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**Case Report**

# Familial Highly Recurrent Molar Pregnancy: A Rare Clinical Condition

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**ABSTRACT:**

Familial Recurrent Hydatidiform Mole (FRHM) is an extremely rare autosomal recessive condition. In this report, we present an unusual case of a 29 years old woman, Gravida 11, with 11 consecutive molar pregnancies without a single intervening viable gestation. Patient was admitted in labor room and evaluated for the 11th consecutive molar pregnancy. After careful examination and assessment, Manual Vacuum Aspiration was planned for the patient. The samples were sent for the histopathological examination and the results confirmed complete molar pregnancy. The facility of genetic studies was not available in the hospital. The patient was counseled for the high risk of GTN and subsequent need for hysterectomy, and referred to the tertiary care hospital for genetic testing and regular follow-up with serial serum human chorionic gonadotropin (beta-hCG) hormone estimation. The couple was also counseled for hysterectomy and adoption.

**Keywords:** hydatidiform mole, familial recurrent molar pregnancy, persistent trophoblastic disease, complete mole, partial mole

## INTRODUCTION:

Gestational Trophoblastic Disease (GTD) is a manifestation of an aberrant fertilization event that leads to proliferative process and potentially to an invasive neoplasm. The Hydatidiform Mole (HM) is the most common type of GTD (80% of the cases) [1]. Raised levels of Beta HCG are associated with all the types of GTD. The early symptoms of molar pregnancy include Hyperemesis Gravidarum, sepsis, pervaginal bleeding [2]. The early detection of HM can be done by ultrasound by the end of the first trimester typically showing central, heterogeneous mass with anechoic spaces, corresponding to hydropic villi. In this report, the discussed patient is married to his paternal cousin for 15 years with positive family history of GTD and having highly recurrent molar pregnancy.

## CASE REPORT:

A 29-years old Gravida 11, Para 0, muslim female with 10 previous hydatidiform moles, was presented to us at 8th week of gestation, with the complaint of per-vaginal bleeding for two days. The Pelvic Ultrasound showed uniform snowstorm appearance in uterine cavity, typical anechoic spaces suggestive of Hydatidiform mole Figure.1. The ovaries were devoid of theca lutein cysts. Her pre-evacuation serum Beta-HCG level was 2790.30 mIU/ml. Her vitals were within normal range; BP= 110/70 mmHg, PR= 98/min, RR= 18/min, $SaO_2$ = 96% at room air. Her pre-operative baseline investigations were also normal, Hb=11 mg/dl, PT= 11, APTT= 38,

INR=1, Hepatitis B and C status = Negative. Liver and renal function tests and Chest X-ray PA view were unremarkable. Patient was diagnosed with 11th consecutive molar pregnancy and counseling of the couple was done. Manual Vacuum Aspiration (MVA) was performed after taking the informed written consent and the sample was sent to the lab for histopathological examination which later revealed Complete Mole. The post operative serum Beta HCG level started to regress gradually and after 6 months, the Beta HCG level was 233.6 mIU/ml.

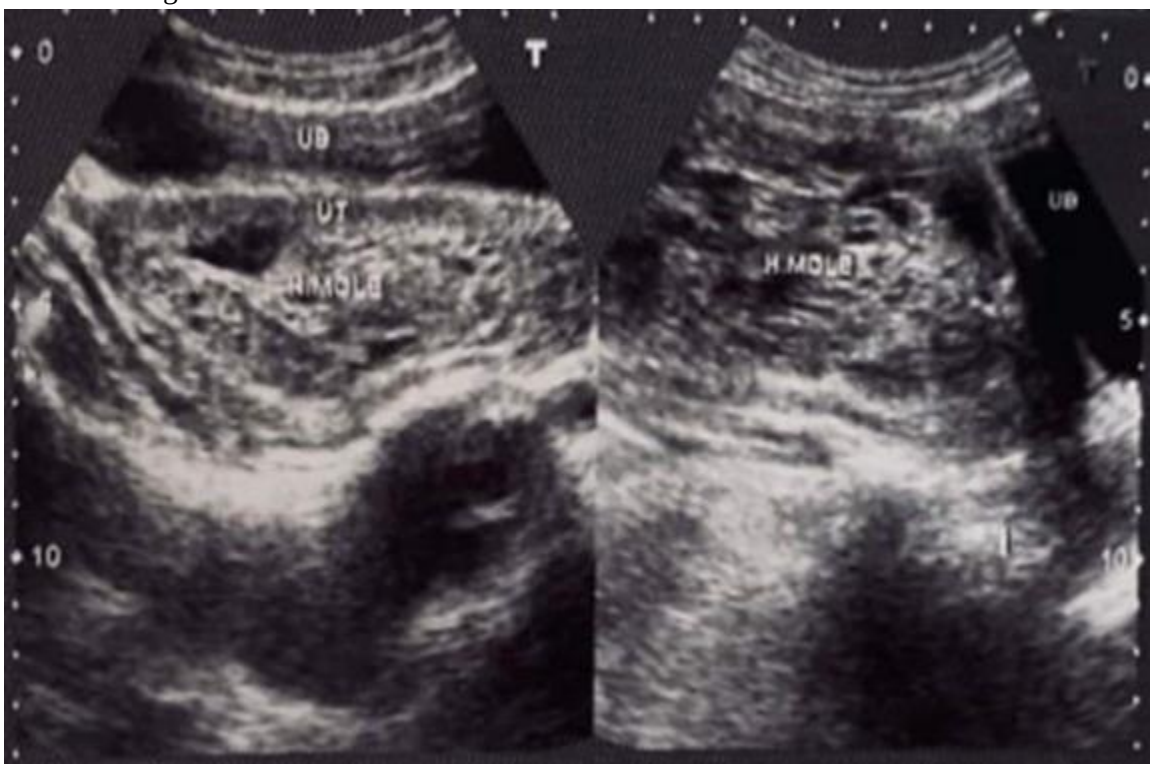


**Figure.1. Transvaginal Sonography (TVS) showing uniform snowstorm appearance in the uterine cavity**

Her previous 10 molar pregnancies occurred over the period of 15 years. Those were evacuated somewhere else. Histopathology of all the samples were done except for the first one. The details of previous 10 HMs are summarized in Table.1.

| Year | Gestational Age | Ultrasound Findings | Procedure Done | Histopathological Findings |
|---|---|---|---|---|
| 2006 | 1st Trimester | Molar Pregnancy | D&E | Not performed |
| 2007 | 1st Trimester | Molar Pregnancy | D&E | Partial Mole |
| 2008 | 1st Trimester | Molar Pregnancy | D&E | Partial Mole |
| 2009 | 1st Trimester | Molar Pregnancy | D&E | Partial Mole |
| 2010 | 1st Trimester | Molar Pregnancy | D&E | Partial Mole |
| 2011 | 1st Trimester | Molar Pregnancy | D&E | Partial Mole |

| | | | | |
|---|---|---|---|---|
| 2012 | 1st Trimester | Molar Pregnancy | D&E | Partial Mole |
| 2015 | 1st Trimester | Molar Pregnancy | D&E | Partial Mole |
| 2017 | 1st Trimester | Molar Pregnancy | D&C | Complete Mole |
| 2018 | 1st Trimester | Molar Pregnancy | MVA | Complete Mole |
| 2020 | 1st Trimester | Molar Pregnancy | MVA | Complete Mole |

**Table.1. The details of previous 10 HMs D&C: Dilatation and Curettage; D&E: Dilatation and Suction Evacuation; MVA: Manual Vacuum Aspiration**

Her sister-in-law (Paternal Cousin) also had a history of 3 consecutive HMs with no viable gestation in between. Due to familial, highly recurrent nature of these moles with no viable conceptions in both relatives, it is likely to be biparental in origin. The genetic and molecular studies of this clinical condition were not feasible in our set-up so we counseled and referred the patient to the tertiary care hospital for the genetic workup, and to explore the possibility of Donor oocyte in-vitro fertilization (IVF). Adoption was also suggested as an alternative option.

## DISCUSSION:

Hydatidiform Mole (HM) is an aberrant fertilization of ovum and sperm characterized by excessive proliferation of placental villi, hyperplastic villous trophoblasts, and severely stunted or absent embryonic tissue growth [1]. HM is further subdivided into 2 types: Complete HM (CHM) and Partial HM (PHM) [2]. CHM are usually androgenetic and are entirely paternal genome derived. However, in Partial HM, two sperms fertilize a single oocyte. The diploid parental genome and haploid maternal genome constitutes the triploid genome with 3 copies of each chromosome. When the two-third of the chromosomal material is derived from the paternal genome, it results in regressed placental and fetal growth along with unregulated human trophoblastic growth [3]. In CHM, macroscopically the chorionic villi get transformed into clusters of vesicles with variable dimensions like bunch of grapes. The uterine enlargement exceeds the gestational age. In 30% of the cases, theca lutein cyst is also observed [4]. There is a complete absence of fetal or embryonic tissue development. Microscopically, the villi is edematous and enlarged with diffused, outrageous growth of trophoblastic tissue. No fetal tissue, RBCs, or amnion are produced during the first trimester. Whereas in PHM, the molar pattern is not diffused, its slight or focal. Excessive uterine enlargement and theca lutein cysts are uncommon. Abnormal Fetal or embryonic tissue is present [4, 5]. In Asian countries, the incidence of molar pregnancy is 1 in 160, which is 10 times higher than in Europe and North America [1, 2]. In United States, the incidence is 1 in 1500 whereas in UK it is 1 in 600 pregnancies. The risk of HM in next pregnancy increases with every subsequent molar pregnancy by 1-2% [3, 4]. The risk of recurrence of HM is slightly higher in case of partial mole as compared to complete mole. Likewise, the risk of HM in subsequent pregnancy decreases with a normal intervening conception. Complete HM has a comparatively higher tendency to progress into Persistent Trophoblastic Disease (PTD) and hence malignancy. Whether complete or partial HM, the Recurrent HM has remarkable clinicopathological as well as psychological implications, including risk of malignancy such as choriocarinoma, poor reproductive performance, early abortions, and significant mental trauma [6, 7]. Familial Recurrent HM (FRHM) is an extremely rare medical condition. Recurrence is defined by the occurrence of two or more molar pregnancies in the same patient regardless of her family history. To the best of our knowledge, there are only 21 affected families are reported with FRHM so far [8]. It is divided into 2 groups depending on the positive and negative family history for molar pregnancy. If the patient has positive family history of molar pregnancy and having recurrent moles and consanguinity, then it is probably

Bi-Parental Complete Hydatidiform Moles (BiCHM). If the patient does not have a family history of HM but still having recurrent moles then this it is usually Androgenetic Complete HM (AnCHM) [8, 9] AnCHM (46 XY, 46 XX) accounts for the 80% of the total incidences of the Complete HM. It occurs when sperm fertilizes with an anucleated oocyte resulting in the reduplication of parental chromosomes, called Monospermic Androgenetic Diploid (46, XX). Unlike BiCHM, AnCHM has some chance to have intervening normal pregnancy [9, 10]. The Bi-Parental HM (69 XXY, 69 XXX, or 69 XYY) is an Autosomal Recessive condition in female germ line with little to no chance of a normal, successful pregnancy. BiCHM has both the chromosomal components, maternal and paternal. In this case, a normal ovum is fertilized with either 2 or 3 sperms resulting in triploid or tetraploid genome [11]. Although the genetic studies/ karyotyping of the patient and her husband was not performed; but the history was suggestive of Bi-Parental HM. Also, it is important to perform genotyping of the molar tissue with polymorphic DNA markers to determine the parental origin and type of mole as the planning and decision of therapeutic options depends on it. The extensive genetic mapping of FBHM indicated defective locus at 19q13.4, localized to a single gene NALP7. This was the first gene defect identified as a cause of HM [12].

The risk of Persistent Trophoblastic Disease is 50% higher in the recurrent familial or sporadic HM. The respective histopathology and the invasiveness increase with every successive HM pregnancy. The incidence is particularly higher in South Asian, muslim females with history of extensive intermarriages [13]. If the patient with recurrent molar pregnancy develops Persistent Trophoblastic disease, then the chemotherapy is almost always suggested as an alternative therapeutic option. However, the recurrent molar pregnancy alone does not necessitate chemotherapy. That is why our patient was not given chemotherapy. Nevertheless, couple counseling was done and patient was referred to tertiary care hospital for the regular follow-up of Beta hCG, risk of GTN and option for hysterectomy, elaborating the significance of genetic workup and highlighting the risk of malignancy with every subsequent molar pregnancy [14, 15]

## CONCLUSION:

Recurrent Molar Pregnancy is a rare phenomenon. Every abnormal pregnancy and abortion results in the significant mental trauma and increased risk of malignancy. The role of genetic study is extremely important in the proper diagnosis and labeling of the pathophysiological background of the disease. The proper diagnosis facilitates the surgeon in the better planning of treatment and management as well as effective guidance and counseling of the couple regarding the possible options and outcomes.

## REFERENCES:


1. Helwani MN, Seoud M, Zahed L, Zaatari G, Khalil A, Slim R. A familial case of recurrent hydatidiform molar pregnancies with biparental genomic contribution. Human genetics. 1999 Aug;105(1):112-5.
2. Al-Hussaini TK, Abd El Aal DM, Van den Veyver IB. Recurrent pregnancy loss due to familial and non-familial habitual molar pregnancy. International Journal of Gynecology & Obstetrics. 2003 Nov 1;83(2):179-86.
3. Fisher RA, Hodges MD, Newlands ES. Familial recurrent hydatidiform mole. a review. 2004;2004:49.
4. Seoud M, Khalil A, Frangieh A, Zahed L, Azar G, Nuwayri-Salti N. Recurrent molar pregnancies in a family with extensive intermarriage: report of a family and review of the literature. Obstetrics & Gynecology. 1995 Oct 1;86(4):692-5.
5. Sebire NJ, Fisher RA, Foskett M, Rees H, Seckl MJ, Newlands ES. Risk of recurrent hydatidiform mole and subsequent pregnancy outcome following complete or partial hydatidiform molar pregnancy. BJOG: an international journal of obstetrics and gynaecology. 2003 Jan 1;110(1):22-6.
6. Eagles N, Sebire NJ, Short D, Savage PM, Seckl MJ, Fisher RA. Risk of recurrent molar pregnancies following complete and partial hydatidiform moles. Human reproduction. 2015 Sep 1;30(9):2055-63.
7. Van Der Smagt JJ, Scheenjes E, Kremer JA, Hennekam FA, Fisher RA. Heterogeneity in the origin of recurrent complete hydatidiform moles:

not all women with multiple molar pregnancies have biparental moles. BJOG: An International Journal of Obstetrics & Gynaecology. 2006 Jun;113(6):725-8.
8. Kumari S, Dhingra M, Ahmad SN, Singh A. Recurrent Molar in Five Consecutive Pregnancies–A Case Report. International Journal of Women's Health. 2020;12:171.
9. Rai L, Shripad H, Guruvayare S, Prashant A, Sunil A. Recurrent familial hydatidiform mole-a rare clinical problem. Journal of the Turkish German Gynecological Association. 2012;13(4):284.
10. Al-Hussaini TK, Abdel-Alim MA. Habitual complete molar pregnancy: a case report. Reproductive BioMedicine Online. 2001 Jan 1;3(2):133-5.
11. Garner EI, Goldstein DP, Feltmate CM, Berkowitz RS. Gestational trophoblastic disease. Clinical obstetrics and gynecology. 2007 Mar 1;50(1):112-22.
12. Buckley JD. The epidemiology of molar pregnancy and choriocarcinoma. Clinical obstetrics and gynecology. 1984 Mar 1;27(1):153-9.
13. Kalogiannidis I, Kalinderi K, Kalinderis M, Miliaras D, Tarlatzis B, Athanasiadis A. Recurrent complete hydatidiform mole: where we are, is there a safe gestational horizon? Opinion and mini-review. Journal of assisted reproduction and genetics. 2018 Jun;35(6):967-73.
14. Koc S, Ozdegirmenci O, Tulunay G, Ozgul N, Kose MF, Bulbul D. Recurrent partial hydatidiform mole: a report of a patient with three consecutive molar pregnancies. International Journal of Gynecologic Cancer. 2006 Mar 1;16(2).
15. Ambani LM, Vaidya RA, Rao CS, Daftary SD, Motashaw ND. Familial occurrence of trophoblastic disease-report of recurrent molar pregnancies in sisters in three families. Clinical genetics. 1980 Jul;18(1):27-9.