PROGNOSIS OF GESTATIONAL CHORIOCARCINOMA AT KHYBER TEACHING HOSPITAL PESHAWAR

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Background: Choriocarcinoma is a highly malignant tumour which originates in developing trophoblast of pregnancy, most commonly following molar pregnancy. It is a potentially fatal disease, but current management protocols have turned the prognosis highly favourable. **Methods:** This study was done on patients with gestational choriocarcinoma presenting to Gynae-B unit of Khyber Teaching Hospital Peshawar, between May, 1996 to December, 1997, 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. **Results:** During this period 5 patients of choriocarcinoma were treated. In 2 (40%) cases choriocarcinoma developed after molar pregnancy whereas in 3 (60%) cases antecedent pregnancy resulted in spontaneous abortion. Four (80%) patients were from poor socioeconomic class, 3 (60%) were above 39 years of age and 4 (80%) were multiparous. Two patients (40%) were medium risk and 3 (60%) were high risk cases. There was no patient with low risk disease. EMA-CO (Etoposide, Methotrexate, Actinomycin-D, Cytocine, Oncovine) regimen was administered to all patients. Maximum number of cycles of chemotherapy given was 8. Only one patient developed drug resistance. Overall cure rate was 80% (4 patients survived out of 5 at two years' follow-up). **Conclusion:** Prognosis of gestational choriocarcinoma 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.

Key words: gestational choriocarcinoma, prognosis, chemotherapy.

INTRODUCTION

Choriocarcinoma is a highly malignant tumour which originates in developing trophoblast. It most commonly follows molar pregnancy, but may ensue after any gestational event and therefore usually occurs in young women in their reproductive years[1]. It is a potentially fatal disease, but availability of different diagnostic aids like Radiology, serum Human Chorionic Gonadotrophin (HCG) and unique sensitivity of tumour to chemotherapy has turned the prognosis highly favourable. It is one of the rare human malignancies that is highly curable even with wide spread metastasis[2]. Prognosis of gestational choriocarcinoma largely depends upon early diagnosis of the disease, comprehensive metastatic workup, selection of appropriate regimen of chemotherapy from outset and carefully planned follow up.

The frequency of the disease is estimated as 1 in 30,000 pregnancies in the West and 1 in 11,000 pregnancies in Oriental communities[3]. Preceding factors in 50% are hydatidiform mole, normal pregnancy in 40% and abortion or ectopic pregnancy in 5%, while the remaining 5% are of non gestational origin. Patients may present with vaginal haemorrhage, abdominal or vaginal swelling, amenorrhea and chest symptoms (due to metastases)[3].

Gestational Trophoblastic Tumours (GTT) are unique in that they may follow a normal or an abnormal pregnancy and almost always contain only paternal genes; as such they are considered to an allograft in the maternal host[4]. A few postmolar choriocarcinomas are biparental, and are considered to represent 'new pregnancies' or 'choriocarcinoma *ab initio*' that has long been proposed[5]. The term Gestational Trophoblastic Disease (GTD) is used to describe the situation where a woman has had a hydatidiform mole and still has persistently raised human chorionic gonadotrrophin (HCG) levels.

MATERIAL AND METHODS

A study was carried out in the Gynaecology B unit, Khyber Teaching Hospital Peshawar for 20 months to assess the frequency of the disease in this setting and the prognostic outcome of management protocols being followed there.

The study includes all patients with gestational choriocarcinoma presenting to Gynaecology B unit from May 1996 to December 1997. On admission detailed history was obtained from each patient and thorough clinical examination was performed including general, systemic and pelvic examination. Diagnosis of choriocarcinoma was mainly based on clinical course of the disease (history, abnormal vaginal bleeding, adnexal masses) and elevated levels of serum b-HCG. Evaluation of metastatic disease was done by thorough clinical examination and set of investigations including chest radiography and ultrasound scan of abdomen and pelvis. Computed tomography of skull was done in one patient. Other investigations included blood cell counts, blood groups of patient and husband, liver function tests and renal function tests. Patients were assigned low, medium and high risk groups according to the prognostic scoring system suggested by WHO in1983 (Table-1).

Table 1: WHO Scoring System based on prognostic factors[1]

	Score			
Prognostic Factors	**0**	**1**	**2**	**4**
Age (years)	<39	>39		
Antecedent Pregnancy	Hydatidi-form Mole	Abortion	Term	—
Interval*	4	4–6	7–12	12
hCG (IU/l)	$<10^3$	10^3–10^4	10^4–10^5	$>10^5$
ABO groups female × male	—	O × A A × O	B AB	—
Largest tumour including uterine tumours	—	3–5 Cm	>5 Cm	—
Site of metastases	—	Spleen Kidney	GIT, Liver	Brain
Number of metastases identified	—	1–4	4–8	>8

Prior Chemo-therapy	—	—	Single Drug	Two or more

The total score for a patient is obtained by adding the individual score for each prognostic factor.

Total score: ≤4 =low, 5–7 =middle risk, ≥8=high risk.

*time interval (months) between end of antecedent pregnancy and start of chemotherapy.

Patients were managed in consultation with the oncologist. All patients were put on EMA-CO regimen after counselling the family. Therapy was monitored by serum concentration of b-HCG, which was estimated fortnightly. Chemotherapy with EMA-CO regimen (Table-2) was given cyclically until complete remission was attained. Patients were vigilantly observed for adverse effects of chemotherapy (vomiting, diarrhoea, liver function, bone marrow depression and alopecia) and supportive treatment was given. Radiotherapy was used only to treat the complications like vaginal haemorrhage. Emotional support was given to the patient and family.

Table 2: EMA-CO Regimen[1]

Course 1 EMA	
Day 1	Actinomycin D 0.5 mg IV stat Etoposide 100 mg/m^2 in 200 ml normal saline over 30 minutes Methotrexate 300 mg/m^2 IV 12 hours infusion
Day 2	Actinomycin D 0.5 mg IV stat Etoposide 100 mg/m^2 in 200 ml normal saline over 30 minutes Folinic acid 15 mg *per os* or IM BD for 4 doses starting 24 hours after the start of Methotrexate
5-day drug-free interval to course 2	
Course 2 CO	
Day 1	Vincristine 1.0 mg/m^2 IV stat (maximum 2.0 mg) Cyclophosphamide 600 mg/m^2 IV infusion over 20 minutes
6-day drug-free interval	

RESULTS

During the 20 months of study 5 patients of choriocarcinoma were detected and treated. Most of the patients (80%) belonged to poor socioeconomic class, one was from middle class and none from high class. The age ranged between 20-42 years, and 60% were above 39 years of age (Table-3).

Table-3: Age of patients (n=5)

Age in years	Number of patients	Percentage
20–39	2	40%
40 and above	3	60%

Out of 5 patients, 4 were multiparous and in only one patient first pregnancy resulted in hydatidiform mole followed by choriocarcinoma. Antecedent pregnancy was hydatidiform mole in two patients (40%) while in remaining 3 (60%) choriocarcinoma was preceded by spontaneous abortion.

None of the cases had localized disease (Table-4). Two patients (40%) had vaginal metastasis, 2 patients (40%) had lung deposits and in one patient disease was widespread with metastasis in lung, vagina, liver and brain (detected by computed tomography of skull).

Table-4: Sites of Metastasis (n=5)

Site	Number of patients	Percentage
Lungs	2	40%
Vagina	2	40%
Widespread (lung, liver, vagina, brain)	1	20%

The b-HCG level was estimated prior to and during chemotherapy. In all patients it was more than 200 IU/L, prior to therapy.

Patients were categorized as low, medium and high risk cases. There were 2 (40%) patients in medium risk group and 3 (60%) in high risk group (Table-5).

Table-5: Prognostic scoring of patients (n=5)

Category	Number of patients	Percentage
Low risk	Nil	—
Medium risk	2	40%
	3	60%

High risk		

Time interval between end of antecedent pregnancy and onset of chemotherapy was recorded. It was less than 4 months in one patient, between 4–7 months in 3 (60%) patients, and in one patient it was more than 12 months (Table-6).

Table-6: Interval between Antecedent Pregnancy and Chemotherapy (n=5)

Interval (months)	Number of patients	Percentage
Less than 4	1	20%
5–8	3	60%
9–12	Nil	—
more than 12	1	20%

Chemotherapy (EMA-CO) was administered to all patients. Radiotherapy was not used as primary treatment, but it was given to 2 patients who developed massive vaginal haemorrhage. No patient was treated with surgical resection.

All the patients had nausea, vomiting, anorexia; three developed alopecia. Bone marrow depression occurred in one patient. No other adverse effects were seen (Table-7).

Table-7: Complications of Chemotherapy (n=5)

Complications	Number of Patients	Percentage
Nausea, Vomiting, Anorexia	5	100
Alopecia	3	60
Bone Marrow Depression	1	20

Only one patient died. Survival rate was 80% (Table-8).

Table-8: Outcome of chemotherapy (n=5)

Patients who received chemotherapy	Patients died	Patients survived at two years follow up
5	1 (20%)	4 (80%)

DISCUSSION

We received 5 cases over the study period of 20 months. Our study showed a frequency of gestational choriocarcinoma that is probably higher than that seen in western countries. Possible reasons for this may be that we receive patients from Afghanistan and large parts of North-West Frontier Province (NWFP) of Pakistan, both of which are medically and socio-economically backward areas. Most of our patients belonged to poor socioeconomic class. Higher frequency of choriocarcinoma in this deprived group may be related to poor nutrition. There is increased incidence of gestational trophoblastic disease (GTD) in the women who consume less meat[6]. Association with dietary deficiencies was also reported by Berkowitz *et al* who noted the progressively increasing incidence of GTD with decreasing level of dietary carotene and animal fat[7]. We found that most of the patients affected by choriocarcinoma were multiparous women and were above 39 years of age. Abnormal ovulation and fertilization in older women may predispose to choriocarcinoma[8]. Knowledge of antecedent pregnancy is important because prognosis depends upon it. Choriocarcinoma most commonly follows molar pregnancy, but in our study in 3 out of 5 patients it followed spontaneous abortion. However 2 of these patients were referred from other hospitals and though they were labelled as abortion, no details of clinical findings or histopathology of conceptus were available. This shows that some times these cases are mismanaged by general practitioners causing delay in diagnosis and management and therefore influencing prognosis. Time interval between antecedent pregnancy and onset of chemotherapy is a crucial factor influencing the prognosis.

It is apparent from the above study that all patients with choriocarcinoma are potentially curable provided the appropriate therapy is given early enough in the course of the disease. In our study 80% patients attained complete remission and they survived with out any morbidity at two years' follow up period. This shows cure rate of 80% which is similar to those achieved in other studies. Lewis reported a cure rate of 80% with the regimen of Etoposide, Methotrexate, Actinomycin-D, Cyclophosphamide and Vincristine sulfate[9].

We had one refractory case, who did not respond to chemotherapy and died within 4 months of diagnosis. This patient had widespread disease at the time of presentation. Wang *et al* mention a case which was not responding to multiple regimens (EMA-CO, EMA-PE, BEP), after which she responded to VIP (Etoposide, Ifosfamide and Cisplatin) regimen and was cured[10].

CONCLUSION

Gestational choriocarcinoma is not rare in our area. It is a life threatening disease but complete remission can be obtained in majority of patients by administration of appropriate chemotherapy from outset. Prognosis depends upon early diagnosis and management. Continued awareness and education is therefore required, so that choriocarcinoma developing after molar or non- molar pregnancy is detected as early as possible, thereby reducing the choriocarcinoma mortality rate.

Advanced maternal age is a poor risk factor regarding prognosis. Trend of large size families and pregnancy in women at the extremes of reproductive age should be discouraged by motivation and provision of effective family planning services.

As choriocarcinoma usually affects poor women, provision of free medical care should be considered for these poor patients to save their lives. These patients should always be managed by team of experts.

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