OLGU SUNUMU CASE REPORT

DOI: 10.24074/tjrms.2023-95782

Recurrent Molar Pregnancy Repeated Seven Times in the Same Patient

Aynı Hastada Yedi Kez Tekrar Eden Rekürrent Molar Gebelik: Olgu Sunumu

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ABSTRACT

Molar pregnancies are benign trophoblastic diseases associated with a risk of malignant transformation. Two or more molar pregnancies are defined as recurrent molar pregnancies (RMP). The genetic mutation rate is very high in these patients. RMP does not always require chemotherapy. In the case presented, the woman had seven molar pregnancies and had no family history. It describes two maternal effect genes, NLRP7 and KHDC3L, responsible from familial cases of recurrent HMs (RHMs). Patient request and according to the results of genetic analysis in patients diagnosed with recurrent moles, IVF or oocyte donation is recommended. However, the couple was counseled for their adoption.

Keywords: Molar pregnancy, recurrent molar pregnancy, IVF, oocyte donation

ÖZET

Molar gebelik malign transformasyon riski bulunan bening trofoblastik hastalıktır. İki veya daha fazla tekrarlanırsa, tekrarlayan molar gebelik olarak tanımlanır ve genetik mutasyon oranı yüksek oranda görülmektedir. Tekrarlayan molar gebelik her zaman kemoterapi ihiyacı doğurmaz. Sunduğumuz olguda hastanın histo-patolojik rapor edilen toplam yedi molar gebelik öyküsü olsa da, aile öyküsü yoktu. Tekrarlayan molar gebeliklerden NLRP7 ve KHDC3L genleri sorunlu olduğu bilinmektedir. Genetik analiz sonuçlarına göre tekrarlayan molar gebelik teşhisi konan hastalarda tüp bebek veya oosit donasyonu önerilir. Ayrıca evli çifte çocuk edinmeleri için danışmanlık da verildi.

Anahtar Kelimeler: Molar gebelik, tekaralayan molar gebelik, IVF, oosit donasyonu

Hydatidiform mole (HM) is characterized by varying degrees of trophoblastic proliferation and vesicular swelling of placental villi that occur during pregnancy. There are two forms of HM; complete HM (CHM) and partial HM (PHM). This classification is based on the following features trophoblast proliferation and presence or absence of fetal tissue.[1] Diagnosis is usually made after histopathological examination of the specimens. Genetically, CHM and PHM are different. CHM is an androgenetically diploid (two sets of paternal chromosomes) while PHM is triploid (one maternal and two paternal chromosomes).[2] If two or more molar pregnancies are repeated, it is defined as a recurrent molar pregnancy. RHM is caused by genetic disorders. So far, three maternal-effect genes, NLRP7, KHDC3L, and more recently PADI6, have been identified as responsible for RHM. Molecular genetic research is important in terms of treatment and prognosis in these patients. Informed consent was obtained from the patients.

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Peer review under responsibility of Turkish Journal of Reproductive Medicine and Surgery.

Received: 29 Jan 2023 ***Received in revised form:*** 08 May 2023 ***Accepted:*** 22 May 2023 ***Available online:*** 30 May 2023

CASE PRESENTATION

A thirty-two-year-old woman has been married for 13 years. She had a child from her first pregnancy and was delivered vaginally at 39 weeks of pregnancy. Her second marriage was six years ago and she had six (G8P1A6) abortions. She gave a history of six previous histologically confirmed molar pregnancies. Histopathological diagnosis was partial hydatidiform moles in five and complete mole in one. The patient has no family history. Ultrasound was performed on the patient with vaginal bleeding and a diagnosis of molar pregnancy was made histopathologically.

In laboratory examinations, serum human chorionic gonadotropin (beta-hCG) was 93,000 mIU/L (milliinternational units/L), TSH was 1.15 mIU/L, complete blood count, kidney and liver function tests were normal. Chest X-ray was also normal. Vacuum aspiration was performed and histological diagnosis was PHM.

Post-procedure, serum beta-hCG levels of the patient were measured weekly until undetectable and then monthly for 6 months. A molecular study of possible causative variants was proposed. But the family refused.

DISCUSSION

Hydatidiform mole (HM) is the most common sporadic and occurs in 1 in 1000 pregnancies characterized by hydropic swelling of the placental villi.[3] RHM is defined by the occurrence of at least two molar pregnancies in the same patient. After a molar pregnancy, the risk of HM increases to 1-2% in the next pregnancy.[4] CHM pregnancy rarely recurs and this probability has been reported as 0.91 percent in the literature. The probability of a PHM pregnancy to recur is lower as 0.28 percent.[5] Some studies revealed that the risk is associated with CHM rather than PHM.[6] There are two groups of recurrent HM: with and without a positive family history.[7] Patients with a positive family history of recurrent CHM and usually biparental, who have negative family history of recurrent moles usually have androgenetic CHM.[7,8] But in the current report patient's histological result was five PHM and one CHM. And patient had no family history. The utility of microsatellite genotyping as a stand-alone method for accurate classification of hydatidiform mole has been reported.[9-11] The patient carries an autosomal recessive mutation that causes the development of complete hydatidiform moles during pregnancy.[12] Three genes have been identified as responsible for RHM, NLRP7, KHDC3L and more recently PADI6.[13,14] This distinction is important because patients with androgenetic CHM may have subsequent normal pregnancies and can reduce the risk of further CHM with IVF and PGD while patients with FRHM need to consider IVF with ovum donation to achieve a normal pregnancy.[15,16]

Studies from various groups and populations concur that NLRP7 is a major gene for this condition and is mutated in 48-80% of patients with at least two HM pregnancies.[14] Mutations in both alleles of NLRP7 cause recurrent biparental HM.[17] Also heterozygosity for NLRP7 NSVs has been observed in patient with classic HM, diploid biparental HM and in patient with NMM, indicating that some NLRP7 NSVs may be associated with these reproductive outcomes even in heterozygous states.[18] A male with NLRP7 compound heterozygous mutations in the present family has been found to have no reproductive problems, because NLRP7 is not required for normal spermatogenesis. A heterozygous NLRP7 mutation increases a woman's risk of early spontaneous miscarriage of reproductive function. Mutations in KHDC3L have previously been found in women with familial diploid biparental HMs.[19]

CONCLUSION

Although recurrent molar pregnancies are rare, there is an increased risk of cancer. Genetic analysis of these patients is very important in terms of prognosis. Because women with androgenetic CHM may have subsequent normal pregnancies and can reduce the risk of further CHM with IVF and PGD while patients with FRHM need to consider IVF with ovum donation to achieve a normal pregnancy.[15,16]

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that pro-

vides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Aytaj Jafarzade;* ***Design:*** *Aytaj Jafarzade;* ***Control/Supervision:*** *Tamer M. Mungan, Aydan Biri;* ***Data Collection and/or Processing:*** *Aytaj Jafarzade;* ***Analysis and/or Interpretation:*** *Aytaj Jafarzade;* ***Literature Review:*** *Aytaj Jafarzade;* ***Writing the Article:*** *Aytaj Jafarzade;* ***Critical Review:*** *Aytaj Jafarzade;* ***References and Fundings:*** *Aytaj Jafarzade.*

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