Recurrent hydatidiform mole transformed into invasive mole with co-morbid depression- a rare case report

Nisha Bhagat¹*, Rajnish Raj²

¹Department of Obstetrics and Gynecology, Government Medical College, Amritsar, Punjab, India
²Department of Psychiatry, Government Medical College, Patiala, Punjab, India

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*Correspondence:
Dr. Nisha Bhagat,
E-mail: nishabhagat07@yahoo.com

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ABSTRACT

The gestational trophoblastic disease is a group of interrelated lesions that arise from abnormal proliferation of placental trophoblast. It comprises of hydatidiform mole (partial or complete), invasive mole, placental site trophoblastic tumor and choriocarcinoma. The occurrence of hydatidiform mole in more than two conceptions is known as recurrent hydatidiform mole. Although, its incidence is less than 2% but it may progress to invasive mole or choriocarcinoma. The case of 26-year old female is reported; she had five consecutive molar pregnancies and the sixth one developed into invasive mole with co-morbid depression that was managed by methotrexate chemotherapy, antidepressant and psychotherapy.

Keywords: Gestational trophoblastic diseases, choriocarcinoma, invasive mole, methotrexate

INTRODUCTION

Hydatidiform mole (HM) is the most common form of gestational trophoblastic neoplasia (GTN). Histologically, it is characterized by chorionic villi abnormalities that consist of atypical trophoblastic proliferation and oedema of villous stroma.¹ The incidence of HM in USA is 1 in 1500 live births; in India 1 in 1000 and in Philippines 1 in 80.² Molar pregnancies in more than two conceptions is known as recurrent hydatidiform mole. However, the incidence of recurrence is 1 in 60 in second pregnancy and 1 in 6.5 in third pregnancy.³

About 92% of HM resolve spontaneously after evacuation.⁴ About 15% of them have potential for developing into local invasive gestational trophoblastic neoplasia (GTN).³ The low risk GTN is treated by single-agent chemotherapy while high risk of GTN requires multi-agent chemotherapy. The overall prognosis is good and most of the patients can preserve their fertility and anticipate normal pregnancy outcomes.

Depression is a major public health problem around the world. Important contributors to etiology include genetic vulnerability, changes in neurotransmitter levels, neuroendocrine function and psychosocial stressors. The female: male prevalence is approximately 2:1. World Health Organization (WHO) projects unipolar depressive disorders as the second leading cause of burden of disease worldwide by the year 2030. There are no specific tests to confirm a diagnosis of depression, but ruling out certain contributors to illness can help and guide treatment. More than 60% of major depressive disorders are prone to risk of recurrence and may require antidepressant treatment. We hereby, report a case of 6th consecutive molar pregnancy in 26-year old female that was transformed into invasive mole with co-morbid...
depression and treated successfully by methotrexate regimen, antidepressant and psychotherapy.

CASE REPORT

A 26-year old, married female, of upper middle income socio-economic status reported to the out-patient department (OPD) of Obstetrics and Gynecology in March 2016 as G6P0A5 with chief complaints of amenorrhea of 3 months; sadness of mood, lethargy, loss of appetite and weight, decreased interest in sexuality and insomnia for the last one month. She was referred from private practitioner with Ultrasonogram (USG) showing molar pregnancy with history of recurrent molar conceptions.

She had her first molar pregnancy 5 years back in April 2011 for which suction evacuation was done. During the follow-up, serial β-human chorionic gonadotropin (β-hCG) and urinary pregnancy test (UPT) was done until there were 3 consecutive negative reports of pregnancy for 6 months. However, it was followed by five complete molar conceptions at an interval of 8-12 months and reported for 6th time with partial mole.

On general physical examination (GPE) patient was calm, conscious well oriented to time, place and person. Abdominal examination showed uterus enlargement of 14 weeks. Per vaginal examination revealed 14 weeks of soft uterus and non-tender fixed mass of 4 cmx3 cm felt through left fornix and right fornix was clear. Her blood group was B-positive. Routine investigations like haemogram, liver function test (LFT), renal function test (RFT), prothrombin index (PTI), platelet count, thyroid function test (TSH) and X-ray chest were normal. USG for pelvic organs revealed multiple-cystic lesions in the uterus with fetal tissue without cardiac activity suggestive of hydatidiform mole with a cyst of 2.5 cm in left ovary along with ectopic left pelvic kidney (Figure 1).

Pre-evacuation β-hCG was 17609 mIU/ml. Suction evacuation was done under short general anestheisia (GA) and products were sent for histopathological examination that confirmed the diagnosis of partial HM. Post-operatively, one unit of blood was transfused; β-hCG level after 48 hours dropped to 9124 mIU/ml.

Patient was discharged in satisfactory condition with instructions for regular follow-up for β-hCG levels and contraception till six months. Her β-hCG levels became normal after 4 weeks.

Unfortunately, her subsequent follow-up was irregular. She again presented in September 2016 with complaints of irregular vaginal bleeding and pain lower abdomen. USG revealed a hyper-echoic nodular lesion of 68x50x45 mm in the left lateral wall of lower uterine segment with cystic areas along with multiple dilated vascular channels on Doppler. A well circumscribed cystic, multi-locular mass with thick septae, measuring 75x72x63 mm was seen in the left fundal region. Multiple nodular lesions were seen in the rest of uterus, bilateral ovaries were normal (Figure 2).

β-hCG level was 22,500 mIU/ml. The clinical history of recurrent molar pregnancies, persistently elevated β-hCG levels and USG findings were suggestive of invasive mole of uterus. Thus, chemotherapy was planned and complete metastatic work-up was done.

As per Federation of International gynecologists and Obstetricians (FIGO) staging system for GTN, she was in stage-1 with prognostic score of 6, indicating low risk. Thus, single agent chemotherapy was started with Methotrexate 1mg/kg intramuscularly and Leucovorin (folinic acid) 15 mg per oral on alternatively day for one week. Her β-hCG level was dropped to 619 mIU/ml after the first cycle. Subsequently, another cycle was given at an interval of 1-week. After two weeks, her β-hCG levels were within normal i.e., less than 0.5 mIU/ml. On USG with colour-Doppler, all her lesions in the uterus of invasive mole disappeared, thus indicating complete recovery. However, she reported sadness, insomnia, loss of weight etc., for which a psychiatric consultation was taken. Mental status examination of the patient revealed...
that she was low on mood; affect appropriate to the mood content. She was lethargic, decreased sexual activity and had lost weight of more than 5 kg during the last one month. However, her higher mental function test, insight and contact with reality were within normal range. Diagnostic and Statistical Manual of Mental Disorder (DSM-5) revealed a clinical diagnosis of 296.22 (F32.1) i.e., Single Major depressive disorder (MDD) with specifier: moderate. She was assessed for severity on MADRS scale; and its impact on sexual experience during the past one week on Arizona sexual experience (ASEX) scale; and Clinical outcome on Clinical Global Impression- Severity (CGI-S) Scale which revealed the scores of 24, 21 and 4 respectively.

These symptoms of depression occurred concurrently with medical illness of sixth molar pregnancy. There was no history of past psychiatric illness. Thus, it could not be attributed to a normative stress reaction of anticipated failure of pregnancy or hormonal derangement or any other substance/drugs etc. Patient was given psycho-education, crisis-intervention psychotherapy and pharmacotherapy with fluoxetine 20 mg per day, which was gradually titrated to the therapeutic level of 40 mg per day and clonazepam 0.5 mg at night for fifteen days that was later on tapered off. After 12 weeks of periodic follow-up, her MADRS, ASEX and Clinical Global Impression- Improvement Scale (CGI-I) scores were 6, 5 and 1 respectively, indicating very much improvement.

DISCUSSION

The exact pathogenesis of molar pregnancy is still unclear. Many risk factors have been identified e.g., paternal age affecting quality of spermatozoa, oral contraceptive pills and gravidity. In India, the incidence is 1 in 1000 whereas in Europe, incidence ranges from 0.6 to 1.1 per 1000 pregnancies. Women older than 35 years of age have a relative risk of 2.0 and more than 40 years of age have 5 to 10-fold increase in their incidence of HM.

In the medical literature, a rare familial predisposition has been reported among 21 families. Genetic studies suggest mutations in maternal Nucleotide-binding oligomerization domain, Leucine rich repeat and Pyrin (NLRP-7) gene, which is located on chromosome 19q13.3-q13.4. In these cases, HM is diploid but biparental rather than androgenetic in origin. These patients are autosomal recessive and cause them to have recurrent molar pregnancies with little chance of normal pregnancy. However, our patient had no family history of any recurrent HM.

Complete moles have potential for local invasion and dissemination. The clinical presentation of an invasive mole includes vaginal bleeding, a sub-involuted uterus on bimanual examination and high urinary or serum β-hCG level, typically after the evacuation of a molar pregnancy. The interval from an antecedent molar pregnancy is usually less than six months. Definitive treatment of GTN is chemotherapy with or without hysterectomy and depends on combined FIGO anatomic staging system with a revised WHO risk factor scoring system for GTN. A score of less than 7 is a low risk of GTN, which is managed by single-agent chemotherapy e.g., either methotrexate or actinomycin in case of female desirous to preserve her fertility. In our case, the GTN score was 6 and was managed successfully, by methotrexate regimen. In case of treatment with methotrexate, complete remission is achieved in most of the non-metastatic and low risk cases even in the presence of disseminated disease. These cases are amenable to treatment with almost 100% survival.

High risk cases require various combination chemotherapy regimens, which include methotrexate/leucovorin, actinomycin-D and cyclophosphamide (MAC); etoposide, methotrexate/leucovorin and actinomycin, followed by cyclophosphamide and oncovin (EMA-CO). Continuous monitoring with β-hCG level for 1 year in low risk cases and for 2 years in high risk cases is mandatory.

Psychiatric disorders following cancer have close links with a patient’s mental state. There have been suggestions that stressful life events predispose to cancer. Likewise, if a patient has already been depressed prior to the diagnosis of depression, it is likely to recur or become exacerbated. However, evidences for these claim is conflicting and subsequent studies did not replicate the observations.

During study, patient developed depression concurrent with ammenorrhea and she had full recovery after chemotherapy and psychopharmacology. It is, therefore, advisable that an interdepartmental consultation-liaison is important for an early screening, diagnosis and treatment of medical illness and depression which may be disabling and can cause considerable risk of suicidality.

CONCLUSION

Gestational trophoblastic tumors are group of cancers that respond to chemotherapy. Complete remission is possible without any adverse effect on future pregnancy outcomes. However, adjunct psycho-education, marital-therapy and psycho-pharmacotherapy can mitigate these problems and help the couples in preserving and strengthening their familial ties and psychological health.

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