Gestational Trophoblastic Disease: Review of Cases Managed at B P Koirala Memorial Cancer Hospital

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Aims: This study was done to analyze the clinical presentation and management outcomes of gestational trophoblastic disease managed at B.P. Koirala Memorial Cancer Hospital, Chitwan, Nepal.

Methods: Descriptive study was conducted at B.P. Koirala Memorial Cancer Hospital. Case records of all gestational trophoblastic cases from January 2001 to December 2007 were analyzed regarding clinical details, investigations and treatment outcomes.

Results: Forty-five cases of 16 to 50 years (mean 29.1 years) had gestational trophoblastic disease, among which 19 (43%) were of Tibeto-Burmese and 15 (33%) Indo-Aryan ethnic group. Hydatidiform mole, invasive mole and choriocarcinoma were observed in 17 (37.8%), six (13.3%) and 22 (48.8%) cases respectively. In seven cases (15.5%) molar pregnancy had occurred in primigravida, seven cases (15.5%) had previous molar pregnancy and in 16 (35.5%) cases GTD had occurred following abortion. Vaginal bleeding was the commonest presentation and 26 (57.8%) cases had anaemia. Eleven (24.5%) cases had theca luteal cyst, 17 (37.8%) had lung metastasis and 4 (8.9%) had brain metastasis. Chemotherapy was administered in 34 (75.5%) cases, among which 15 (33.3%) received single agent and 18 (40%) received multiagent chemotherapy. Hysterectomy was done in nine (20%) cases. Brain irradiation was done in a case with brain metastasis. Five (11.2%) cases with high WHO risk score left the hospital against medical advice. There were three (6.6%) mortalities. Thirty-seven (72.1%) cases were in remission and follow-up.

Conclusions: Early diagnosis of disease and proper management strongly influences the outcome of GTD. Even in disseminated state GTD can be cured.

Keywords: chemotherapy, choriocarcinoma, molar pregnancy, gestational trophoblastic disease.

INTRODUCTION

Gestational trophoblastic disease (GTD) represents a spectrum of histologically distinct pathologies including molar pregnancy, invasive mole, placental site trophoblastic tumour and choriocarcinoma. Invasive mole, placental site trophoblastic tumour and choriocarcinoma grouped as gestational trophoblastic tumours (GTT) has been referred to as "God's first cancer and man's first cure".[1] Prior to 1956, GTT treatment usually involved surgical removal of the primary or metastatic lesions or perhaps radiotherapy. The treatment failure occurred in metastatic disease with fatal outcome in almost all patients.[2] In 1956, at Maryland, the first patient with metastatic choriocarcinoma was cured by methotrexate.[3]

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The incidence of GTD in Japan and Mexico were 2/1000 and 2.5/1000 pregnancies respectively are three times higher than in Europe or North America (0.6 – 1.1/1000 pregnancies).[4,5] The malignant potential of GTD is also higher in South Asia (10-15%) compared to western countries (2-4%).[6] It is undetermined whether such differences are attributable to genetic characteristics or to shared cultural factors.[7]

The primary treatment of molar pregnancy is suction curettage, while that of choriocarcinoma is chemotherapy. Surgery is required in some patients.[8]

This study tried to explore the epidemiology, management and outcome of patients with GTD in Nepal.

METHODS

This review was conducted at B.P. Koirala Memorial Cancer Hospital, Chitwan, Nepal from January 2001 to December 2007.

The case records of all the gestational trophoblastic diseases during the study period were analyzed regarding their identification, illness history, clinical examination, investigations, treatment and follow-up. The main outcomes were measured in terms of age, ethnicity, duration, parity, antecedent pregnancy, histopathology, investigations, treatment, follow-up and mortality associated with this disease. All the patients having trophoblastic disease with elevated ß-hCG, radiological or hispathological evidence of the disease were included in the study. Choriocarcinoma was diagnosed on the basis of histopathology or clinical presentation along with raised level of serum ß-hCG and metastatic lesions detected by radiological examination. Statistical analysis was done using descriptive statistics: mean, range and standard deviation.

RESULTS

A total of 45 cases of gestational trophoblastic diseases (GTD) from 26 districts of Nepal received during the study period. There were 17 cases (37.8%) of hydatidiform mole, six of invasive mole (13.3%), four of persistent gestational trophoblastic tumour (8.9%) and 22 patients (48.8%) of choriocarcinoma (Table 1).

Table 1. Classification of GTD observed (n=45).

GTD Type	Number	Percentage
Hydatidiform Mole (n=17)		
Complete Mole	12	26.6
Partial Mole	1	2.2
Persistent GTT	4	8.9
Choriocarcinoma (n=22)		
HPE proven	8	17.8
↑ Serum ß-hCG and positive radiology	14	31.0
Invasion Mode	6	13.3

The age of the patients ranged from 16 to 50 with a mean age of 29.1 years (SD 9.4 years). The highest percentage of GTD, 51.2% (n=23) was observed in 21 – 30 years and choriocarcinoma was more common (56.5%) in this age group. Magar women constituted 24.4% (n=11) of the GTD with higher percentage (54.4 %, 6/11) of malignant progression as well. Nine-teen (43%) belonged to Tibeto-Burmese ethnic group and 15 (33%) to Indo-Aryan ethnic group. Malignant sequelae in Tibeto-Burmese and Indo-Aryans were 52.6 % and 46.5% respectively.

The gestational period at presentation in 32 (71%) cases was between two to five months, in 12 (26.6%) cases it was less than two months and only in one (2.2%) case it was more than five months (Table 2).

Table 2. Distribution of age, parity and gestational age at presentation (n= 45).

Characteristics	Number of Cases	Percentage
Age		
< 20 years	8	17.8
21 – 30 years	23	51.2
31 – 40 years	6	13.2
> 40 years	8	17.8
Parity		
1	7	15.5
2	11	24.5
3	10	22.3
≥ 4	17	37.7
Gestational age		
1 - 2 months	12	26.6
2 - 5 months	32	71.2
> 5 months	1	2.2

In seven cases (15.5%), molar pregnancy had occurred in the first conception; another seven cases (15.5%) had previous molar pregnancy and 16 (35.5%) cases of GTD had occurred following abortion (Table 3).

Table 3. Antecedent pregnancy (n=45).

Obstetric History	H. Mole	Invasive Mole	Choriocarcinoma	Total
Primigravida	4	1	2	7
Spontaneous abortion	2	-	1	3
Induced abortion	4	1	8	13
Molar pregnancy	4	-	3	7
Ectopic pregnancy	-	-	1	1
Term pregnancy	3	4	7	14
Total	17	6	22	45

The most common presenting symptom was vaginal bleeding (82.2%) and 26 (57.8%) patients had anaemia. Twenty-six (62%) cases had uterus large for date, in 10 cases (24%) uterine size corresponded with gestational age and six cases (14%) had uterus small for date.

Fifty percent cases of molar pregnancy had ultrasonographic picture of snow storm pattern. Theca leuteal cyst was detected in 11 (24.4%) of the cases. Seventeen (37.8%) cases had lesions in chest X-ray, suggestive of lung metastasis which was further confirmed by CT scan among which only six (13.3%) presented with haemoptysis. Four (8.9%) cases had clinical features of cerebral involvement and CT scan of brain detected the metastatic lesions. Disseminated disease was detected radiologically in 7.5% (3/40) of the cases.

Suction evacuation and follow-up with serial serum ß-hCG was the mainstay of treatment in molar pregnancy. Of 45 cases, 29 (64.4%) had already undergone suction evacuation elsewhere and another six (13.3%) were treated with suction evacuation only. Nine (20%) underwent hysterectomy for invasive mole (n=6) and complications like uterine perforation (n=1) and excessive hemorrhage (n=2).

Final histopathology, WHO modified risks score and the results of serum ß-hCG guided adjuvant treatment. The risk scoring was done taking into consideration: age, antecedent pregnancy, interval of antecedent pregnancy, serum ß-hCG level, largest tumour size, number of metastasis and prior chemotherapy. Cases with total score from 0 to 6 were regarded as low risk and ≥ 7 high risk. Based on the above criteria, 22 (48.8%) cases fell in low risk and 23 (52.2%) cases fell in high risk group. Low risk group requiring chemotherapy received single agent and high risk group received multi-agent chemotherapy. Adjuvant chemotherapy was administered in 34 (75.5%) cases among which 15 (33.3%) underwent single agent chemotherapy with methotrexate; 18 (40%) underwent multiagent chemotherapy with EMA-CO regimen and only 1 (2.2%) high risk score case underwent MAC regimen. Chemotherapy was given until serum ß-hCG was negative or below normal value and then after continued for a further two to three cycles. One case required second-line chemotherapy with EMA-EP regimen. A case with brain metastasis required brain irradiation and intrathecal methotrexate. Single agent methotrexate resulted 86.6 % (13/15) complete remission after 3 to 8 cycles. Complete remission was obtained after 4 to 10 cycles of multiagent EMA-CO regimen in 73.7% (14/19) of cases.

Five (11.1%) cases with disseminated disease and high WHO risk score left the hospital against medical advice. There were three (6.6%) mortalities and remaining 37 (82.2%) of the cases were in remission and follow-up (Table 4).

Table 4. Treatment and outcome (n=45).

Treatment Modality	Number (%)
Surgical	
Uterine suction evacuation	35 (64.4%)
Abdominal hysterectomy	9 (20%)
Surgical resection (nephrectomy)	1 (2.2%)
Chemotherapy	34 (75.5%)
Single agent (MTX+FA Regimen)	15 (33.3%)
Multi-agent (EMA-CO, MAC Regimen)	20 (44.4%)
Complete Remission (CR)	37 (82.2%)
Left against medical advice (LAMA)	5 (11.2%)
Mortality	3 (6.6%)

DISCUSSION

This study revealed more cases of GTD among Tibeto-Burmese ethnic group with higher incidence of malignant sequelae as well which is similar to observation made in Hawaii study where higher incidence of GTD and metastatic disease was observed among East Asian countries (Japan, Philippines).[9] The highest frequency of GTD observed among 21 – 30 years in the study was reported as significantly lower incidence in the other study.[9] However, mean age is consistent with other studies.

With regards to etiological factors, nulliparity was associated with molar pregnancies in several studies.[8, 10] But, in present study less percentage of women had GTD in the first pregnancy. Previous history of hydatidiform mole is another well-established risk factor.[11] Seven (15.5%) of cases in our study had molar pregnancy in the past among which three were found to have metastatic disease. In 50 %, choriocarcinoma is preceded by hydatidiform mole; in 25 % it follows abortion or ectopic pregnancy and in remaining 25%, delivery of a normal fetus.[12] Similar risk factors were observed for choriocarcinoma.

Experience from England and the United States reveals that complete mole is being diagnosed earlier in gestational age.[4] A study done in Saudi Arabia showed that 50% of the patients are diagnosed during their first trimester and present infrequently with the classical signs and symptoms.[13] Majority (71%) of GTD in our study presented with 2-5 months of amenorrhea which is consistent with classical description but is not consistent with recent studies from US, England and Saudi Arabia.

Although there have been advances in development of effective chemotherapy to improve survival rate, surgery has crucial role in management of GTD. In family completed elderly patients, abdominal hysterectomy offers advantage

of simultaneous evacuation and sterilization. Additionally, hysterectomy has shown to reduce the risk of malignant sequelae to approximately 3.5% from 20% anticipated for patients treated with suction curettage.[8] Nine (20%) of our patients, with family complete, underwent hysterectomy mainly for invasive mole for the advantage of sterilization, reducing morbidity and also reducing malignant squeal.

Cure rates of 90-100% have been reported in patients with non-metastatic and low-risk metastatic disease if treated appropriately.[14-16] In cases having low risk score, single agent chemotherapy with methotrexate resulted 86.6% complete remission and in cases having metastatic disease and high risk score, EMA-CO resulted in 73.7% complete remission. Overall cure rate achieved in our study is slightly lower than that of other studies.

CONCLUSIONS

Gestational trophoblastic disease was more prevalent among young women of Tibeto-Burmese ethnicity with higher rate of progression into malignancy. Early diagnosis of disease and proper management strongly influenced the outcome of GTD and it is potentially curable even in disseminated state. The frequency of trophoblastic disease could not be obtained as our hospital is the national cancer hospital without obstetrical services. Thus, a larger multicentre study involving obstetrical department is required.

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