Recurrent hydatidiform mole: A case report of six consecutive molar pregnancies complicated by choriocarcinoma, and review of the literature

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ABSTRACT

Hydatidiform mole (HM) is the most common form of gestational trophoblastic neoplasia. Recurrence of HM is extremely rare. Here, we report the case of a patient with six consecutive partial HMs without normal pregnancy. A 42-year-old lady who was referred to us at King Fahad Hospital of the University, Al Khobar, initially as a case of 26-year-old with persistent trophoblastic disease after three recurrent molar pregnancies that were confirmed histologically in the referring hospital. She underwent evacuation and curettage and was followed up by serial β-human chorionic gonadotropin levels, and did not require chemotherapy. She then had three more molar pregnancies in 1995, 1996, and 2004; all molar pregnancies were evacuated by suction curettage at her base hospital, but in the last event, she complained of shortness of breath and abdominal pain. Diagnostic workup in our hospital confirmed choriocarcinoma, for which she received multiple regimen chemotherapy and was cured. Unfortunately, she lately presented with symptoms suggestive of premature menopause.

Key words: Choriocarcinoma, hydatidiform mole, recurrent mole

INTRODUCTION

Hydatidiform mole (HM) is characterized by atypical hyperplastic trophoblasts and hydropic villi. It forms a heterogeneous group of disorders, with an incidence ranging from 1 in 500 to 1 in 1 500 pregnancies in the Western World. The incidence in our region was reported to be 1 in 452 pregnancies, whereas the incidence is higher in Asia reaching 1 in 80 pregnancies. Although recurrent molar pregnancies are a rare occurrence seen in 1 to 2% of cases, it is clear that women who have had a previous mole have a higher risk of recurrence than the general population. We present here a case with repeated HM in six consecutive pregnancies.

CASE REPORT

A 26-year-old Saudi patient was first referred to our outpatient department (OPD) at King Fahad Hospital of the University in January 1994 as a case of recurrent molar pregnancy for the third time with persistent trophoblastic disease. She gave a history of three previous histologically proven molar pregnancies since her marriage two years ago, treated in a peripheral hospital. The patient continued to have vaginal bleeding for a month after the procedure. The serum β-human chorionic gonadotropin (β-hCG) was found to be 15,444 IU and a chest X-ray, renal and liver function tests were normal. She underwent a repeat uterine curettage in her base hospital which showed necrotic endometrial tissue. Unfortunately, she continued to have intermittent vaginal bleeding and hence referred to our hospital after 10 days. Her β-hCG on presentation was 4 458 IU and the ultrasound showed endometrial thickening, so she underwent dilatation and curettage.
Histopathology reported necrotic decidua only. The patient was given the oral contraceptive pill and followed up regularly in the OPD with serial quantitative \( \beta \)-hCG estimations until it was undetectable after 4 weeks.

Her subsequent clinic attendance at our hospital was irregular. The patient returned to the OPD in June, 2004 and reported to have had three more molar pregnancies treated at her initial hospital with suction and curettage in May, 1995; June, 1996; and three weeks prior to presentation. Histopathology report revealed avillous sheets of trophoblastic cells with hemorrhage and necrotic background. She was followed up in her base hospital in the last two pregnancies with serial quantitative \( \beta \)-hCG, until it became negative. By the time she came to us after 3 weeks of her last molar pregnancy, she complained of abdominal pain and shortness of breath. A chest X-ray showed bilateral cannon ball opacities in both lung fields which were thought to be due to metastatic choriocarcinoma; her \( \beta \)-hCG was 987 576.5 IU. The ultrasound of the pelvis showed an enlarged uterus (12.5 \( \times \) 6.6 cm) with some cystic changes in the endometrial cavity and hypervascularity of the hypoechoic areas and intramyometrium on color Doppler. The left ovary showed three cysts, the largest was 1.7 cm. The CBC, RFT, LFT, PT, and PTT were normal.

The patient was referred to our Medical Oncology department for chemotherapy with a diagnosis of metastatic choriocarcinoma. Multiple drug regimen consisting of etoposide, methotrexate, actinomycin, cyclophosphamide, and vincristine was started. The patient required a total of 10 courses. Her last course ended in July, 2007 when she was asymptomatic, the lung shadows had disappeared, and the \( \beta \)-hCG was negative.

Her last visit to the follow-up clinic was in February, 2010, at 42 years of age, when she complained of six-months of amenorrhea and mood changes. \( \beta \)-hCG was negative, but the FSH was 36 IU/ml. She was considered to be in the phase of menopause and was given a further follow-up appointment after 3 months.

**DISCUSSION**

The cause of molar pregnancy is unclear; however, there are several risk factors. Molar pregnancies occur at extremes of the childbearing age. For women over 40 years of age, there is a 10-fold increase, compared with only 1.3-fold increased risk in teenagers.\(^9\) Other factors postulated to increase the risk of HM have included diet, gravidity, and contraception.\(^{2,5}\)

The incidence of recurrent molar pregnancy ranges from 5- to 40-fold increase in the current literature.\(^{22}\) In a report from the United Kingdom for women who had already had two molar pregnancies, the subsequent risk increases to 1 in 6.5 pregnancies.\(^{18}\) This risk diminishes if there is a normal pregnancy following the HM. Familial predisposition has recently been evaluated. Familial recurrent HM are considered exceedingly rare, with only 21 families reported in the medical literature. In these cases, the HM are diploid, but biparental, rather than androgenetic in origin. These patients appear to have an autosomal recessive condition, causing them to have recurrent molar pregnancies and they have very little chance of a successful pregnancy. However, this patient had no known family history of recurrent HM. Genetic studies suggest mutations in the NLRP7 gene, also known as NALP7 gene, which is located on chromosome 19q13.3–q13.4, a maternal gene, as a cause of Familial biparental HM, and possibly responsible for causing recurrent spontaneous abortions, stillbirths, and intrauterine growth retardation.\(^8\)

Follow up of patients with HM by measuring serial \( \beta \)-hCG levels is very crucial to allow early detection of persistent gestational trophoblastic disease (PTD) which has high potential to malignant change. Malignant transformation may be life-threatening to the mother and needs urgent treatment. Patients with complete molar pregnancies have an increased risk of PTD, considered to be 5% compared with patients with partial molar pregnancies where it is <1%.\(^3\)

Women who receive chemotherapy for GTD are likely to have an earlier menopause.\(^9\) Furthermore, multiagent chemotherapy which includes etoposide increases the risk of developing secondary cancers, such as acute myeloid leukemia, colon cancer, melanoma, and breast cancer for those who survive more than 25 years.\(^{18}\) These risks would necessitate long-term follow-up of these patients treated with chemotherapeutic agents. Our patient started to develop early menopause as diagnosed in her last visit.

In conclusion, doctors diagnosing and managing molar pregnancies should be aware of the potential malignant transformation and the genetic predisposition for early detection and proper referral and counseling regarding the prognosis of future pregnancies.

**ACKNOWLEDGMENT**

The author would like to thank Professor M.S. Rahman, Consultant obstetrician and gynecology/oncology, and Dr. J Rahman Associate Professor, Consultant Obstetrics and gynecology, University of Dammam, for their continuous support and advice during the write up of the manuscript.
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How to cite this article: Al-Ghamdi AA. Recurrent hydatiform mole: A case report of six consecutive molar pregnancies complicated by choriocarcinoma, and review of the literature. J Fam Community Med 2011;18:159-61.

Source of Support: Nil, Conflict of Interest: Nil