GESTATIONAL TROPHOBLAST NEOPLASIA-GYNAECOLOGICAL & NON GYNAECOLOGICAL MODES OF PRESENTATION: REQUIRING RECOGNITION BY CLINICIANS OF MULTIPLE DISCIPLINES

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ABSTRACT

Objective: To analyze the modes of presentation of Gestational Trophoblast Neoplasia(GTN) in our set up and raise awareness among clinician of all disciplines about wide range of symptoms and clinical findings of these rare but highly curable gynaecological malignancies.

Study design: Rertospective cohort study

Place& duration of study: From June 2005-June 2014 at Department of obstetrics & gynaecology, Hayatabad Medical Complex, Peshawar, Pakistan.

Materials & methods: 90 patients with diagnosis of GTN were included in the study. After staging work up patients were assigned figo risk score and given chemotherapy accordingly. Patients demographic profile, age, parity, antecedent pregnancy, serum β-hCG levels, site of metastasis, type of chemotherapy, were recorded on performa and computerized record was kept.

Results: In 90 patients diagnosed with GTN. 73(81.1%) patients were aged less than 40 years with 20(22.2%) patients being nullipara. Antecedant pregnancy was mole in 50(55.6%) patients. Serum β-hCG level was between 10,000-100,000 IU/ml in 34(37.8%) & >100,000IU/ml in 27(30%) patients . 43(47.8%) patients presented with complaints of P/V bleeding.13(14.4%) cases presented with pain abdomen while post evacuation rise of β-hCG was seen in 12 (13.3%) patients. Hemoptysis was seen in 4(4.4%), cough& breathlessness in 4(4.4%) and paresis/convulsion in 2(2.2%) cases.

Conclusions: Gestational trophoblast neoplasia are rare but highly curable malignancies. High index of suspicion required in case of unexplained systemic pulmonary, neurological ,genitourinary symptoms in women of reproductive age group.

Key words: Gestational Trophoblast Neoplasia(GTN), Choriocarcinoma, FIGO Risk Score.

INTRODUCTION

Gestational trophoblastic disease (GTD) is comprised of a spectrum of conditions, each of which is characterised by low incidence and high cure rates. The diagnosis range from the generally benign, pre-malignant partial and complete molar pregnancies to the malignant invasive mole, choriocarcinoma, placental site trophoblastic and epithelioid trophoblastic tumours (PSTT/ETT). The malignant forms are often referred to as gestational trophoblastic neoplasia (GTN). Choriocarcinoma develops in around one in 50,000 deliveries and PSST accounts for 0.2% of GTN in UK.[1]

Most commonly, GTN is diagnosed following molar pregnancy with rising (β-hCG), but it can also occur after any gestation including miscarriages and term pregnancies. Any form of GTN can metastasize and the most common metastatic site is lung (80%) followed by vagina (30%), brain and liver (10%).[2,3]

The most frequent presentation is with vaginal bleeding which can be severe, either from a mass within the uterus or from vaginal metastases. Pulmonary involvement may cause cough, dyspnoea, hemoptysis and pleuritic chest pain due to pulmonary infarction or pleural space invasion. Intra-abdominal metastases can produce intra-peritoneal bleeding, malaena and severe pain, whilst neurological manifestations may include headaches, seizures, loss of consciousness and hemiplegia.[4,5]

As a result of the broad range of presentations, clinicians should be alert to the possibility of cho-

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riocarcinoma in any a woman of child-bearing age with central nervous system symptoms, postpartum cerebrovascular accidents or evidence of a metastatic cancer of unknown origin. In all of these cases, a simple laboratory serum hCG measurement may be life-saving, as even in advanced cases with cerebral metastases the expectation is cure with effective treatment.[6,7]

Patients with molar pregnancies make up the large majority of the cases of GTN and approximately 10% of them will require additional therapy following uterine evacuation. The patients who develop malignancy after a molar pregnancy should rarely prove difficult to treat and in areas with well organised care overall cure rates approaching 100% are reported[8,9]. Unfortunately an approach of 'no structured follow up' is still the case in many areas of the world including ours and in these settings patients re-present with more advanced GTN with a variety of symptoms including severe haemorrhage, anaemia and lung metastases. In this situation the diagnosis of GTN after the evacuation relies on the patient's presentation and investigation by their primary care physician The optimal care of patients with these rare conditions relies on effective team working between obstetricians, gynaecologists, physicians, radiologists, pathologists, oncologists, nurses and an effective post molar pregnancy follow-up team. This management approach clearly leads to diagnosis with more advanced cases and potentially less favourable outcomes.[4]

The objective of our study was to analyze the modes of presentation of GTN in our set up and raise awareness among clinician of all disciplines about extremely wide range of symptoms and clinical findings of these rare but highly curable gynaecological malignancies.

MATERIALS & METHODS

This study was carried out at Department of Obstetrics & Gynaecology, Hayatabad Medical Complex, Peshawar, from June 2005 to June 2014: total of 90 patients with GTN, were treated at our institution. We retrospectively analysed the clinical record of these patients. The diagnosis of GTN was made by both clinical and histopathologic criteria. The inclusion criteria were patients diagnosed to have GTN, post-molar, miscarriage or full-term pregnancy. After the diagnosis of GTN was made, staging work-up was performed. Along with complete history and physical examination, patients underwent laboratory tests: complete blood counts, quantitative serum β-hCG level, renal and liver function tests. Chest X-ray with computed tomography(CT) scan of the chest, abdomen, and pelvis were regularly performed, as well as either CT scan or magnetic resonance imaging (MRI) of the brain if other scans showed metastatic disease.

Based upon the staging work-up, patients with GTN were categorized according to the World Health Organization (WHO) scoring system called the prognostic scoring index. The WHO risk factor scoring system was determined by age, antecedent pregnancy, interval from antecedent pregnancy, pre-treatment hCG level, largest tumor size, site of metastasis, number of metastasis, and previous failed chemotherapy. Patients with score ≤6 were considered low-risk, whereas patients with score ≥7 or more were considered high-risk group. Low risk category patients were given weekly single agent chemotherapy while high risk category patients were given multiagent EMA-CO chemotherapy as per international standards.[4]

The clinical data about the patient and disease characteristics, including age, antecedent pregnancy, presenting complaint, interval from pregnancy, clinico-pathologic diagnosis, pre-treatment serum β-hCG levels, site of metastasis and treatment were recorded on performa and computerized record was kept.

Data was analyzed by statistical package for social sciences(SPSS) version 16.0. Mean & standard deviation were calculated for numerical data and percentages, frequencies for categorical variables.

RESULTS

In 90 patients diagnosed with GTN. 59(65.6%) patients were low risk and 31(34.4 %) were in high risk category. 73(81.1%) patients were aged less than 40 years while 17(18.9%) were aged more than 40 years with 20(22.2%) patients being nullipara & 18(20%)were multipara (parity≥5). Antecedant pregnancy was mole in 50(55.6%),miscarriage in 20(22.2%) and term pregnancy in 20(22.2%) patients. Interval from antecedent pregnancy was <4 months in 42(46.7%) patients while serum β-hCG level was between 10,000-100,000 IU/ml in 34(37.8%) & >100,000IU/ml in 27(30%) patients. 43(47.8%) patients presented with complaints of P/V bleeding, while 7(7.8%) had life threatening hemorrhage.13(14.4%) cases presented with pain abdomen while post evacuation rise of β-hCG was seen in 12 (13.3%) patients. Non gynaecological complaints like

Table 1: Type of Antecedent Pregnancy

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid Mole	50	55.6	55.6	55.6
Miscarriage	20	22.2	22.2	77.8
Term pregnancy	20	22.2	22.2	100.0
Total	90	100.0	100.0	

Table 2: Presenting Complaints in Patients with GTN

Presenting Complaint	Frequency	Percent	Valid Percent	Cumulative Percent
Valid "P/V bleeding"	43	47.8	47.8	47.8
Life threatening hemorrhage	7	7.8	7.8	55.6
secondary ammenorrhea	1	1.1	1.1	56.7
"Pain Abdomen"	13	14.4	14.4	71.1
"Hemoptysis"	4	4.4	4.4	75.6
"Paresis/Seizures"	2	2.2	2.2	77.8
"Palpitations"	1	1.1	1.1	78.9
"Cough & Breathlesness"	4	4.4	4.4	83.3
"Swelling/Mass in external genitalia"	2	2.2	2.2	85.6
"Post evacuaton with rising β-hCG "	12	13.3	13.3	98.9
"increased β-hCG in follow up"	1	1.1	1.1	100.0
Total	90	100.0	100.0	

hemoptysis was seen in 4(4.4%), cough& breathlessness in 4(4.4%) and paresis/convulsion in 2(2.2%) cases. Metastatic disease was seen in 23(25.5%) cases out of which lungs were major site of mets in 26%,liver metastasis in 21% & both lungs,vagina metastasis in 13%.

DISCUSSION

The majority of women diagnosed with GTN can be cured with overall worldwide survival rate of low-risk group approaching 100%, and 80–90% for high-risk group[4]. However, these tumors are rare in any individual hospital and most treatment recommendations are based on the observational studies from larger series. Our Unit has been a referral center and many patients were directed to our center from all across the KPK & neighbouring Afghanistan. In this series of 90 patients spanning over 10 years of period, we confirm the previously reported highly curable rates of GTN when therapeutic decisions are based on FIGO prognostic scoring index.

In our study most of women 73(81.1%) were aged less than 40 years years which seems similar to what is published in the peer-reviewed English literature[12]. In this age group women with GTN have to confront potentially life threatening diagnosis, delays in future child bearing and overall anxiety and negative perceptions on fertility & conceiving again in future.[10]

90% were referral cases.70 patients were Pakistani national while 20 patients were afghan, because of proximity of our unit to border area between Pakistan & Afghanistan.

43(47.8%) patients presented with abnormal vaginal bleeding while 7 patients had life threatening hemorrhage necessitating transfusion of blood & blood products. This presentation is somewhat very similar to what is reported in different case series world wide[11,12,13]. Abnormal vaginal bleeding in women of reproductive age with raised serum β-hCG level should raise the suspicion of GTN. Diagnosis of GTN becomes easier in patients who had prior history of molar pregnancy with raised or rising serum β-hCG during follow up as seen in 13 out 90 GTN patients. Nevertheless its non gynaecological complaints that pose a diagnostic challenge to clinicians who have limited experience in dealing with these relatively rarer malignancies.

In our study 13(14.4%) patients presented with chief complaints of pain abdomen. Intrabdominal metastsasis (hepatic,splenic,renal,intestinal) leads to intraperitoneal bleeding & severe pelvic, abdominal pain. Surgeons, physicians dealing with such complaints in women of reproductive age should have this differential diagnosis in the mind after excluding important causes to ensure early diagnosis and prompt treatment.[14,15]

Metastases to the lung are present in over 80% of women with choriocarcinoma and pulmonary involvement may cause cough, dyspnoea, hemoptysis and pleuritic chest pain due to pulmonary infarction or pleural space invasion. In our study 4(4.4%) patients presented with cough& breathlessness while other 4(4.4%) presented with hemoptysis and one patient with palpitations. Cardio respiratory physicians should have high index of suspicion in case of unexplained systemic & pulmonary symptoms in reproductive age women about the likelihood of this diagnosis to avoid undue delays[16,17].

In our case series 2(2.2%) patients presents with neurological symptoms and both had radiological/evidence of brain metastasis as well. Both these patients survived and achieved remission after multi agent chemotherapy, similar to results shown in study by Xiao C, &Savage P.[18,19]

CONCLUSIONS

Gestational trophoblast neoplasia are rare but highly curable malignancies. Reproductive age women with gynaecological complaints and non gynaecological ones like un explained pulmonary, neurological, gastrointestinal symptoms with near or remote history of gestational event should have their serum β-hCG done to diagnose these potentially life threatening but highly curable malignancies.

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