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Original Article

Outcome of Gestational Trophoblastic Neoplasia: Experience from a Tertiary Cancer Centre in India

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Abstract

Aims: Gestational trophoblastic neoplasms (GTN) comprise a spectrum of interrelated conditions originating from the placenta. With sensitive assays for human chorionic gonadotropin (β-hCG) and current approaches to chemotherapy, most women with GTN can be cured with preservation of reproductive potential. The purpose of this analysis was to address the outcome of GTN from a developing country, as data are largely sparse from this region.
Materials and methods: We undertook a retrospective review of GTN cases treated at our centre from 2001 to 2008. Patients of GTN were assigned to low-risk (score ≤ 6) or high-risk (score ≥ 7) categories as per the modified World Health Organization scoring system. The low-risk group was treated with single-agent methotrexate (MTX) and the high-risk group received the EMA/CO regimen. Salvage therapies were EMA/EP or BEP. Treatment was continued until serum β-hCG values were normal for three consecutive chemotherapy cycles, after which the patients were kept on follow-up.
Results: In total, 70 GTN patients were treated at our institution during this period; 48 (68%) were low-risk and 22 (32%) were in the high-risk category. The median β-hCG level was 50 000 IU/l. The lung was the most common site of metastasis, seen in 15 (21%) patients. Among 48 low-risk patients, 37 (77%) received chemotherapy, of whom 25 (68%) were treated with MTX and 24 (96%) achieved a complete response. Twelve low-risk patients (32%) received EMA/CO therapy; 10 (83%) achieved a complete response. The 22 high-risk patients received EMA/CO and of these 16 (73%) achieved a complete response, two (9%) progressed, two (9%) died of progressive disease and two (9%) were lost to follow-up. Grade 3/4 toxicities with MTX included mucositis in two (8%) and neutropenia in five (21%) patients. At a median follow-up of 16.6 months, overall survival in the low- and high-risk groups was 100 and 88.8%, respectively.
Conclusion: Risk-stratified treatment of GTN was associated with acceptable toxicity and resulted in outcome that was comparable with international standards.

Key words: Chemotherapy; choriocarcinoma; gestational trophoblastic neoplasia; treatment outcome

Introduction

Gestational trophoblastic neoplasia (GTN) encompasses a spectrum of disorders that arise from placental tissue [1]. GTN refers to patients with persistent or metastatic trophoblastic disease that requires the use of chemotherapy. Most women with GTN can be successfully treated with preservation of normal reproductive potential. GTN is a highly chemo-sensitive tumour that can be cured even in patients with advanced-stage disease. The reported 5 year overall survival for low-risk GTN is 100% [2] and for high-risk GTN 75–90% [3], in the presence of liver metastasis 27%, in the presence of brain metastasis 70% and with both brain and liver metastasis around 10% [4]. The data regarding the outcome of GTN from developing countries are scant. We report the clinical characteristics and outcome of consecutive GTN patients treated at our centre over an 8 year period.

Materials and Methods

The data were extracted by retrieving all case records of GTN patients registered during the study period. The abstracted information included history and examination

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findings; chest X-ray, pelvic ultrasound, computed tomography brain (if carried out), serum human chorionic gonadotropin (β-hCG) and histopathological evaluation of biopsy or curettage specimen, if available. Using this information patients were categorised as low risk or high risk (Table 1) according to the modified World Health Organization (WHO) scoring system [5]. Patients with a score of ≤6 were treated with methotrexate (MTX) at 1 mg/kg (50 mg maximum single dose) [2], given intravenously on days 1, 3, 5 and 7 with oral leucovorin 15 mg single dose on days 2, 4, 6 and 8. The cycle was repeated every 2 weeks. Serum β-hCG levels were measured once every week, including before the start of every chemotherapy cycle; any patient who had two static or one increasing value on treatment was defined as having drug-resistant disease. The latter patients were given multi-agent chemotherapy using the EMA/CO regimen (etoposide, methotrexate, actinomycin on day 1, cyclophosphamide and vincristine on day 8) [3]. Patients with a score ≥7 were classified as high risk and started on the EMA/CO regimen. Patients who failed the EMA/CO regimen were subsequently treated with EMA/EP (Etoposide, methotrexate, actinomycin on day 1, etoposide and cisplatin on day 8) [6] or BEP (bleomycin, etoposide and cisplatin) [7] regimens. Patients underwent a hysterectomy if there was no response to chemotherapy or if they had intractable bleeding not amenable to control by medical measures. Treatment was continued until β-hCG values were normal (< 5 IU/l) at the beginning of three consecutive chemotherapy cycles. After the last chemotherapy cycle, patients were kept on regular follow-up using regular β-hCG monitoring as per standard guidelines [8,9]. Specifically, β-hCG level was measured 6–8 weeks after the end of any future pregnancy to exclude disease recurrence [10,11]. Patients were also advised standard contraceptive measures [12]. The response to therapy was defined as follows: complete response as β-hCG values in the normal range for 3 consecutive weeks, a partial response as more than 50% decline in β-hCG levels compared with baseline, no response as less than 50% decline over baseline values and progressive disease as an increase of at least 25% in the size of any measurable lesion or appearance of any new lesion with increasing β-hCG levels. Recurrence was defined as elevation of β-hCG level after more than three normal values in the absence of a confirmed pregnancy [13].

Statistical Analysis

Clinical data were entered into Predictive Analytics Software (PASW, Version 18; Chicago, IL, USA). Overall survival was calculated using the Kaplan–Meier method.

Results

Of the 70 analysable patients, diagnosis was based on histopathological evidence in 30 (43%) and elevated β-hCG with history consistent with GTN in 40 (57%) patients. Table 1 shows the important characteristics of these patients, including stage and various elements of the WHO scoring system. In the low-risk category, nine patients (19%) had confirmed choriocarcinoma based on histopathology (five patients) or evidence of metastasis (lung metastasis in four patients). Sixteen (23%) patients were diagnosed with a

Table 1
Demographic and baseline characteristics and outcome

Patient characteristics	Low risk ≤ 6 ($n = 48$)	High risk ≥ 7 ($n = 22$)
Age (in years)		
<40	47 (98%)	21 (96%)
≥40	1 (2%)	1 (4%)
Diagnosis		
Choriocarcinoma	9 (19%)	22 (100%)
Invasive mole	8 (17%)	0
Vesicular mole	16 (33%)	0
GTN not classified	15(31%)	0
FIGO stage		
I	36 (75%)	0
II	7 (15%)	6 (27%)
III	5 (100%)	9 (41%)
IV	0	7 (32%)
Antecedent pregnancy		
Mole	33 (69%)	6 (27%)
Abortion	10 (21%)	10 (46%)
Term	5 (10%)	6 (27%)
Interval between pregnancy and chemotherapy (in months)		
<4	27 (56%)	3 (14%)
4–6	16 (33%)	6 (27%)
7–12	5 (11%)	5 (23%)
>12	0	8 (36%)
β-hCG (in IU/l)		
<1000	4 (8%)	1 (4%)
1000–10 000	12 (25%)	3 (14%)
10 000–100 000	17 (35%)	2 (9%)
>100 000	15 (32%)	16 (73%)
Site of metastasis		
Lung	4 (8%)	11 (50%)
Gastrointestinal	0	2 (9%)
Liver/brain	0	6 (28%)
Tumour size (in cm)		
<3	41 (85%)	12 (55%)
3–4	5 (11%)	2 (9%)
≥5	2 (4%)	8 (36%)
Number of metastasis		
0	42 (87%)	6 (27%)
1–4	4 (9%)	10 (45%)
5–8	2 (4%)	3 (14%)
>8	0	3 (14%)
Previous failed therapy		
None	40 (83%)	16 (73%)
Single drug	6 (13%)	4 (18%)
≥2 drugs	2 (4%)	2 (9%)
Surgery		
No	46 (96%)	16 (73%)
Yes	2 (4%)	6 (27%)
Response		
Complete response	36 (97.2%)	16 (72.7%)
Partial response	1 (2.7%)	0
Progressive disease	0	2 (9%)

β-hCG, human chorionic gonadotropin; FIGO, International Federation of Gynecology and Obstetrics; GTN, gestational trophoblastic neoplasia.