73.91%) patients followed protocol for 3–6 months. **Conclusion**: Frequency of trophoblastic disease was high in this series compared to world literature. Therefore, emphasis should be on the early diagnosis of disease as proper management in the early stages strongly influences the outcome of disease. Histopathology proved to be gold standard in diagnosis. Suction evacuation and follow – up are ideal treatments for Benign trophoblastic disease.

Keywords: Trophoblastic disease, malignancy, management, surgery, chemotherapy.

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INTRODUCTION

Gestational trophoblastic disease is a heterogenous group of diseases that includes partial and complete hydatidiform mole, invasive mole, choriocarcinoma and placental site trophoblastic tumour. In recent years, new entities like epithelioid trophoblastic tumour have been added[1]. The incidence of GTD varies in different parts of the world, for example, in Japan the incidence is 2/1000 deliveries, while in Malaysia the incidence of molar pregnancy and gestational trophoblastic neoplasia is 2.8/1000 and 1.59/1000 deliveries respectively[2,3]. Meanwhile, in North America, its incidence is reported up to 2.5/1000 pregnancies[4]. Highest incidence of 12.1/1000 deliveries is reported from Turkey[5]. The malignant potential of this disease is higher in South East Asia where it as high as 10-15% in comparison to 2-4% in the western countries[6]. GTD is characterized by the secretion of a distinct tumour marker, the beta-HCG. This condition is highly curable even in the presence of metastasis. The major well established risk factors for the disease are advanced maternal age and past history of GTD[7]. The predisposing factors include low socioeconomic status, dietary deficiency in protein, folic acid and iron. The exact aetiology of the disease is not known. But, the cytogenetic studies show the stronger genetical association. Common clinical presentations include vaginal bleeding in early trimester, uterus larger than gestational age and the absence of fetal parts after 20

weeks of gestation. Ultrasonography is a reliable non invasive tool for diagnosis of GTD in the clinical setting. Since this group of disorders is now one of the highly curable neoplasms, early diagnosis and prompt treatment is necessary. The rates of GTD are decreasing and survival has dramatically improved in different parts of the world[8,9]. The objective of this study was to find out the frequency, common presentation, histopathological findings, type of the GTD, extent of the disease, treatment modalities and the outcome in a cohort of local population.

PATIENTS AND METHODS

This descriptive case review was conducted at the department of Pathology, NRI Medical college from March 2014 to March 2015.The case records all these patients who were admitted with trophoblastic diseases and neoplasm were analyzed retrospectively regarding the age, parity, signs and symptoms, duration of previous treatment, histopathology, investigations, type of trophoblastic disease, type of surgical treatment, chemotherapy, follow up and mortality associated with this disease. All those patients having trophoblastic disease with elevated bHCG, ultrasonic and histopathological evidence of the disease were included in the study. However, histopathological findings were the gold standard for the diagnosis of GTD. Choriocarcinoma was diagnosed on the basis of clinical presentation of the patients as well as investigations which included X-ray chest having canon ball appearance along with routine test. Brain metastasis was detected through CT scanning of the patients. Patients having irregular bleeding per vagina without any evidence of trophoblastic disease were excluded.

RESULTS

There were total of 100 gynaecology admissions during the study period which included 27 cases (27%) trophoblastic diseases in which Hydatidiform mole was seen in 23 cases (85.18%). Mean age of patients was 22 years. Two were less than 20 years (7.40%) and two were above 30 years (7.40%) of age. Out of 27 patients, 25 patient (92.59%) were para one, while one (3.703%) was para four and another was para three (3.703%). The antecedent of pregnancy was hydatidiform mole in one (3.703%) patient. Hydatidiform mole was diagnosed in 23 patients(85.18%) of which complete mole in 12 cases(52.17%), partial mole in 11 cases(47.8%), invasive mole in 1 case (3.703%), choriocarcinoma in 1 cases (3.703%), placental site trophoblastic tumour in 1 case (3.703%) and epithelioid trophoblastic tumour in 1 case (3.703%). Out of these 27 patients, 24 patients (86.9%) underwent suction evacuation and only 3 cases (13.04%) underwent hysterectomy. Indication for hysterectomy was emergency presentation with heavy bleeding.3 Four (17.39%) patients received chemotherapy. Among them three (13.04%) received single drug therapy and only one (4.34%) received multiple drug therapy. Chemotherapy was given for 6 months. Among all the27 patients, 20 patients (86.9%) fully recovered and 3 patients (13.04%) died because of extensive disease (metastasing to brain). Follow up of the patients was carried out by clinical examination and investigations such as serum b HCG level, ultrasound examination and X-ray chest.

Table 1: Clinical presentation of cases (n=27 cases)

Symptoms	Number of cases	Percentage (%)
Bleeding per vagina	27	100%
Pain in lower abdomen	25	92.59%
Hyperemesis gravidarum	27	100%
Dyspnea	23	85.1%
Passage of moles	24	88,88%

Table 2: Distribution of age, parity and gestational period of cases (n=27 cases)

Age(in years)	Number of cases	Percentage (%)
< 20 yrs	2 cases	7.40%
20-30 yrs	23 cases	85.18%
>30 yrs	2 cases	7.40%
Parity status		
0-1	25 cases	92.59%
2-4	1 case	3.703%
>4	1 case	3.703%
Gestational status		
1-2 months	13cases	48.14%
2-5 months	12cases	44.44%
>5 months	2 cases	7.04%

DISCUSSION

Gestational trophoblastic disease encompasses a unique group of uncommon but interrelated conditions derived from placental trophoblasts, with a wide range of histological appearances and clinical behaviours[10]. In vitro models for human trophoblasts were initially established more than three decades ago from isolated choriocarcinomas[11]. They have proven to be extremely valuable for the study of cellular, molecular and endocrine aspects of human trophoblasts. Molecular analysis can determine the nuclear DNA origin of complete hydatiform mole and allow us to define the patients with higher risk of malignant transformation usually to gestational choriocarcinoma[12,13]. This kind of trophoblast pathology has geographic differences in the expression[14]. The forms of TD have clinical manifestations that are not specific. There are principles especially histopathological examination which is taken into account, could help the clinicians put the right diagnosis.GTD has higher incidence in Asia[6]. This

frequency is also higher within our country if compared to hospital –based studies from Peshwar and Karachi[15,16]. The reasons for high frequency of GTD in this study might be the fact that hospital is major referral centre with large catchment area. However, the high incidence in Asia is generally attributed to low socioeconomic status and malnutrition[17]. In this study disease was more common in the younger reproductive age group. It is consistent with studies in Singapore and Karachi[16,6]. Vaginal bleeding was the most common presenting symptom in this study and is also reported by other studies such as Kim and Zalel et al[19]. Another study conducted by Moodley et al have also reported the same findings[2]. Complete hydatiform mole showed early and uniform hydatid enlargement of villi in the absence of an ascertainable fetus or embryo, the trophoblast is consistently hyperplastic with varying degrees of atypia and villous capillaries are absent. Complete mole results from fertilization of an empty egg by two sperms (dispermy) with a duplicated haploid sperm 46XX /46XY and the product is entirely of paternal origin (Diandry). Trophoblastic neoplasia follows complete mole in 15 - 20% of cases[22,23]. In our study there were 12 cases of complete hydaditiform mole and 2 cases progressed to trophoblastic neoplasia. Partial hydaditiform mole demonstrate identifiable fetal or embryonic tissue, chorionic villi with focal edema that vary in size and shape, scalloping and prominent stromal trophoblastic inclusions, and a functioning villous circulation, as well as focal trophoblastic hyperplasia with mild atypia only. Less than 5% of partial moles will develop postmolar GTN; metastases occur rarely and a histopathologic diagnosis of choriocarcinoma has not been confirmed after a partial mole[24,25]. Partial mole results from fertilization of a viable egg by two sperms (dispermy= paternal extra chromosome) 23XX +46X/Y= 69XXY.In our study there were 11 cases of partial hydatiform mole none progressed to trophoblastic neoplasia. Invasive mole is a benign tumour that arises from myometrial invasion of a hydatidiform mole via direct extension through tissue or venous channels. Approximately 10-70% of hydatidiform moles will result in invasive mole and about 15% of these will metastasize to the lungs or vagina. Invasive mole is diagnosed clinically rather than pathologically based on persistent hcg elevation after molar evacuation and is frequently treated with chemotherapy with or without a histopathologic diagnosis[26]. There was a single case of invasive mole diagnosed histopathologically and presented with metastasis to lung and vagina. Placental site trophoblastic tumour is an extremely rare disease that arises from the placental implantation site and consists predominantly of mononuclear intermeidiate trophoblasts without chorionic villi infiltrating in sheets or cords between myometrial fibers. PSTT is associated with less vascular invasion, necrosis and hemorrhage than choriocarcinoma and has propensity for lymphatic metastasis. We had a single case of placental site trophoblastic tumour. Choriocarcinoma is a malignant disease characterized by abnormal trophoblastic hyperplasia and anaplasia, absence of chorionic villi :hemorrhage and necrosis, with direct invasion into the myometrium and vascular invasion resulting in spread to distant sites, most commonly to lungs, brain, liver, pelvis, vagina, kidney, intestines and spleen. Immunohistochemistry shows positivity for Cytokeratins and Beta HCG. We have a single case of choriocarcinoma. Epthelioid trophoblastic tumour is recently described unusual type of trophoblastic tumor that is distinct from placental site trophoblastic tumour and choriocarcinoma. It resembles a carcinoma. A tumour is composed of a monomorphic population of intermeidiate trophoblastic cells resembling those of chorionic laeve(membranous chorion). On immunohistochemistry show positivity for Cytokeratin (AE1/AE3, cytokeratin 18), Epithelial membrane antigen, E-Cadherin, Epidermal growth factor receptor and Inhibin alpha. Hyperemesis gravidarum was found in100 % of patient. The cause is unknown but it could be because of high level of human chorionic gonadotrophin. The diagnosis of trophoblastic disease was based on clinical and histopathological features, bHCG, ultrasonography especially by using high resolution vaginal ultrasonography that can diagnose the disease much earlier. Choriocarcinoma is potentially fatal disease but current management protocol has turned the prognosis highly favourable. We had a single case of choriocarcinoma which was diagnosed on histopathology and prompt treatment helped in survival. Izhar from Peshawar has also reported cure rate of 80%. Similar to other studies, in this study, majority of patients with molar pregnancy were treated with suction curettage twenty four patients (86.9%) and only 3 patients(13.4%) needed hysterectomy; one had invasive mole and other had persistent bleeding per vagina, after evacuation, were treated with single drug chemotherapy. The duration of treatment ranged from 3-6 months with three doses of chemotheraphy till the serum Bhcg level was undetectable One patient died and main reasons of death in this patients was extensive disease (metastasizing upto brain) and poor general health.

CONCLUSION

In this series, frequency of GTD was higher compared to national and international literature. The disease was common in low para women. Patients with regular follow up recovered fully while mortality was associated with

complications, delay in recovery and receiving no proper treatment. Histopathology proved to be Gold standard in diagnosis. Proper management in the early stages strongly influences the outcome of the diseases. Hence, emphasis should be given to detect the disease in its early stage to decrease the mortality and morbity from the condition.

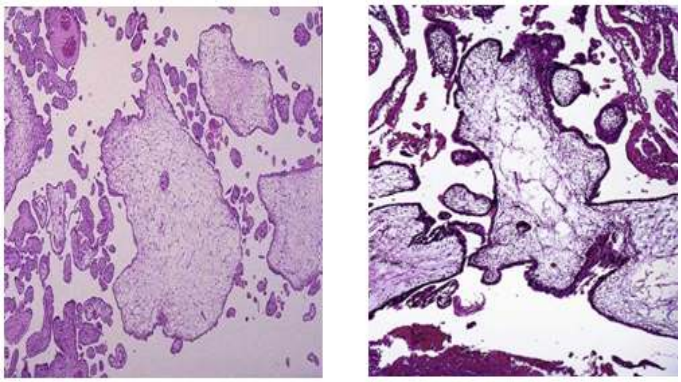

Figure 1: Partial mole hpe 100X (scalloping of villi and partial trophoblastic activity)

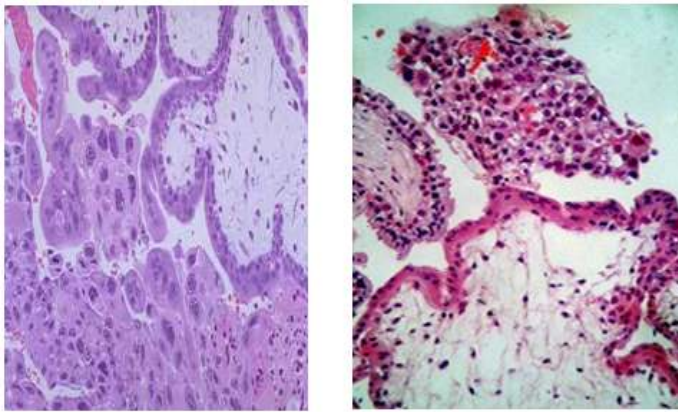

Figure 2: Complete mole hpe 400X &100X (circumferential trophoblasic activity)

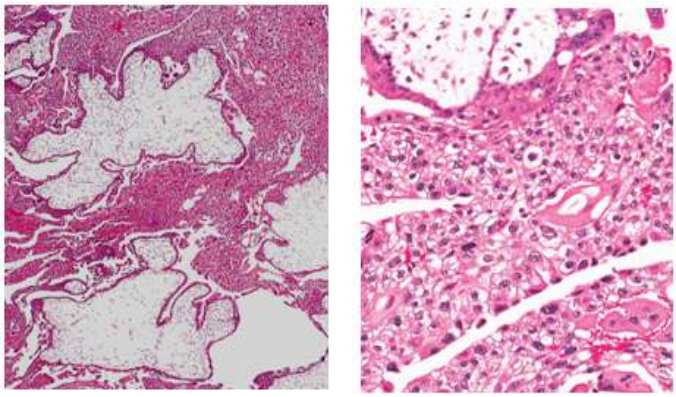

Figure 3: Complete mole hpe 100x &400 xs

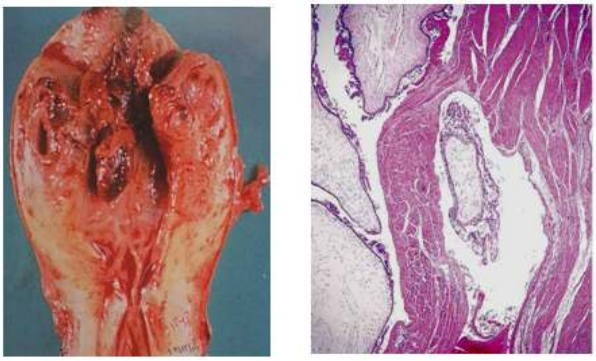

Figure 4: invasive mole gross & hpe x100 (Villi invading myometrium)

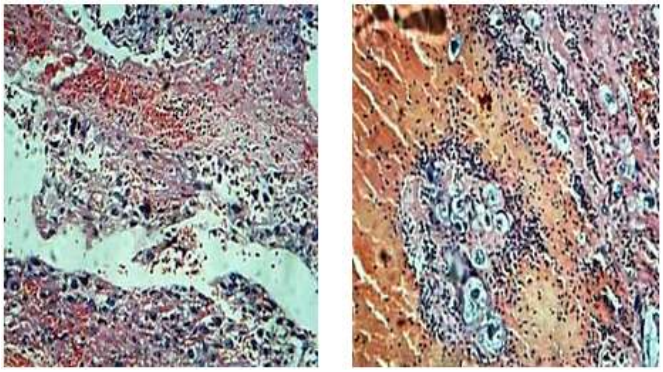

Figure 5: Choriocarcinoma microscopy hpe x 100& x 400 (Extensive areas of necrosis and hemorrhage)

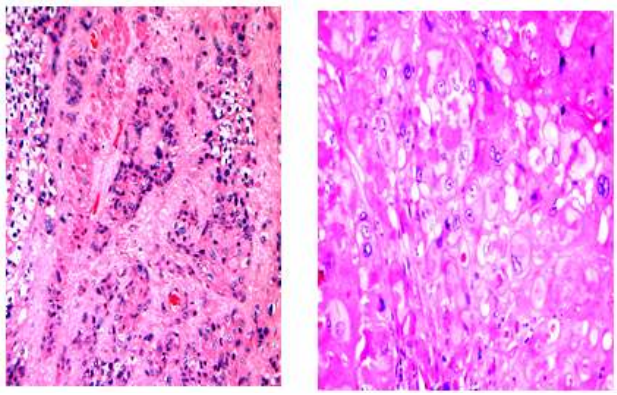

Figure 6: Epithelioid trophoblastic tumour HPE X100 & X 400

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