

## Recurrent Molar Pregnancy: An Obstetric Dilemma?

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### ABSTRACT

Approximately 1% of women with a molar pregnancy may have a recurrence. Chemotherapy is not indicated for recurrent molar pregnancies. An adequate interconception interval is important to ensure that the serum beta-human chorionic gonadotropin ( $\beta$ -hCG) from a new pregnancy does not interfere with the follow-up of the molar pregnancy that is done to detect persistent disease. We discuss the case of a nulliparous woman who had four molar pregnancies and her future reproductive options.

**Keywords:** Gestational trophoblastic disease, Recurrent molar pregnancy, Assisted reproductive technologies, Fertility issues.

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### INTRODUCTION

The incidence of gestational trophoblastic disease (GTD) varies from 0.6 to 2/1,000 pregnancies worldwide.<sup>1</sup> The risk of persistent trophoblastic disease varies from 20% after complete hydatidiform mole to 4% after partial hydatidiform mole.<sup>1</sup> The recurrence risk after one molar gestation is around 1%.<sup>1</sup> We present the case of a woman with four molar pregnancies to discuss the prognosis and fertility options.

### CASE REPORT

A 26-year-old nulliparous lady presented to us at 9 weeks of gestation in her fourth pregnancy, which was an assisted conception (ovulation induction). She gave a history of three histologically confirmed molar pregnancies elsewhere in the past 6 years. We could not, however, access obstetric and management details of these previous pregnancies. Prior investigations revealed her blood group to be O positive and karyotype of both partners to be normal. Ultrasound in the fourth pregnancy was suggestive of partial mole with clots inside the uterine cavity. Her serum beta-human chorionic gonadotropin ( $\beta$ -hCG) was 2,15,560 mIU/ml and histopathological examination (HPE) revealed chorionic villi with polar trophoblastic proliferation with no evidence of molar change or malignancy. Serum beta-hCG

normalized in 11 weeks. Her fifth pregnancy, 2 years later, ended in a missed miscarriage at 9 weeks. The beta-hCG, which was 76,750 mIU/ml normalized after 16 weeks. HPE showed products of conception corresponding to first-trimester of pregnancy.

She conceived for the sixth time 9 months later and had a molar pregnancy complicated by hyperthyroidism. Her thyroid profile showed thyroid stimulating hormone (TSH) of 0.1 mIU/ml and elevated free T3 and free T4 levels and HPE confirmed partial molar tissue. The initial beta-hCG of >2,00,000 mIU/ml fell to 20,015 mIU/ml in 10 days and we did not resort to chemotherapy. The patient was followed up with weekly beta-hCG titers till three consecutive values were negative and monthly thereafter for 6 months.

### DISCUSSION

The risk of a second molar pregnancy ranges from 0.7 to 1.8%.<sup>2,3</sup> This risk is highest in the second year after diagnosis and increases to 10% after two molar pregnancies.<sup>3</sup> The risk of recurrence is higher for women of Indian and Pakistani origin and those with blood group B.<sup>2</sup> Around 81% of the recurrent moles may have a similar histology after complete moles and 68% of the recurrent moles may have a similar histology after partial moles.<sup>3</sup> A complete mole may recur as a partial mole or a choriocarcinoma or a complete mole.<sup>2</sup>

Routine use of prophylactic chemotherapy at the time of molar evacuation is controversial as the tumors persist in only 20% of women. Chemotherapy may be useful in the management of high-risk complete moles with serum beta-hCG >10<sup>5</sup> mIU/ml, especially when hormonal follow-up is unavailable or unreliable. In our case, we did not administer chemotherapy although the initial beta-hCG titers in the sixth pregnancy were high as there was a clinically satisfactory drop in titers. Repetitive molar pregnancy is not an indication for chemotherapy unlike persistent disease which definitely warrants it.<sup>4</sup>

Pregnancy is permissible after an additional 6 months follow-up, if beta-hCG falls by one log per week and becomes negative by 8 weeks. The woman requires at least 2 years follow-up, if the fall in titers is slow and takes more than 8 weeks.<sup>5</sup> This case had adequate spacing between pregnancies.

The molar chromosomes are entirely of paternal origin in a complete mole and the extra haploid set is usually derived from the father in a partial mole.<sup>1</sup> An oocyte defect

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has been suspected after recurrent GTD due to abnormal triploid embryos after *in vitro* fertilization (IVF) of the retrieved oocytes raising the possibility that donor oocyte IVF could be an alternative.<sup>6</sup> Intracytoplasmic sperm injection (ICSI) coupled with preimplantation confirmation of diploidy (guards against partial moles) and selection against transfer of 46 XX embryos (prevents complete moles) was employed to prevent a repeat molar pregnancy in a patient with two previous episodes of GTD.<sup>7</sup>

Although most complete moles are androgenetic in origin, highly recurrent hydatidiform moles, which can be familial are biparental variants.<sup>8,9</sup> There have been reports of women with up to seven molar pregnancies.<sup>9,10</sup> The likelihood of having a normal pregnancy in the future appears to be remote in these couples.

Risk factors have been described for persistence but have not been described for predicting recurrence of molar pregnancy. Donor oocytes and assisted reproductive technologies are still costly and may not be a viable alternative for many women with molar pregnancies. Counseling on subsequent pregnancies remains an obstetric dilemma that has to carefully consider the needs of the woman, the family, and the costs involved besides the obvious psychological aspects of a recurring miscarriage.

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