OUTCOME OF TREATMENT OF GESTATIONAL TROPHOBLASTIC DISEASES IN HMC

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ABSTRACT

Objective: The objective of this study is to know the prognosis of the patients turning up in the tertiary care hospital with Gestational trophoblastic disease.

Method: This was a descriptive study done on patients with gestational trophoblastic disease presenting in the Gynae-A Unit of Hayatabad Medical Complex Peshawar, between January 2009 to December, 2010, diagnosed on the basis of clinical course and elevated level of HCG. Metastatic evaluation of the disease was done to assign different risk groups to the patients before selecting appropriate chemotherapy regimen for each patient. Results of the therapy were monitored by serial estimation of HCG levels. A questionnaire was developed on which the data was transferred from the patient charts.

Results: There were a total of 1030 obstetric admissions during the study period, which included 34 cases of trophoblastic disease. Hence, frequency of GTD was 1 per 45 live births. Of these 23 cases, 19 (82.6%) patients had hydatidiform mole and 4 patients had malignant trophoblastic disease. Eight patients (34.7%) received chemotherapy while rest of the patients had suction evacuation and follow-up.14 patients (40%) were low risk and 20 (60%) were high risk cases. EMA-CO (Etoposide, Methotrexate, Actinomycin-D, Cytocine, Oncovine) regimen was administered to all patients. Among all patients, 32 (91.3%) fully recovered and 2 (8.69%) died because of extensive disease/ metastasis. Overall cure rate was 96% (4 patients survived out of 5 at two years' follow-up).

Conclusion: Prognosis of gestational trophoblastic disease is favourable provided the appropriate therapy is administered early in the course of disease. Provision of free medical care should be considered for these patients to save their lives.

Keywords: trophoblastic disease, malignancy, management, chemotherapy, prognosis.

INTRODUCTION

Gestational Trophoblastic Disease (GTD) is a heterogeneous group of diseases that includes partial and complete hydatidiform mole, invasive mole, choriocarcinoma and placental site trophoblastic tumor. In recent years, new entities like epithelioid trophoblastic tumor have alsobeen added.[1] A study in Finland done by Loukovaara et al (2001) revealed that, broad variations in the incidence of gestational trophoblastic diseases have been reported in different parts of the world. The incidence, for example, in Japan, 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 is as high as 10-15% in comparison to 2-4% in the western countries.[6] GTD is characterised by the secretion of a distinct tumor 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 a past history of GTD.[7] The predisposing factors include low socioeconomic status, dietary deficiency in protein, folic acid and iron. The exact etiology of the disease is not known. But, the cytogenic studies show the stronger genetically association. Common clinical presentations include vaginal bleeding in early trimester, uterus larger than gestational age and absence of fetal parts after 20 weeks of gestation. The availability of ultrasonography and quantitative measurement of hCG levels now allows earlier diagnosis. Symptoms are more likely to be dramatic with complete mole than with a partial mole.[8]

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.[9,10] The objective of this study was to find out the frequency, common presentation, type of the GTD, extent of the disease, treatment modalities and the outcome in a cohort of local population.

METHODOLOGY

This descriptive case review was conducted at the Gynae-A Unit of Hayatabad Medical Complex Peshawar from January 2009 to December 2010. The

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case records of all those patients who were admitted with trophoblastic disease and neoplasm were analyzed retrospectively regarding the age, parity, district of residence, investigations, type of trophoblastic disease, FIGO risk scoring, chemotherapy, follow-up and mortality associated with this disease. Allthose patients having trophoblastic disease with elevated bHCG and ultrasonic or histopathological evidence of the disease were included in the study. Metastasis was detected through CT scanning. Patients havingirregular bleeding per vagina without any evidence of trophoblastic disease were excluded. The main outcomes were measured in terms of duration of antecedent pregnancy, investigations, treatment, mortality and follow-up. Data was analyzed by using Epi Info software program.

RESULTS

There were a total of 1180 obstetric admissions during the study period which included34 cases of trophoblastic disease. Hence, the incidence of the disease was 34/1180 pregnancies or the frequency of GTD was 1 per 3

5 live births in this study. Most of the patients belonged to the extreme of ages;5 (15%) were less than 20 years and 22(64%) were between 20-40 years and

Table- 1: Age of Patients

No.	Age	pts.	%age
1	<20	5	15
2	20-30	12	35
3	30-40	10	29
4	>40	7	21
	Total	34	100

Table-2: Parity status of patients

No.	Parity	pts.	%age
1	0-1	15	44
2	2-4	6	17.5
3	4-6	8	23.5
4	>6	5	15
	Total	34	100

Table-3: Geographical distribution

No.	Area	pts.	%age
1	Peshawar & surr.	9	26
2	North KPK	4	12
3	South KPK	3	09
4	Punjab	1	03
5	FATA	7	20.5
6	Afghanistan	8	23.5
	Total	34	100

Table-4: Type of disease

No.	Type	pts.	% age
1	H. Mole	25	73.5
2	Invasive mole	6	17.5
3	Choriocarinoma	3	09
	Total	34	100

Table-5: Prognostic scoring

No.	FIGO score	pts.	% age
1	<6	16	47
2	>6	18	53
	Total	34	100

Table-6: antecedent pregnancy and start of chemotherapy

No.	Interval in months	pts.	%age
1	<4	6	17.5
2	5-8	18	53
3	8-12	4	12
4	>12	6	17.5
	Total	34	100

Table-7: Complications of Chemotherapy

No.	Complications	pts.	%age
1	Nausea, vomiting, anorexia	34	100
2	Alopecia	18	53
3	Stomatits	17	50
4	Bone marrow depression	7	21

Table-8: Outcome of treatment

No.	Indicator	pts.	%age
1	Patients who survived at two years follow up	32	94
2	Patients who died	2	6
	Total	34	100

Table-9: b-HCG level at start of treatment.

No.	HCG level (miu/l)	pts.	%age
1	<50,000	5	15
2	50,000-100,000	20	59
3.	>100,000	9	26
	Total	34	100

7(21%) wereabove40 years of age.

Out of 34 patients, 15 (44%) were Paraone, while 39% were Para 4 and above.

The patients turning up at HMC were mostly from Afghanistan i.e. 23.5%. 20.5% were from FATA, 26% from Peshawar and its surroundings while 19%

were from the northern and southern districts of Khyber Pakhtunkhwa. The frequency of patients therefore does not show an exact estimate of the incidence and prevalence of this disease in Peshawar city.

The antecedent of pregnancy was hydatidiform mole in 14(60.86%) patients, abortion in 7 (30.43%) and full-term pregnancy in 2 (8.69%) patients. The gestational period in 14(60.86%) patients was between 2-5 months, in 5 (21.7%) patients it was between 1-2 months and in only 2 (8.69%) patients, it was more than 5 months.

Hydatidiform mole was diagnosed in 25(73.5%) patients, invasive mole in 06(17.5%) and choriocarcinoma in 03 (09%).

Out of 23 patients, 21 underwent surgical treatment. In 19 (82.6%) patients, suction evacuation was done and only 2 (8.69%) cases underwent hysterectomy. Fourteen (63.63%) patients received no adjuvant therapy.

According to the FIGO scoring method 16(47%) were less than 6 score i.e. low risk while the other 18(53%) were diagnosed as high risk patients.

All 34 patients received chemotherapy. Among them, 6 (75%) received single drug therapy and only 2 (25%) received multiple drug therapy. Chemotherapy was given for 3-6 months. Common complications associated with chemotherapy were nausea, vomiting, weight-loss (100%), alopecia (53%), stomatitis (50%) and bone marrow depression (21%).

Among all the 34 patients, 32(94%) fully recovered and 2 (6%) died because of extensive disease (metastasizing up toliver and lungs).

Follow-up of the patients was carried out by clinical examination and investigations such as serum bHCG level, ultrasound examination and X-ray chest. Initially, it was carried out monthly, then after every 3 months till the bHCG level was undetected. In patients having benign hydatidiform mole, the serum bHCG level was undetectable within 3 months period.

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 behaviors.[11] In vitro models for human trophoblasts were initially established more than three decades ago from isolated choriocarcinoma.[12] They have molecular and endocrine aspects of human trophoblasts. Molecular analysis can determine the nuclear DNA origin of complete hydatidiform mole and allow us to define the patients with higher risk of malignant transformation usually to gestational choriocarcinoma.[13] This kind of trophoblastic pathology has geographic differences in the expression.[14] The clinicians often fail to consider the possibility of trophoblastic disease due to its low incidence rate. The forms of TD have clinical manifestations that are not specific. There are principles, which taken into account, could help the clinicians put the right diagnosis.

GTD has high incidence in Asia.[15] In this study, its frequency was 1 per 35 live births, which is quite significant. This frequency is also higher within our country if compared to hospital-based studies from Peshawar.[16] and Karachi.[17] The reasons for the high frequency of the GTD in this study might be the fact that the hospital is a major referral Centre with large catchment area. However, the high incidence in Asia is generally attributed to low socioeconomic status and malnutrition.[18] Dietary etiology is not supported by conclusive data.

In this study, disease was more common in the extreme of reproductive ages. It is consistent with the findings of studies from Karachi.[19] Antecedent pregnancy in invasive mole was hydatidiform mole while in choriocarcinoma both the patients had full-term pregnancy one year back. Vaginalbleeding was the most common presenting symptom in this study and it is also reported by other studies such as Zalel et al.[20] Hyper emesis gravidarum was found in 17.3% of patients. Hyper emesis gravidarum is a multifactorial disease. The cause is unknown but it could be because of high level of human chorionic gonadotropin.

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. Ultrasonography and serum bHCG are the sensitive detectors of trophoblastic disease. These tests are simple, non-invasive, and inexpensive and yield quick result. Ultrasound is the modality of choice for evaluating normal or abnormal first trimester pregnancy. When the monographic appearance is correlated with the clinical presentation, accurate diagnosis is possible in most cases of GTD. Sonography and Doppler imaging are helpful in diagnosing gestational trophoblastic disease, in determining whether invasive disease is present, in detecting recurrent disease, and in following the effectiveness of chemotherapy.[21] Most of patients in this study were having hydatidiform mole while 18% were having malignant trophoblastic disease in the form of choriocarcinoma and invasive mole. Choriocarcinoma is a potentially fatal disease but current management protocol has turned the prognosis highly favorable. Izhar[22] 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, i.e. 82.6% and only 2 patients needed hysterectomy; one had invasive mole and other had persistent vaginal bleeding, which did not settle with evacuation and chemotherapy. The patients with malignant trophoblastic disease were treated with multiple agent chemotherapy and those patients who had increased serum bHCG or those with persistent bleed-

ing per vagina, after evacuation, were treated with single drug chemotherapy. The duration of treatment ranged from 3-6 months with three doses of chemotherapy till the serum bHCG level was undetectable. One patient who had extensive malignant trophoblastic disease was in poor general health and unfit for chemotherapy so he received only symptomatic treatment. Overall complete cure was achieved in 91.3% patients in this study. However, 2 patients (8.69%) died during therapy. Main reasons of death in these patients were extensive disease (metastasizing up to 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 and grand multiparous women. Patients with regular follow-up recovered fully while mortality was associated with complications, delay in recovery and receiving no proper treatment. 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 morbidity from this condition.

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