Recurrent Hydatiform Mole: Report of A Case with Fourth Recurrence

Rengin KARATAYLI, Kazım GEZGİNÇ, Dilay GÖK, Ali ACAR

Konya, Turkey

In this report, it is objected to demonstrate 4th recurrence of molar pregnancy in a patient with a past history of 3 suction curettages for 2 complete and 1 partial moles. A 31-year-old woman was referred to our hospital with diagnosis of mole. There was no history of consanguinity. The mother of the patient had history of molar pregnancy and both sisters had primary infertility and IVF failures. Karyotype analysis of the patient and her husband was normal. The calculated serum β-hCG level was 188000IU/ml and she had an endometrial thickness of 40mm with a crumb like image. Thyroid function tests were normal. Suction curettage was performed and histopathological examination revealed complete HM. The patient is still being followed up with serial serum β-hCG levels. Families who have recurrent molar pregnancies should be informed about that subsequent pregnancies are at increased risk of having molar conception.

Key Words: Recurrent molar pregnancy, Diagnosis, Treatment

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Introduction

Hydatiform mole (HM), the most common form of gestational trophoblastic neoplasia, is characterized by atypical proliferation of placental villi and absence of, or abnormal, embryonic development.[1,2] Based on histology and karyotype data, HM is divided into two types: complete hydatidiform moles (CHM) and partial hydatidiform moles (PHM). Complete moles are usually diploid and androgenetic, demonstrating minimal embryonal development with hydropic chorionic villi and trophoblastic hyperplasia. Partial moles are usually paternally derived triploid conceptions in which embryonic development occurs in association with trophoblastic hyperplasia.

The etiology of HM is still unknown. Several epidemiologic risk factors for the development of molar pregnancy are recognized, but at present the exact mechanism is unclear. It is known that previous HM increases the risk of recurrence.[3] Several groups have looked at the incidence of recurrent molar pregnancies, and data from these studies indicate that approximately 1.3-2% of mothers who have had a molar pregnancy would be expected to have a recurrence.[4,5] We report a case which a patient had recurrent partial molar pregnancies without having a normal viable pregnancy.

Selcuk University Meram Medical School, Department of Obstetrıcs and Gynecology, Konya

Address of Correspondence: *Rengin Karatayl*ı
Selçuk University Meram Medical School, Department of Obstet. and Gynecol Akyokuş, Konya
renginkaratayli@hotmail.com

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Case Report

A 31-year-old woman with gravidity 7, parity 0, abortion 3 and suction curettage 3 was referred to our hospital with diagnosis of mole. The history revealed that patient had experienced three consecutive molar pregnancies, in 2001, 2003 and 2010. For all three, she had conceived spontaneously with the same partner. Her husband was a 30-year-old healthy man. There was no history of consanguinity. Family history revealed that her mother had history of molar pregnancy and her both sisters had primary infertility and IVF failures. Karyotype analysis of the patient and her husband was normal.

In 2001, she had a missed abortion in her first pregnancy at 9 weeks of gestation, but histopathological examination revealed a PHM. The serum β-human chorionic gonadotropin (β-hCG) level was within normal limits 3 months after evacuation. In 2003, she has admitted to hospital with the complaint of missed menses for 6 weeks and vaginal bleeding. Suction curettage was performed. Histopathological examination revealed CHM. After these hydatiform moles in 2005, 2007 and 2009 she was done revision curretage for 3 consequent missed abortions. Histopathologic examinations of all three pregnancies revealed decidual reaction. In 2010 another molar pregnancy was diagnosed by ultrasonography. Molar pregnancy was confirmed histopathologically after evacuation of the uterus by aspiration and curettage at the 11th week of gestation. Further histopathologic examination revealed CHM. In her last application to our clinic she was so desperate and in depression. The calculated serum β-hCG level was 188000IU/ml and she had an endometrial thickness of 40mm with a

crumb like image. Renal and liver function tests, thyroid function testes, hemogram, and chest x-ray were all within normal limits. So the suction curettage was performed and histopathological examination revealed CHM. The patient is still being followed up with serial serum β-hCG levels.

Discussion

Hydatiform moles are abnormal conceptions, which occur in about 1 in 500-1000 pregnancies.[1] This incidence varies between ethnic groups and reaches 1 in every 250 pregnancies in Eastern Asia.[1,2] After a molar pregnancy, the risk of further complete and partial mole rises to 1-2%. After two molar gestations, the risk of a third mole is 15-20%, and changing the partner does not decrease the risk.[6]

PHMs are nearly all triploid and occasionally tetraploid consisting of both maternal and paternal DNA. In PHMs, the uterus is often not enlarged for gestational age and vaginal bleeding tends to occur in the second trimester, and occasionally patients present with a missed or incomplete abortion.[7] CHMs are nearly always androgenetic in origin and result from the fertilization of an ovum lacking maternal genes by a single sperm, 23X, which then duplicates to form the homozygote 46XX. Very occasionally the CHM is biparental in origin, when the maternal nuclear DNA is retained. In 25% of cases, fertilization can occur by two spermatozoa, resulting in either the 46XX or 46XY genotype; the 46YY genotype has not yet been reported in cases of CHM.[8]

Familial recurrent cases of HM are extremely rare. Findings from some studies show that patients with recurrent disease can have biparental molar rather than typical androgenetic disease, which might be familial or sporadic.[9] Genetic studies in such families showed that the related genes are at chromosome 19q13.3-13.4,31 and subsequent analysis noted mutations in this region.[10] The function of the normal protein and the mechanism by which mutations are associated with imprinting abnormalities and gestational trophoblastic disease are unknown. Data show clustering of mutations in the leucine-rich region of NLRP7, suggesting that this region is crucial for normal function.[11] Some androgenetic diploid complete moles and possibly even triploid partial hydatiform moles might also carry NLRP7 mutations, but confirmation from large studies is needed.

N.J Sebire at all[4] studied women having a pregnancy affected by a histologically confirmed complete or partial hydatiform mole may be counseled that the risk of repeat mole in a subsequent pregnancy is about 1 in 60 and if this were to occur, the majority of cases will be of the same type of mole as the preceding pregnancy. However, >98% of women who become pregnant following a molar conception will not have a further hydatiform mole and these pregnancies are at no increased risk of other obstetric complications.[12]

The classical macroscopic 'bunch of grapes' appearance is usually seen when molar pregnancy presents in the second trimester, and is due to swelling of chorionic villi. Ultrasound plays an important role in helping to raise suspicion that a pregnancy is abnormal and could be molar, but in the absence of histology, this imaging modality is not diagnostic. Suction curettage is the preferred method of evacuation irrespective of uterine size in patients with suspected HM who want to preserve fertility.[13] Intraoperative ultrasonography can reduce the risk of uterine perforation. Patients who are rhesus-negative should receive rhesus immunoglobulin at the time of evacuation because rhesus D factor is expressed on trophoblast. Hysterectomy is rarely recommended but might be considered for women who do not want further children or have life-threatening hemorrhage.[14]

Some women who miscarry or have medical terminations will have had unsuspected molar pregnancies. Because ultrasonography cannot reliably confirm molar disease and histological examination of products might not be done after pregnancy termination, delayed diagnosis of gestational trophoblastic neoplasia, and hence substantial morbidity with the need for complex chemotherapy and surgery, can result. Histological examination after every termination would be impracticable, so checking of hCG concentrations at 3-4 weeks after treatment to ensure a return to a value within the normal range is recommended.

In conclusion, the etiology of recurrent HM remains obscure, and further studies at the molecular level are needed. Families who have recurrent molar pregnancies should be informed about the subsequent pregnancies that past molar pregnancies increase the risk of having a molar conception on the other hand when they become pregnant after a molar conception these pregnancies are at no increased risk of other obstetric complications.

Tekrarlayan 4. Molar Gebelik: Olgu Sunumu

Biz bu olgu sunumunda 2 kez komplet, 1 kez parsiyel molar gebelik geçirmiş 4. reküran molar gebelikli bir hastayı sunmayı amaçladık. 31 yaşında hasta molar gebelik ön tanısı ile kliniğimize sevk edildi. Hastanın anamnezinden daha önce 2 kez komplet, 1 kez parsiyel molar gebelik geçirmiş olduğu, eşi ile arasında akrabalık olmadığı öğrenildi. Hastanın soygeçmişinde annesinin de 1 kez molar gebelik geçirdiği, 2 kız kardeşinin de primer infertil olup, tekrarlayan IVF başarısızlıkları olduğu öğrenildi. Hastanın ölçülen serum β-hCG seviyesi, 188.000 IU/ml olarak geldi. Bakılan ultrasonografide endometriyal kalınlık 40mm olarak ölçüldü ve ekmek içi görünümü mevcuttu. Tiroid fonksiyon testleri normal sınırlarda idi. Hasta ve eşinin karyotip analizleri normal olarak bildirildi. Hastaya genel anestezi altında suction küretaj yapıldı. Patolojisi komplet molar ge-

belik olarak bildirildi. Bu nedenle molar gebelik geçirmiş hastalar sonraki gebelikleri konusunda bilgilendirilmelidirler.

Anahtar Kelimeler: Tekrarlayan Molar Gebelik, Tanı, Tedavi

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