

## Choriocarcinoma - Varied Presentations

SN BEGUM

### Summary:

*Choriocarcinoma is a highly malignant tumour that originates in developing trophoblast of pregnancy. It is a potentially fatal disease but current management protocol has turned the prognosis highly favourable.*

*Gestational choriocarcinoma is not a rare disease in our country. Various mode of presentation sometimes makes it difficult to diagnose.*

*Eleven cases of choriocarcinoma were presented here along with treatment modalities and prognosis. Two patients expired during treatment while other respond well with chemotherapy. Early diagnosis and appropriate treatment have better prognosis.*

*(J Bangladesh Coll Phys Surg 2012; 30: 145-150)*

### Introduction:

Choriocarcinoma is a highly malignant epithelial tumour arising from the trophoblastic tissue of any gestational event.<sup>1</sup> It is a potentially fatal disease, but availability of different diagnostic aid (ultrasonogram, serum  $\beta$ -hCG) and its unique sensitivity to chemotherapy has turned the prognosis highly favourable.

It is one of the rare human malignancy which is completely curable even with wide spread metastasis<sup>2</sup>.

It has an incidence of 0.05 to 0.23 per thousand live births. 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.<sup>3</sup>

Preceding gestational events are hydatidiform mole (50%), term pregnancy (20%), non molar abortion (5%) and ectopic pregnancy (5%).<sup>4</sup>

Patients may present with irregular vaginal bleeding, amenorrhoea, abdominal or vaginal swelling or symptoms of metastasis like haemoptysis.<sup>4</sup> It can virtually spread anywhere in the body through haematogenous or lymphatic route. Most commonly it spreads to lungs (80%), lower genital tract (cervix, vagina, vulva), brain and liver.<sup>5</sup> It can spread to small bowel producing intestinal obstruction, renal mass with hematuria, splenic metastasis with intraperitoneal bleeding with severe anaemia.<sup>3,6,7,8</sup>

Gestational trophoblastic tumour always contain only paternal genes as such they are considered to an allograft in the maternal host.<sup>9</sup> A few postmolar choriocarcinomas are biparental, and are considered to represent 'new pregnancies' or 'carcinoma *ab initio*'.<sup>10,11</sup> Most of the choriocarcinoma patients belong to poor socioeconomic class and that may directly related to poor nutritional status.

The clinical presentation, treatment modalities and outcome of 11 cases of choriocarcinoma are discussed here.

### Methods:

This prospective study on 11 cases of choriocarcinoma with varied clinical features was undertaken in Sylhet MAG Osmani Medical college.

All data regarding clinical presentation, investigation and treatment with outcome was recorded meticulously for analysis.

### Result:

Sociodemographic characteristic of the patients were presented in Table I. Mean age of the patient were 33.39 yrs (range 18-46 yrs), among them six were > 40 years of age. 73.75% were multipara (n=8) out of which four were grandmulti. All but one belongs to poor social class. Blood group was O in seven cases while rest have A or AB group.

Time interval between antecedent pregnancy and diagnosis of disease varies from 3 months to 13 yrs. Antecedent pregnancy events were term pregnancy (n=5), abortion (n=5) and molar pregnancy (n=1) in this study.

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**Received:** 8 January, 2012

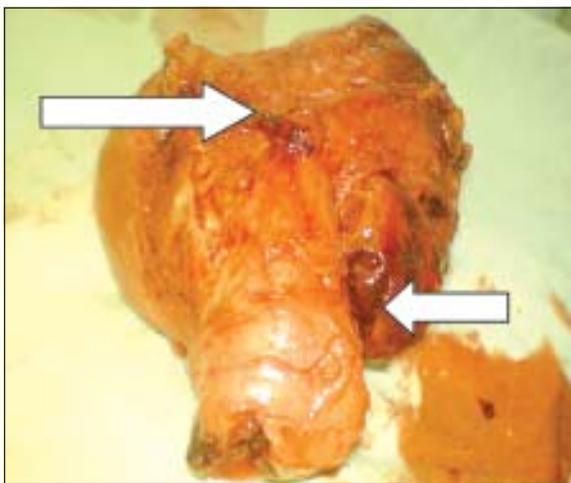
**Accepted:** 11 June, 2012

Clinical presentation was depicted in Table II. Irregular per vaginal bleeding was the common presentation in all case. Other clinical features were lower abdominal pain (case2,3,4,5,6), bleeding from vaginal growth (case1,8) and Shock (case1,4). Two patients (case 4,6) present with acute abdomen for internal haemorrhage needed emergency laparotomy. Uterus was enlarged (about 10-20cm. size) in seven cases due to myometrial involvement and misdiagnosed as fibroid uterus by ultrasonogram. Case 7 was diagnosed as cervical fibroid by USG. Serum  $\beta$ -hCG level varies from 412-15,00,000 miu/ml. Pulmonary metastasis was present in 7cases. Case 1 had metastasis in vagina, lungs and brain. Histopathology showing features of choriocarcinoma in 8 cases.

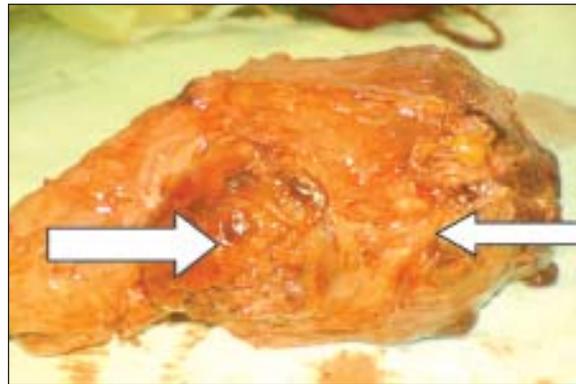
Regarding treatment 63.63% (n-7) patients had total abdominal hysterectomy (TAH) due to severe bleeding with extensive involvement of myometrium. Four patient had internal haemorrhage as the growth invade the uterine wall. Chemotherapy was given in 81.80% of cases. EMA-CO regime was given in six patient while three received MTX. Both surgery (TAH) and chemotherapy was needed in seven cases.

Regarding treatment outcome, seven had good recovery while two patient expired . Two patient lost to follow-up. Case no.6 expired suddenly on 2<sup>nd</sup> POD following TAH due to respiratory problem (? pul.embolism). Case no.8 having vaginal and pulmonary metastasis with high  $\beta$ hCG level, treated with surgery (TAH) and chemotherapy but the patient succumb suddenly on 7<sup>th</sup> POD.

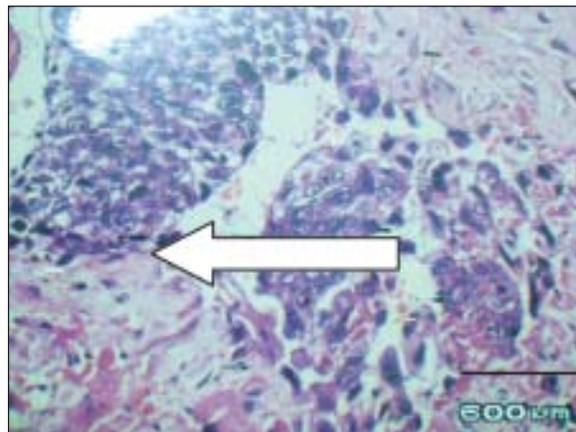
Autopsy examination was needed to confirm the cause of death in such cases.



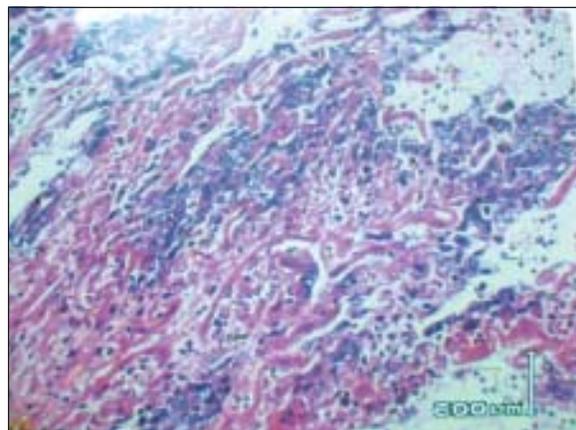
**Fig.-1:** Haemorrhagic growth in lat. and ant wall of ut.(case3)



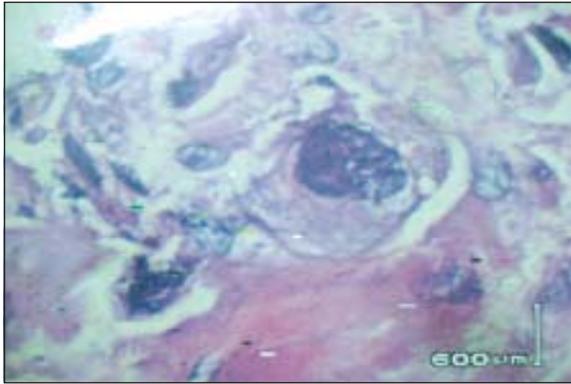
**Fig.-2:** Haemorrhagic growth (case4)



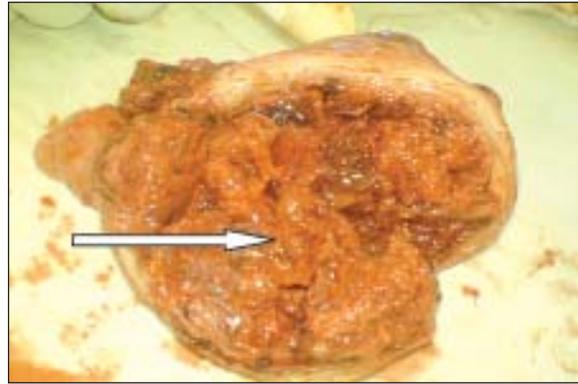
**Fig.-3:** Photomicrograph of choriocarcinoma(case4)



**Fig.-4:** Photomicrograph (low power) (case5)



**Fig.-5:** Photomicrograph (high power)(case5)



**Fig.-6:** Cut section of ut. showing growth(case-6) Fig.7 Growth in vagina.(case-8)

**Table-I**

<i>Sociodemographic profile of cases</i>						
Case no.	Age	Parity	Socioeconomic condition	Interval of preg. & disease	Antecedent pregnancy	Blood group
1	40	2+0	Poor	13yrs	Term preg.	O
2	20	0+1	Poor	1 yrs	H.Mole	O
3	40	7+0	Poor	7 yrs	Term preg	A
4	20	0+1	Poor	1.6yrs	Abortion	O
5	26	4+0	Poor	1.6yrs	Term preg	O
6	45	8+1	Poor	10yrs	Term preg.	O
7	18	0+1	Poor	3 month	Abortion	A
8	25	1+1	Poor	1yrs	Abortion	O
9	42	3+1	Poor	1.6yrs	Abortion	AB
10	45	10+1	Middle class	2.6yrs	Abortion	A
11	46	7+1	Poor	11 yrs	Term preg.	O

Table showing age of the patient were between 18-46yrs, parity 0-10, mostly following term pregnancy, majority were from poor class family, common blood group were O(OO) .

**Table-II***Management outcome of cases-*

Case no.	Clinical presentation	Metastasis	Investigations	Treatment	Outcome
1	PVB, Vaginal growth Shock,.	Vagina , Lungs, Brain	$\beta$ -hCG - 107,000 CXR-pul.matastasis SOL in brain	EMACO RT	good
2	Irreg. PVB, Severe LAP & mass abd.	myometrium	$\beta$ -hCG - 25,300 USG-Ut.growth (highly vascular)	MTX	good
3	PVB, LAP, mass abd. severe anaemia	Lungs, myometrium	$\beta$ -hCG - 30,500 USG-RPC/fibroid CXR-pul.matastasis Histopath.-chorio-ca	TAH, EMACO	Lost to follow up
4	PVB, mass abd. Acute abd., shock	myometrium	$\beta$ -hCG 89,425 USG- ut.mass . Histopath.-chorio-ca	TAH,EMACO	Good
5	PVB, LAP, Severly anaemia mass abd.	Lungs myometrium	$\beta$ -hCG - 41,600 CXR-pul.matastasis USG- ut.mass . Histopath.-chorio-ca	TAH, Refuse chemo	Lost to follow up
6	PVB, Acute abd. haemoptysis, anaemia	Lungs, myometrium	$\beta$ -hCG - 711 USG- ut.mas CXR-pul.matastasis Histopath.-chorio-ca	TAH	Expired
7	PVB, fever mass in cx,	Lungs, cervix	$\beta$ -hCG - 1,60,000 USG-Cx. Fibroid CXR-pul.matastasis	EMACO	Good
8	PVB, cough, resp. distress vag.growth	Lung s Vagina.	$\beta$ -hCG - 15,00,000 CXR-pul.matastasis. Histopath.-chorio-ca	MTX	Expired
9	PVB, Cough, resp.distress, wt. loss	Lungs, myometrium	$\beta$ -hCG – 422 USG- Ut,mass CXR-pul.matastasis. Histopath.-chorio-ca	TAH EMACO	Good
10	PVB Enlarged ut..	myometrium	$\beta$ -hCG - 64,000 USG- Ut.mass Histopath.-chorio-ca	TAH, EMACO	Good
11	PVB Enlarged ut	myometrium	$\beta$ -hCG - 107,640 USG- Ut.mass Histopath.-chorio-ca	TAH, MTX	Good

**Discussion:**

11 cases Choriocarcinoma were admitted and studied over a period of 20 months in Sylhet MAG Osmani Medical College Hospital. This study showed a higher frequency of gestational choriocarcinoma in this region.

Most of the patient were from poor socioeconomic class. Higher frequency of choriocarcinoma in this deprived group may be related to poor nutrition.

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. This correlates with the study in Pakistan where similar socioeconomic condition is prevailing<sup>12</sup>

In this study 73.75% (n=8) patients were multipara out of which four were grandmulti. Mean age of the patients were 33.39yrs (range 18-46yrs), among them six were >40yrs of age. Abnormal ovulation and fertilization in older women may predispose to choriocarcinoma. Knowledge of antecedent pregnancy is important because prognosis depends upon it. Choriocarcinoma commonly follows molar pregnancy. But in this study 5 patients had abortion, 5 had delivery at term & only one had molar pregnancy. However 3 of these patients labeled as abortion, no details of clinical findings or histopathology of conceptus were available. So this misdiagnosis causing delay in initiation of treatment and thus influence prognosis. In a study by RN Baergen *et. al* showed that age greater than 35 years, interval from antecedent pregnancy of >2 years, and prior term pregnancy were the significant prognostic factors.<sup>14</sup>

Haemoptysis in pulmonary metastasis frequently confused with tuberculosis which is common in our country making diagnosis late. Choriocarcinoma is a highly malignant neoplasm that metastasize readily to vagina, lungs, liver & brain. Rarely it can metastasize in intestine, spleen, kidney and lymph nodes.

In this study site of metastasis was lungs (n=7), vagina (n=2), brain (n=1) and cervix (n=1). Uterine myometrium was involved in 8 cases.  $\beta$ hCG level was high in 9 cases. Two patients (case 6,9) had low  $\beta$ -hcg (<100iu/L) presented with irregular p/v bleeding, uterine mass & pulmonary metastasis. Case 6 had emergency hysterectomy for severe intra-peritoneal haemorrhage but she suddenly expired on 7<sup>th</sup> POD (? pul. embolism). Case 9 also had hysterectomy &

chemotherapy. Both the cases were probably metastatic placental site trophoblastic tumour (PSTT) which is a variant of GTD. In PSTT exaggerated invasion of trophoblastic tissue in the myometrium necessitate treatment by hysterectomy. Metastatic PSTT need chemotherapy in addition to surgery.<sup>13</sup>

Intraperitoneal haemorrhage following spontaneous perforation of uterus may simulate ectopic pregnancy as in case 5. Rapid growth & haemorrhage makes the tumour a medical emergency. In this study, 63.63% (n=7) cases had total abdominal hysterectomy(TAH) which has similarity with the study by RN Baergen where hysterectomy with or without salpingoophorectomy was performed in 85% of cases. Five cases developed acute abdomen due to intra-peritoneal bleeding needed hysterectomy. 5 cases were treated with combined surgery and chemotherapy. Six patients received EMACO therapy and responded well. Two patients died suddenly probably due to pulmonary embolism.

Anatomical staging emerged as the most important prognostic factor. Other significant factors include interval from previous pregnancy, prior term pregnancy, high level, deep myometrial invasion, high mitotic rate, coagulation necrosis. Time interval between antecedent pregnancy and onset of chemotherapy is also a crucial prognostic factor. The number and size of metastasis will obviously influence the response, but the site is also important. Tumour involving the brain, liver and gastrointestinal tract have a poor response. The level of  $\beta$ hCG prior to starting of treatment is important in predicting the response to therapy. Patients with serum  $\beta$ hCG levels above 100,000 miu/ml have a poor response<sup>15</sup>.

**Conclusions:**

Gestational choriocarcinoma is not a rare disease in our country. It is a life threatening disease but complete remission can be obtained in majority of patients by appropriate chemotherapy.

Choriocarcinoma should be suspected when there is irregular uterine bleeding following hydatidiform mole, abortion or pregnancy. Prognosis depends upon early diagnosis and management. High index of suspicion and continued vigilance is required for early detection & treatment in order to reduce choriocarcinoma mortality.

These patients should be managed by team of experts. It is important to individualize treatment for GTN based

upon risk factor. Using less toxic therapy for low risk cases and aggressive multi agent therapy for high risk cases. As choriocarcinoma usually affects poor women, provision of free medical care should be considered to save their lives.

Advanced maternal age is a high risk factor regarding prognosis. Trend of large size families and pregnancy at the extremes of reproductive age should be discouraged by motivation and provision of effective family planning services. Development of Molar Card and its implementation is an essential step for follow up and early detection of post molar complications.

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