

Case Series on Gestational Trophoblastic Neoplasia and Its Varied Management

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Abstract:

Heterogeneous group of lesions that arise from abnormal proliferation of placental trophoblasts that have the property for local invasion and metastasis to distant organs is referred to as gestational trophoblastic neoplasia (GTN). Locally invasive GTN develops in about 15% of patients after evacuation of a complete mole and infrequently after other gestations. Metastatic GTN occurs in about 4% of patients after evacuation of a complete mole, but it is seen more often when GTN develops after non-molar pregnancy. Approximately 50% of cases of GTN arise from molar pregnancy, 25% from miscarriage or tubal pregnancy, and 25% from term or preterm pregnancy. Treatment is based on the total WHO score which signifies the risk of the patient developing single-agent drug resistance. Patient who had both first line and second line chemotherapy had faster decline in Beta HCG than the others with first line single agent chemotherapy.

Here we reporting a 5 case series of GTN, we had at our institute Sri Ramachandra Institute of Higher Education and Research (SRIHER, Chennai) during the year of 2015-2020.

Keywords: Gestational trophoblastic neoplasia, beta HCG.

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I. Introduction

Gestational trophoblastic disease (GTD) is the term used to describe the heterogeneous group of lesions that arise from abnormal proliferation of placental trophoblasts. GTD lesions are histologically different and can be benign or malignant. Complete and partial hydatidiform mole are the benign lesion whereas malignant lesions consist of invasive mole, placental-site trophoblastic tumor (PSTT), and choriocarcinoma. This subset of malignant lesions that have the property for local invasion and metastasis to distant organs is referred to as gestational trophoblastic neoplasia (GTN) ^(1,2).

GTD usually presents with symptoms such as uterine enlargement greater than gestational dates, vaginal bleeding, hyperemesis, pregnancy-induced hypertension and hyperthyroidism or incidental finding in ultrasound.

Clinical diagnosis is based on history, physical examination, pelvic ultrasound and serum β -HCG quantification. Primary treatment is urgent surgical evacuation and curettage, and pathologic examination of the curettage specimen confirms the diagnosis ⁽³⁾.

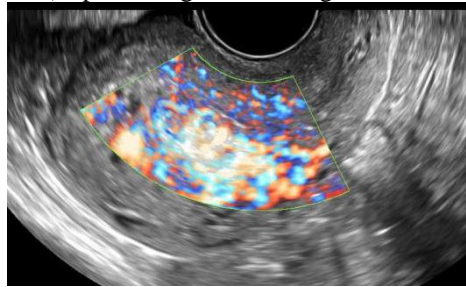
Here we reporting a 5 case series of GTN, we had at our institute Sri Ramachandra Institute Of Higher Education and Research (SRIHER, Chennai) during the year of 2015-2020.

Case Report 1:

Mrs X, a 26 year old Primigravida with LMP of 26/11/2019, ovulation induction conception confirmed by Urine Pregnancy test after 45 days of amenorrhea. Dating scan was done on 04/01/2020, showed an early IUGS ~ 5 weeks 5 days and no fetal pole. Repeat scan on 25/01/2020 also showed an early IUGS with no fetal pole. Scan done of 08/02/2020 as well did not suggest a Fetal Pole. B-HCG was done on 11/02/2020, reported 1,70,600 mIU/ml. In view of failing pregnancy, Dilatation and Curettage was done at a private clinic on 11/02/2020. Serial BHCG done weekly post dilatation and Curettage, since it was elevated, Patient was then referred to SRIHER in view of increasing trend of BHCG and HPE report suspicious of Partial Molar pregnancy. TVS pelvis done at SRIHER on 03/03/2020 showed an ET of 21mm, thickened cavity with irregular cystic anechoic spaces. Color doppler showed increased vascularity. BHCG was 39,950 mIU/ml. Medical Oncology opinion was obtained, advised Single Agent Chemotherapy using Methotrexate 88mg IM. Patient was administered with 11 doses of the same. BHCG was monitored prior to administration of each dosage. BHCG

values were 2695 mIU/ml, at the start of treatment and weekly Beta HCG was on decreasing trend and since 12th and 13th week beta HCG was 2.8mIU/ml, 0.9 mIU/ml treatment was stopped.

Figure 1 (Representing molar changes with vascularity)



Case Report 2:

Mrs Y, 30year old, G3A2 with h/o 32 days of amenorrhea, presented with complaints of spotting pv. Serum BHCG done was reported 4147.5 mIU/ml. TVS Pelvis suggested an early intrauterine gestational sac. 2 weeks later, repeat viability scan showed thickened ET with echogenic area and reported ? incomplete Abortion? Molar pregnancy. BHCG done on the same day as the scan was 5899 mIU/ml. Hence patient underwent Dilation and Curettage. HPE reported Decidua with degenerated villi and no molar changes. One and half months later, patient presented with excessive bleeding per vagina and BHCG of 28298.2 mIU/ml, hence TVS Pelvis was done and suggested fluid in the endometrial cavity with echogenic area. Following which MRI Abdomen Pelvis was done, which suggested a bulky uterus with well-defined heterogenous mass in the uterus with myometrial involvement and diagnosed as Invasive Mole. Patient was referred to Medical Oncologist, CT Chest and CT Brain done was normal. 4 cycles of multi dose regimen of EMACO was administered. Initial Beta HCG before treatment was 1161.20 mIU/ml, weekly beta HCG was on decreasing trend, with the 8th and 9th week beta HCG was 17mIU/ml and 0.7mIU/ml, treatment was stopped.

Case Report 3:

Mrs W, 25 years old, Primigravida 10 weeks 1day presented with complaints of brownish discharge per vagina. TVS Pelvis showed endometrial cavity filled with echogenic material and multiple cystic spaces suggestive of Vesicular Mole and BHCG was 2,70,000 mIU/ml. Suction Evacuation was done and HPE reported Partial Mole. Medical Oncology opinion was obtained and patient was administrated with 5 doses of Inj Methotrexate and started on second line chemotherapy with one dose of Injection Actinomycin and Injection Cyclophosphamide. Weekly BHCG values were monitored, the 1st week Beta HCG was 96,508 mIU/ml, and was on decreasing trend, the 6th and 7th week Beta HCG being 1.3mIU/ml, and 1.1mIU/ml, treatment was stopped.

Case report 4:

Mrs x, 27 years old G2P1L1A2/ 8weeks by dates, presented with complaints of amenorrhea for 1 month followed by increased bleeding PV for past 1 month, TVS pelvis was done at a private hospital which showed echogenic mass measuring 4.3x 3.6cm containing multiple regular cystic areas and few areas of mixed echogenicity S/O retained products of conception. D and C was done and histopathology showed products of conception, following which patient had increased bleeding Per vagina, TVS pelvis done showed retained products of conception and Beta HCG correlation. Patient was referred to SRIHER, Beta HCG done was 50,878. TVS pelvis showed distended cavity with fluids and echogenic mass seen with multiple cystic spaces S/O Gestational trophoblastic neoplasia. Suction evacuation was done. Beta HCG post evacuation was 32,000 and histopathology reported as retained products of conception with clinical correlation. Post evacuation Beta HCG was 86,813. Since Beta HCG was on increasing trend patient was referred to medical oncology and was started on Injection Actinomycin, and Injection cyclophosphamide 8 cycles of chemotherapy was given. Weekly Beta HCG was monitored and treatment was stopped since 9th and 10th week of Beta HCG was <0.6mIU/ml and was same one month and 6 months later.

Case report 5:

Mrs Y 29 years old G2A1/ 17 weeks/ DCDA twin. NT scan done at 12weeks showed one fetal demise with coexisting mole, and fetus B with normal NT of 1.2mm. Scan done at 17 weeks showed same finding, Beta hcg was 2,71,800. Hence admitted for Medical termination of pregnancy. Suction and evacuation was done and histopathology reported as. One week after evacuation Beta hcg was 76,663. Weekly beta hcg was monitored and it was on decreasing trend. Since Beta hcg started to rise on ninth week, patient was referred to medical oncology and was started on single chemotherapy regimen, Injection methotrexate ten cycles and was normal

from week nineteen (Beta hcg- 0.8 mIU/ml) and hence chemotherapy was stopped and followed up six months later and was normal.

Figure 2 (Representing fetus with co existent mole)



Table no 1: Summary of all the cases

	Case 1	Case 2	Case 3	Case 4	Case 5
Age	26	30	25	27	29
Parity	Primi	G3A2	Primi	G3P1L1A1	G2A1
Gestational age	8weeks+5days	6weeks	10weeks+1day	8weeks	17weeks
Initial Beta HCG in mIU/ml	1,70,600	4147.5	2,70,000	50,878	2,71,800
TVS pelvis	ET of 21mm, thickened cavity with irregular cystic anechoic spaces. Color doppler showed increased vascularity.	Fluid in the endometrial cavity with echogenic area.	Endometrial cavity filled with echogenic material and multiple cystic spaces suggestive of Vesicular Mole	Distended cavity with fluids and echogenic mass seen with multiple cystic spaces s/o Gestational trophoblastic neoplasia	One fetal demise with coexisting mole, and fetus B with normal
Management	11 doses of Injection methotrexate	4 doses of EMA-CO	5 doses of Methotrexate, with 1 dose of second line Actinomycin and cyclophosphamide	8 doses of Injection Actinomycin and cyclophosphamide	10 doses of Injection Methotrexate
Follow up Beta HCG in mIU/ml	Post evacuation- 5550 Week four - 39,958	Post evacuation 28298.2	Post evacuation - 96,508	Post evacuation- 86,813	Post evacuation- 76,663.
Week Eight	6.8	17	10.6	1.1	0.9
Beta HCG value at which treatment was discontinued	Week thirteen- 0.9	Week nine- 0.7	Week seven- 1.1	Week nine- <0.6	Week nineteen- 0.8
Resumption of menstrual cycle	4 months after chemotherapy	3 months after chemotherapy	1 month later	1 month after chemotherapy	2 months later chemotherapy
Future pregnancy	Not yet planned	1 cycle of IVF failed, not yet conceived	Not yet planned pregnancy	Conceived spontaneously	Conceived spontaneously
WHO scoring	2	1	2	1	2
Metastasis	Nil	Nil	Nil	Nil	Nil
Complications	Amenorrhea	Infertility	Nil	Vomiting	Thrombocytopenia

II. Discussion:

Gestational trophoblastic disease (GTD) is a spectrum of disorders that may develop following abnormal fertilization.⁽⁴⁾

All patients are between age group 25-30years.2 out of four patients were primigravida

4 patients presented with complaints of bleeding PV and hence suction evacuation has been done for miscarriage or features S/O vesicular mole and one patient was diagnosed on routine ultrasound then in follow up of beta Hcg was diagnosed to have Gestational trophoblastic neoplasia. Post evacuation Beta HCG was raised in two patients than the initial Beta HCG.

Patient who had both first line and second line chemotherapy had faster decline in Beta HCG than the others with first line single agent chemotherapy.

Patient who had maximum doses of chemotherapy had resumption of menstrual cycles later than others.

Two of them conceived spontaneously, one had failed IVF, two of them have not planned pregnancy since last dose of chemotherapy is within six months.

Ova from older women may be more susceptible to abnormal fertilization, resulting in a complete hydatidiform mole. Ultrasonography (TVS pelvis) is a reliable and sensitive technique for the diagnosis of molar pregnancy. In complete mole the chorionic villi exhibit diffuse hydropic swelling, absence of fetal tissue, In partial mole focal hydrophobic swelling are present with fetal parts.

Locally invasive GTN develops in about 15% of patients after evacuation of a complete mole and infrequently after other gestations. Metastatic GTN occurs in about 4% of patients after evacuation of a complete mole, but it is seen more often when GTN develops after nonmolar pregnancy. The most common sites of metastases are lung (80%), vagina (30%), pelvis (20%), liver (10%), and brain (10%)⁽¹⁾

FIGO prognostic scoring is based on individual risk factors such as age, antecedent pregnancy, interval from index pregnancy, pretreatment beta hCG, largest tumor size, site and number of metastases, and previous failed chemotherapy regimens. The sum of individual scores denotes the FIGO prognostic score of low-risk GTN (score <7) or high-risk GTN (score ≥7).

This prognostic scoring system is not valid for the Epidermoid trophoblastic tumor and Placental site trophoblastic tumor. Monitoring of Beta HCG is done weekly once until three negative values, and then monthly once for 6 months. Stage 1 and stage 2,3 low risk tumor are treated with single drug chemotherapy or hysterectomy. Stage 2,3 high risk and stage 4 are treated with combination chemotherapy with or without surgery and radiation therapy⁽⁵⁾.

III. Conclusion

Gestational trophoblastic neoplasia though a rare neoplasia, it can be diagnosed at early stage with regular follow up with Beta Hcg and can be completely cured with chemotherapy regimens without any metastasis.

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ABBREVIATION:

GTD-Gestational Trophoblastic Disease
GTN-Gestational Trophoblastic Neoplasia
PSTT- Placental-Site Trophoblastic Tumor
BHCG-Beta Human Chorionic Gonadotropin
LMP-Last Menstrual Period
IUGS-Intra Uterine Gestational Sac
ET-Endometrial Thickness
TVS-Transvaginal Sonography
HPE-Histopathology Examination
D and C – Dilatation and Curettage

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