THE MANAGEMENT OF GESTATIONAL TROPHOBLASTIC TUMORS USING THE WHO PROGNOSTIC SCORING SYSTEM

LUBNA HASSAN, FARHAT NAHEED AND SHAFIQ AHMAD

Department of Gynaecology and Obstetrics,
Hayat Abad Medical Complex, Peshawar.

SUMMARY

In a prospective study all diagnosed cases of Gestational trophoblastic tumours (GTT) are placed in a risk group, low risk, medium risk, high risk using the WHO prognostic scoring system. Single agent or multiple agent chemotherapy is then commenced and the efficacy and safety evaluated. The second objective is to see if it is possible to manage these patients in a general gynaecological ward and to find constraints if any. Seven patients have so far received treatment in our unit acording to the new prognostic scoring system. Two wee in the low risk group and so received methotrexae and folinic acid rescue chemotherapy, one medium risk and four high risk. All responded well to therapy as judged by the regression in the beta DCG levels. Three patients have achieved a biochemical remission (cured) by first line chemotherapy. The treatment of the rest is ongoing. None had major side effects from the chemotherapy. None have so far developed resistance to the allotted chemotherapuetic regime.

INTRODUCTION

Gestational trophoblastic disease consists of a group of interrelated diseases, including molar pregnancy, placental site trophoblastic tumor and chorioncarcinoma. Chorioncarcinoma was the first tumor to be cured with chemotherapy even in the presence of distant and widespread metastases.[1] The modern management of gestational trophoblastic disease (GTD) has resulted in a cure rate in excess of 90%.[2-4] Important advances in the past include the standardization of terminology, the concept of the assignment of risk and the use of staging system, the centralization of care and the establishment of regional registries, and the development of the aradioimmunoassay for the beta subunit of human chorionic gonodotropin. Chemotherapy remains the mainstay of treatment. Single agent treatment with methotrexate was once the golden standard. This was replaced by the triple drug MAC regime, with which a 50% remission rate could be expected in high risk patients[5] This has now been replaced by methotrexate alone with folinic acid rescue in the low risk patient, the more elaborate regime for medium risk patients and the EMA CO regime for high risk patients with which a 70% remission rate can be expected and the patients can be assured of return to fertility.[5]

A note of caution regarding multi agent therapy is essential, however, with the recent reports in the literature regarding the association of secondary tumors with etoposide exposure[6] etoposide must only be given if indicated.

MATERIAL AND METHODS

All patients in the reproductive age group presenting at our unit with unexplained irregular bleeding following a pregnancy irregardless of the period of gestation or type of pregnancy, including molar pregnancy are requested a serum Beta

HCG level. Early detection of persistent trophoblastic tumors depends on careful post molar gonadotropin follow up and a high index of suspicion for consideration of the diagnosis in any woman of the reproductive age group with unexplained gynaecologic/ systemic symptoms. The diagnosis in our unit is based on the gonodotropic levels and not always on histology. The patients are assessed according to a standard protocol. Following a full physical examination, blood is analyzed for a full blood count, ABO grouping and biochemistry including liver and renal function tests. Beta hCG is assayed in serum initially and then prior to every treatment course. Chest X-Ray and ultrasound are performed on every patient. Computerized tomography and isotope scans are performed as and when required.

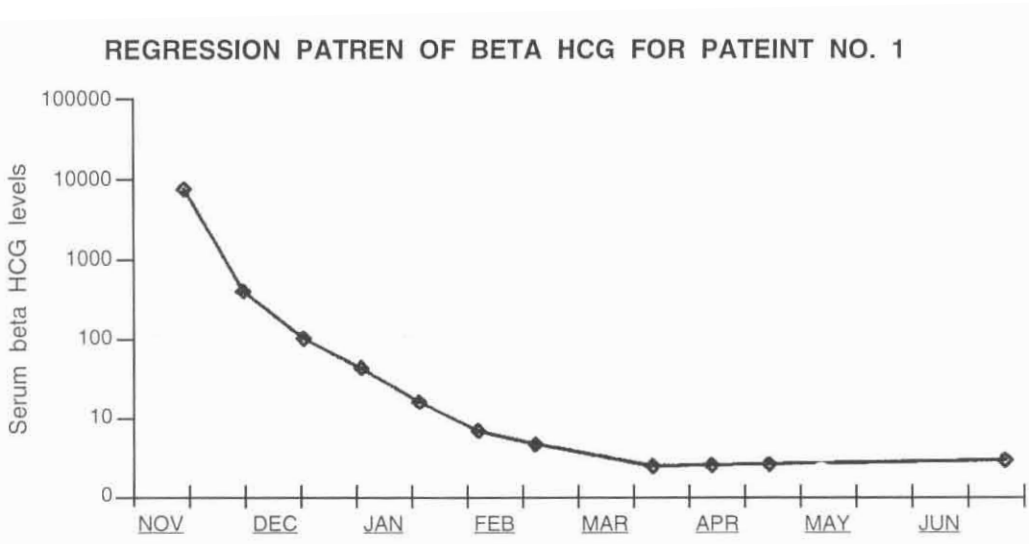
Once the diagnosis is made the prognostic criteria of the world health organization, as used in the department of OB/GYN at the Hayatabad Medical Complex assigns the patients to one of three risk groups depending on features such as age, antecedent pregnancy, the presenting level of hCG, blood group, the number, size and site of metastases, the size of the largest mass and the use of prior chemotherpay. High risk patients score > 9 points, while low risk patients score < 5 points. All patients are then treated, with single agent if in the low risk group and multiagent chemotherapy when in the medium and high risk, with curative intent.

Serial Beta hCG are done as a method for follow up. Three further treatment courses are given once the Beta hCG becomes undetectable. The patients are then followed up with monthly Beta HCG levels for six months and then twice over the next year. Contraception in the form of the oral contraceptive pill is prescribed. After one year of treatment those who desire to conceive are allowed to do so. Follow up by annual B hCG is life long.

TABLE – I

CLINICAL DETAILS OF PATIENTS

AGE (YEARS) (N=7)	
• ≤ 39	4
• > 39	3
ETHINIC GROUP	
• Pathans (Pakistan)	5
• Afghans	2
BLOOD GROUP	
• O	4
• A	1
• B	2
• AB	0
PARITY	
• Nulliparous	2
• 1 – 3	2
• ≥ 4	3
ANTECEDENT PREGNANCY	
• Term	1
• Non Molar abortion	4
• H. mole	2
INTERVAL BETWEEN PREVIOUS PREGNANCY & GTT	
• < Months	2
• 4 – 6 Months	2
• 7 – 8 Months	2
• > 12 Months	1
BETA HCG LEVELS	
• < 1000	0
• 1000 – 10,000	2
• 10,000 – 100,000	1
• > 100,000	3
EXTENT OF DISEASE	
• With metastasis	2
• Non metastatic	5
PRIOR CHEMOTHERAPY	
• No prior chemotheapy	6
• Single agent	0
• Multiple agent	1



RESULTS

Seven patients have so far received treatment in our unit according to the prognostic scoring system. Table-I shows demographic and clinical feature of these cases. Two in the low risk group and so received methotrexate ad folinic acid rescue chemotherapy, there was one in the medium risk and four in the high risk group. All responded well to therapy as judged by the regression in the beta HCG levels (fig-I). Beta HCG decay curves are plotted for each patient. The beta HCG decay curves convey useful information of the chemosensitivity of the tumor, and may assist in determining the time required for treatment and early changes in treatment for determining the time required for treatment and early changes in treatment for the chemoresistant tumor.[7] Three of our patients have achieved a biochemical remission (cured) by first line chemotherapy. Two suffered moderate and one severe myelotoxicity which necessitated a delay in treatment. Both the single agent group have completed their treatment and are now enrolled for follow up. Two patients had severe life threatening hemorrhage one from vaginal secondaries, and the other a nulliparious 22 year old had profuse uterine bleeding. The bleeding from the vaginal secondaries was arrested by stitches, the uterine bleeding was arrested by an evacuation of the uterus which alone was not enough to arrest the bleeding and since preservation of fertility was a major concern in this case, internal iliac artery ligation was performed. She successfully completed her chemotherapy without any further bleeding. Hemorrhage is a serious complication and arresting it may be a problem.

Two patients had vaginal metastasis, which had resolved by the fourth treatment course in both cases. One patient had metastasis in both lungs which have significantly reduced by the sixth course.

All the patients suffered nausea and anorexia that lasted through treatment course. Most of them had at least one complication that necessitated postponement of a course of treatment.

DISCUSSION

Important advances have been made in the diagnosis and management of gestational trophoblastic tumors (GGT) over the last decade. The patients are in the prime of life and early diagnosis is possible due to a highly reliable tumor marker. In our unit we have radically changed our management

and as detailed in the methods. Our experience has shown that our policy of nursing these patients in the same ward has had a very positive effect on the moral of the patients. They tend to exchange notes and new arrivals feel very encouraged by the progress of the earlier patients. We do not have the facility to barrier nurse during treatment to reduce the chances of infection, but we have not had any serious problems with cross infection.

One of our greatest constraints has been financial. The drugs, the long term follow up and investigations are not subsidized by the government. The patients are all from very poor backgrounds. We have so far been able to get the necessary funds from donations. Neutropenaia invariably occurred wit the EMA-CO regime in all our patients on the regime. A novel strategy to combat the occurrence of neutropenia has been tried by Hartenbach and co workers. They describe the treatment schedule.[9] The addition of G-CSF to the EMA-CO regimen may benefit patients by achieving dose intensity in the treatment of high risk gestational trophoblastic disease.

We have not encountered any resistant cases but ours is admittedly a very small series. About 25% of women with high risk metastatic disease become refractory to EMA-CO and fail to achieve a complete disease become refractory to EMA-CO and fail to achieve a complete remission.[10] Currently there is no standard salvage chemotherapeutic agent for EMA-CO failure however high dose chemotherpay consisting of etoposide, carboplatin, and ranimustine (MCNU), which can penetrate the blood brain barrier, followed by autologous bone marrow transplantation (ABMT) appears to be quite effective in cases that present with relapsing multiple brain metastases.[11] Taxo (Paclitaxe) has been shown to be a potent inhibitor of cell growth for a variety of tumors. Marth cultured human chorio-carcinoma cells and treated them with Taxol. He found that Taxol is a highly effective antineoplastic agents in chorio-carcinoma cells.[12] Taxol has been used in the treatment of resistant cases of chorio-carcinoma with significant response.[13]

CONCLUSION

The multiple chemotherapy used in our unit according to the WHO criteria is, as recorded previously in the literature, effective and safe. Our new protocol for treating GTT requires commitment from the staff and greater vigilance, but we have found it feasible in a general gynecological unit. Our greatest constraint is finances as the drugs are expensive and all seven patients are from the low socio-economic strata. There is an urgent need to centralize care for these patients that would result in better diagnostic surveillance, treatment modalities and essential follow-up.

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