ORIGINAL RESEARCH PAPER

Volume-6 | Issue-10 | October-2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

# PREVENTABLE ONCOLOGIC CATASTROPHE IN HIGH RISK GESTATIONAL TROPHOBLASTIC NEOPLASIA: A CASE REPORT

Oncology

**Dr. Swati Jain** M.B.B.S.Post Graduate student. M. B.B.S., Gynaecology Oncology, Gujarat Cancer and Research Institute, Ahmedabad

**Dr. Meeta Mankad** M.D. Professor and Head of Unit M.D., Gynaecology Oncology, Gujarat Cancer and Research Institute, Ahmedabad

## ABSTRACT

Early recognition of gestational trophoblastic neoplasms (GTN) will maximize the chances of cure with chemotherapy. Some patients present with many different symptoms months or even years after the causative pregnancy making diagnosis difficult. Clinicians should be aware of the possibility of GTN in reproductive age woman with bizarre neurological, gastrointestinal symptoms or radiographic evidence of metastatic tumor of unknown primary origin. We report a case of metastatic gestational trophoblastic neoplasm with metastasis to brain presenting with unusual manifestations.

## KEYWORDS

Gestational Trophoblastic Neoplasm, Chemotherapy, Metastasis

## INTRODUCTION

Gestational trophoblastic disease (GTD) encompasses hydatidiform mole (complete and partial) and gestational trophoblastic neoplasia (GTN), which includes invasive mole, choriocarcinoma, and placental site trophoblastic tumor.[1] Risk factors for choriocarcinoma include prior complete hydatidiform mole, ethnicity, and advanced maternal age. Trophoblastic neoplasia (invasive mole or choriocarcinoma) follows complete mole in 15-20% of cases. It infrequently develops after normal pregnancies, ectopic pregnancies, and spontaneous or therapeutic abortions. [2]

Presenting symptoms and signs of gestational choriocarcinoma are highly variable. The invasive nature of this tumor often leads to early metastasis which is diagnosed long after the antecedent gestation and is widely disseminated. In patients with GTN, gynaecological symptoms are sometimes ignored, attributed to normal peripartum or postabortal state, with misdiagnoses by non-gynaecologists due to lack of classic manifestations.[3]

β hCG is a disease-specific tumor marker specific to GTD. It is easily measured quantitatively in both urine and blood which correlates with the burden of disease.[4] It is used for diagnosis, monitoring the treatment, relapse and for prognosis of the patient.

GTN is now one of the most curable of all human tumors, with a cure rate exceeding 90%.[1] Improvements in survival are attributed to advances in chemotherapy, better assays for the tumor marker hCG, development of specialized treatment centres, identification of prognostic scoring systems to predict treatment response and enhance individualization of therapy, and use of combined modality treatment with chemotherapy, radiation, and surgery to treat the highest-risk patients.[1] However, rarity and malingering signs and symptoms of other diseases leads to delay in diagnosis of GTN.

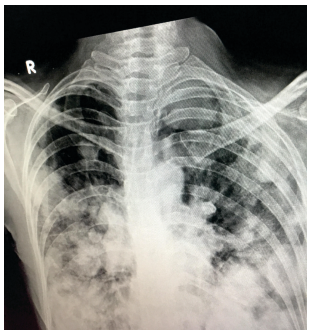
## CASE REPORT

A 35 year old woman, P1A1L1 (last delivery 12 years back and abortion 6 years back) was referred to oncology department at Gujarat Cancer Research and Institute (GCRI), Ahmedabad with a provisional diagnosis of non hodgkins lymphoma. She presented with cough, abdominal pain and generalised weakness since 2 months. She had history of amenorrhea since 3 months followed by bleeding per vaginum for which she had undergone hysterectomy. Ultrasonography prior to hysterectomy revealed a 7×7cm hypoechoic lesion in uterus. Clinical and operative notes with histopathological report of hysterectomy were unavailable. Chest X-ray revealed 'cannon balls' like nodular shadows. She was referred to the department of gynaecologic oncology to rule out primary gynaecological malignancy.

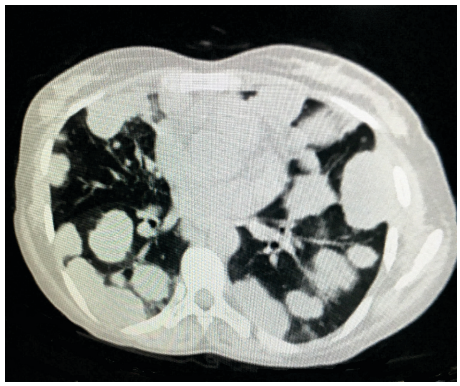
On examination, the patient was pale with pulse rate of 90/min, blood pressure of 110/70 mm Hg and Karnofsky performance score of 90. On per abdomen examination, previous laparotomy scar was present, abdomen was soft, non tender. Vaginal examination revealed a globular mass of approximately 4×4 cm size in left fornix. Urine pregnancy test done with high suspicion of GTN (gestational trophoblastic neoplasia) was found to be positive.

On further investigation ,her Hb was 4.2 gm/dl, WBC was 14.50×10$^3$ /cmm, platelets were 592×10$^3$/cmm, CA 125 was 55.72 U/ml, serum β hCG was 927323 IU/L, CSF β hCG was 9615 IU/L. Ultrasonography of abdomen and pelvis revealed presence of few target lesions in both lobes of liver largest measuring 34×23 mm in segment IV of liver, presence of 30×30 mm sized heterogenous echotexture lesion in lower pole of spleen, presence of 36×42 mm sized heterogenous echotexture lesion in lower pole of left kidney, presence of 26×15 mm sized hypoechoic lesion in intramuscular plane of left iliac fossa, all suggestive of metastasis. Magnetic resonance imaging (MRI) of brain revealed well defined altered signal intensity lesions in right frontal and left occipital region, suggestive of metastasis. Computed tomography (CT) scan of thorax revealed well defined nodular soft tissue opacities in both lung fields, suggestive of metastasis.

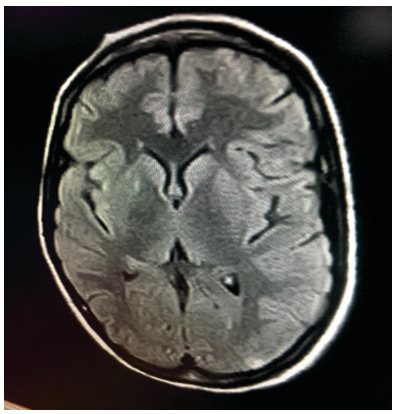
High risk GTN, FIGO stage IV was diagnosed with WHO score 20. Chemotherapy with serial monitoring of serum β hCG was started. Considering the high load of disease with risk of tumor necrosis syndrome, two cycles of low dose induction chemotherapy with etoposide (100mg/m$^2$/day) and cisplatin (20mg/m$^2$day) were given. Etoposide, methotrexate, actinomycin D (EMA) regime was planned but delayed as the patient developed febrile neutropenia, vomiting and diarrhoea. 6 units of packed cell volume were transfused, Injection G-CSF 300 ug was administered to correct neutropenia. Triple intrathecal therapy (methotrexate 12mg, hydrocortisone 50mg, cytosar 70mg) biweekly was started with monitoring of CSF cytology and CSF β hCG. Whole brain radiotherapy was not given as the patient was asymptomatic neurologically. Her serum β hCG and CSF β hCG dropped to 255542 IU/L and 1388 IU/L from 927323 IU/L and 9615 IU/L respectively. The patient was discharged on request and could not be contacted, possibly she succumbed to her illness.



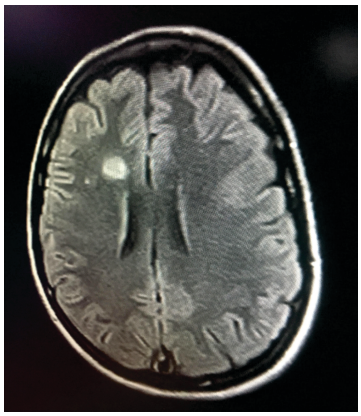

**Chest X-ray- cannon ball opacities**



**CT scan (Thorax)- multiple nodular opacities in both lung fields**



**MRI Brain- hyperintense lesion on T2w in left occipital region**



**MRI Brain-hyperintense lesion on FLAIR in right frontal region**

## DISCUSSION

Gestational trophoblastic disease is potentially curable. The overall cure rate is reported to be 90–100%. It is extremely responsive to chemotherapy therefore, chemotherapy is the treatment of choice in patients with metastatic GTN. Management of GTN is based on FIGO staging and WHO prognostic scoring system.[3] The key to successful management of GTN is based on early diagnosis of the disease but due to its unusual presentations, it is often missed

GTNs are characterised by aggressive propensity for widespread metastasis due to early vascular invasion and dissemination, especially choriocarcinoma. However, any form of GTN can metastazise and the most common site is lung (80%) followed by vagina (30%), brain and liver (10%).[5] Savage et al demonstrated the mean age of patients with GTN to be 32 years.[6] The clinical symptoms may vary from abnormal vaginal bleeding, bleeding from metastatic sites in the abdomen, lung or brain; pulmonary symptoms and neurological signs from spine or brain metastasis.

In our case, 35 year old patient had amenorrhea followed by bleeding per vaginum. The first investigation which could have guided the diagnosis was a simple urine pregnancy test. However, ultrasonography was done which revealed a mass lesion in the uterus for which patient underwent hysterectomy. The specimen of uterus should have been sent for histopathological examination to formulate the diagnosis of benign or malignant lesion which could have guided further management. β hCG being a characteristic and unique tumor marker for gestational trophoblastic disease could have been used to rule out GTN. Her Chest X ray was suggestive of multiple metastasis. It is a dictum in medicine that a woman of reproductive age group with multiple lung metastasis should be evaluated for serum β hCG levels as the most common site of metastasis in GTN is lung. Thereafter patient was referred to our institute with a provisional diagnosis of non hodgkins lymphoma. The diagnosis of high risk GTN, FIGO stage IV and WHO score 20 was established after thorough history and clinical examination, blood and radiological investigation. The value of a lumbar puncture to measure the cerebrospinal fluid: serum hCG ratio, which should be less than 1:60 is used in some centres.[7] In our case it was less than 1:60. The patient might have harboured the disease when she first had amenorrhea which due to diagnostic fallacies progressed to stage IV GTN at the time of presentation to GCRI.

The management of GTN is based upon the FIGO stage and WHO scoring system. Patients with persistent GTN and stage I or score ≤6 (low risk) should be managed with single agent chemotherapy (Methotrexate or Actinomycin), but patients with stage IV or score ≥7 (high risk) need combination chemotherapy (EMA–CO). Stage II and Stage III but low risk patients are treated with primary single-agent chemotherapy and high-risk patients are managed with primary combination chemotherapy.[3] Some patients present with very advanced disease either causing or at high-risk for organ failure. Patients may also have poor prognostic factors such as liver or brain involvement.[7] Commencing such individuals on standard EMA/CO regime or other multiagent chemotherapy can cause severe hemorrhage or worsening organ failure resulting in early deaths. This can be avoided by using induction therapy with low-dose etoposide 100 mg/m2 and cisplatin 20 mg/m2 before commencing standard chemotherapy.[8] In those patients with liver and brain metastases who have the worst long-term outcome, the subsequent uses of EP/EMA regime seem sensible. Patients with high risk features may benefit from 8 rather than 6 weeks of consolidation therapy with a normal hCG.[7] A hysterectomy may be required in patients with metastatic GTN in order to control uterine hemorrhage or sepsis. Furthermore, in patients with extensive uterine tumors, a hysterectomy may substantially reduce the trophoblastic tumor and limit the need for multiple courses of chemotherapy.[9] All hysterectomy specimen should be sent for histopathological examination. The use of whole-brain radiotherapy is controversial, given the long-term toxicity issues and lack of evidence that it significantly improves survival.[7]

The reported case indicates that GTN is a highly metastatic tumor and hence prompt diagnosis and early referral to experienced centres is inevitable in the management of the disease. This would minimise the catastrophic cascade leading to progression of the disease and demise of the patients.

## CONCLUSION

GTN may present in an unlimited number of ways. Clinicians should be able to secure the diagnosis if it is considered and appropriate history, examination, laboratory, radiological and pathological techniques are employed. Clinicians should be aware of the possibility of GTN in reproductive age woman with bizarre central nervous system symptoms, pulmonary symptoms or radiographic evidence of metastatic tumor of unknown primary origin. Histology of the hysterectomy specimen could have averted the catastrophe in this case. Omission of this event delayed the formulation of diagnosis in an otherwise salvageable patient. Effective use of b-hCG assay and therapy for individualizing the identified risk factors, the aggressive use of multi-agent chemotherapy and irradiation, and surgical intervention are the major contributing factor

## REFERENCES

[1] Hoekstra AV, Lurain JR, Rademaker AW, Schink JC. Gestational trophoblastic neoplasia: treatment outcomes. Obstetrics & Gynecology. 2008;112(2, Part 1):251-8.
[2] Balagopal PG, Pande M, Chandramohan K, Somanathan T, Kumar A. Unusual presentation of choriocarcinoma. World J Surg Oncol 2003;1;1-4.
[3] Ashraf-Ganjooei T, Ghaemmaghami F. Patients with presenting unusual manifestations with gestational trophoblastic neoplasm: case series and review of literatures. Archives of gynecology and obstetrics. 2008;277(5):465-70.
[4] Lurain JR. Gestational trophoblastic disease I: epidemiology, pathology, clinical

presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. American journal of obstetrics and gynecology. 2010;203(6):531-9.
[5] Al-Husaini H, Soudy H, Darwish A, Ahmed M, Eltigani A, Edesa W, Elhassan T, Omar A, Elghamry W, Al-Hashem H, Al-Hayli S. Gestational trophoblastic neoplasia: treatment outcomes from a single institutional experience. Clinical and Translational Oncology.2015;17(5) : 409-15.
[6] Savage P, Kelpanides I, Tuthill M, Short D, Seckl MJ. Brain metastases in gestational trophoblast neoplasia: An update on incidence, management and outcome. Gynecologic oncology. 2015; 137 (1): 73-6.
[7] Seckl MJ, Sebire NJ, Fisher RA, Golfier F, Massuger L, Sessa C, ESMO Guidelines Working Group. Gestational trophoblastic disease: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of oncology. 2013;24(suppl_6):vi39-50.
[8] Alifrangis C, Agarwal R, Short D, Fisher RA, Sebire NJ, Harvey R et al. EMA/CO for high -risk gestational trophoblastic neoplasia: good outcomes with induction low-dose etoposide- cisplatin and genetic analysis. J Clin Oncol. 2013;31:280-6.
[9] Berkowitz RS, Goldstein DP (2005) Gestational trophoblastic neoplasia. In: Berek JS, Hacker NE (eds) Practical gynecologic oncology, 40th edn. Williams & Wilkins, Baltimore, pp 603–625.