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Case Report:

Reproductive Wastage in Recurrent Partial Hydatidiform Mole: A Clinical Dilemma.

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Abstract: Recurrent partial Hydatidiform mole is an extremely rare clinical entity which represent a part of the gestational trophoblatic neoplasia spectrum. Since the first case was reported by Honore. LM in 1987 about eight cases of , recurrent partial moles have been reported in the English medical literature. Present two cases are the 9th and 10th case with recurrent partial moles to be described. We have discussed the aetiology, environmental factors, dietary habits , clinicopathologic features, the clinical dielemmas faced by us while counselling, follow up and pregnancy outcome in women presenting with two and three recurrent partial moles respectively. We have also reviewed the literature.
Key Words: Recurrent Partial Hydatidiform moles; Dietary habits; Pregnancy outcome.

Introduction

The incidence of hydatidiform mole varies from 2 up to 12 per 1000 pregnancies in Southeast Asia, Indonesia, India and Turkey.(1) Recurrent partial hydatidiform (RPHM) moles are extremely rare.(2) First case of recurrent partial mole was published by Honore LH in 1987.(3) To date 8 cases of recurrent partial hydatidiform moles have been reported(4-8) in the English medical literature. We present the ninth and the tenth cases of recurrent partial moles, who successfully achieved normal pregnancies.

Case Report:

Case 1: A 25 years old, gravid 3,para 0, living 0 with two recurrent partial moles (histologically proven-2006, 2007) (Figure-1), presented with pregnancy corresponding to 10 weeks ,with inevitable abortion, for which suction curettage was done. It was a second-degree consanguineous marriage and all the three pregnancies were with the same partner. She had irregular cycles since menarche , used oral contraceptives for 10 months, blood group was B positive and thyroid profile was normal. Serum Beta humanchorionic gonadotrophin (S. β HCG) was 50 mIU/mL done one week after evacuation. Karyotyping was normal in both the partners. Partial hydatiform mole was confirmed histologically. She did not require additional treatment on follow up, as she was asymptomatic and had no elevation of S. β HCG levels for 6 months of follow up.

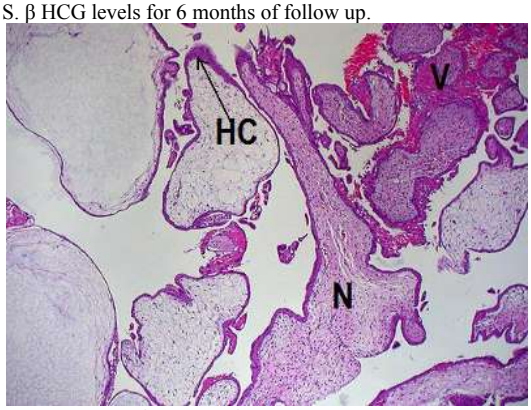

Figure-1: HC-focal proliferation and hydropic chorionic villi, V-vascularity is maintained. N-normal villi.

Case 2: A 27 years old gravid 1, para 0, living 0, had one partial mole (histologically proven-2006). She presented with bleeding per vaginum and a scan report of pregnancy of 9-10 weeks and absent fetal cardiac activity(Figure-2). She underwent medical method of termination of pregnancy, Histopathology was of a partial mole. She had a second degree consanguineous marriage and both the pregnancies were with the same partner. She was on oral contraceptives for cycle regulation for three years, her first cousin sister had a molar pregnancy. Karyotyping was normal in both the partners. Thyroid profile was normal. The S β HCG was 98,550 mIU/mL one week post evacuation (rare in partial moles), which made us suspect if she could progress to a persistent trophoblastic disease. However, on close follow up she had a satisfactory logarthimic S. β HCG fall, by 8 weeks following evacuation. She had normal beta hcg value by the 9

week . She was asymptomatic and did not require any further treatment. She was kept on close follow up for 6 months and maintained normal S. β HCG levels with no evidence of disease persistence.

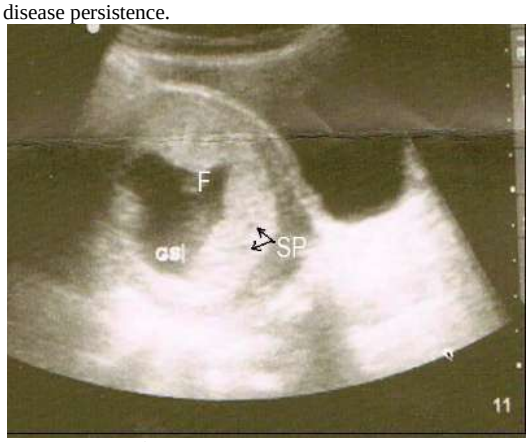

Figure-2: F-fetal component, SP- cystic spaces in the placenta.GS- gestational sac.

The clinical dilemmas faced by us when questioned by these women whether they can they have normal pregnancy and children were:

1. How to prevent these forms of reproductive wastage and reverse the infertility of women with recurrent moles?
2. Is it familial, so change the partner(socially not accepted)?
3. Should we consider IVF-Donor egg and sperms, Intracytoplasmic sperm injection (ICSI) and pre-implantation genetic diagnosis in this sub group of women. Very expensive?
4. What are the chances of persistence of the disease or the malignancy potential?

Therefore, after a complete search of literature we formulated a treatment protocol, follow up and counselling for these women as the expensive treatment modalities and socially unacceptable methods in a low resource setting was not possible.

These women belonged to the socioeconomically deprived group, surviving on a south Indian diet consisting of rice and sambhar followed by butter milk or coffee which are rich in phytates and some calcium ,poor in fat soluble vitamins, carotene. antioxidants and essential vitamins and minerals. Bioavailability of such a diet was questioned and hence, we emphasised on a balanced diet which included green leafy vegetables(50 grams), sprouts and lentils(150 grams), jaggery(50 grams) , one carrot per day, avoid coffee and alcohol. Barrier method was advised for contraception purpose for 6 months following normalization of the S. β HCG levels. Both had adhered to the advice. S.β hcg values and ultrasound of pelvis were normal at the end of 6 months. Both the women conceived spontaneously about a year and half after the diagnosis and are having living healthy babies(2010)

Discussion:

Both the cases, presented above have many clinical and social implications. First, recurrent consecutive partial HM is a rare clinical entity. Second, these women were desperate to have living children, as they felt psychologically betrayed due to recurrent pregnancy wastage and belonged to economically weaker section who could not afford expensive treatment methods. Third, these women had a risk for worsening of histology and possibility of persistence of disease had to be considered.

The excat etiology of HM is still unclear. Current data show the association of NLRP7 mutations with several types of hydatidiform moles and with triploid spontaneous abortions.(9) NLRP7 (NALP7) has been identified as the major gene involved in the inherited predisposition to recurrent molar pregnancies, a rare recessive condition in which affected individuals have complete hydatidiform moles of diploid biparental origin (BiCHM). NLRP7 mutations do not represent a major cause of androgenetic origin AnCHM.(10) Both the women and their partners had normal karyotype, further genetic analysis was not performed in our study.

Both women had same histology of partial moles as the preceding pregnancies and they did not have any pregnancy associated complications ,during antepartum, intrapartum or post partum. Follow up S. β HCG at 6th week post delivery and placental histology was normal. Similar experience has been reported by Sebire NJ et al and they also opined complete and partial moles are associated with similar recurrence risks as 1.9% and 1.7% respectively.(11)

There were no pathognomonic clinical features of these pregnancies, they were similar to other causes of abortion and were proved histopathologically as partial molar pregnancies. Some authors have reported hyperemesis and thyrotoxicosis during a partial molar pregnancy.(6) In both the cases average time of termination of pregnancy was 9-10 weeks, age was 25 and 27 years respectively. Authors have reported pregnancy between 8-18 weeks (3-8), age ranged from 25-39 years, 6 women had living children and 2 women were yet to have living issues, similar to our report. Five women had previous 2 partial moles, 1 had 3 previous partial moles, 2 had 4 previous partial moles, all reported with the same partners similar to our study. All women underwent surgical evacuation except one woman in our study who had medical method of termination of pregnancy (Table-1). High levels of serum beta HCG 98,550 miu/ml, was noticed in the second case, hence we had weekly serial monitoring of S. β HCG to diagnose persistent disease and need for chemotherapy, which would have an effect on further conception; similar experience has been reported by S Koc et al.(8)

There is conflicting evidence, regarding blood group B, irregular cycles and use of oral contraceptives, affected first cousin (familial or non familial) and a diet deficient (rice and sambhar) in proteins, multivitamins, carotene and antioxidants, excess use of beverages like coffee posing as risk factors.(1,2,12) May be a balanced diet rich in naturally available carbohydrates, proteins, vitamins, carotene, antioxidants, avoidance of coffee and alcohol for a period of 6-12 months pre-conceptionally, in the south Indian context, can hopefully improve the reproductive outcome as experienced in the present study.

We reasoned that the alternative options to prevent reproductive wastage in these women, like change of partner, was not socially acceptable. Reubinoff BE et al had developed a strategy for the prevention of repeated molar pregnancies by using intracytoplasmic sperm injection (ICSI) coupled with preimplantation genetic diagnosis (PGD) with fluorescence in-situ hybridization (FISH).(13) Due to financial constraints it was impossible in our study.

It is important to note 37 cases of partial hydatiform moles have required chemotherapy for persistent disease or for invasive partial moles. Hence, persistent Gestational Trophoblastic neoplasia requiring chemotherapy can occasionally occur after PHM; surveillance of all cases continues to be recommended. No choriocarcinoma has been reported following partial hydatiform moles.(8,14-17) With the help of this information from the literature we kept a close follow up of both the women for 6 months following normalization of S. β HCG and advocated the use of barrier contraceptives.

Table-1: Review of cases in literature(3-8).							
References	**Year**	**Age**	**GPAL**	**No. of Molar Pregnancies**	**Therapy**	**Chemotherapy**	**Gestational age at diagnosis**
Honore´(3)	1987	25	3, 1, 0, 1	2 Partial	Evacuation	—	18, 16
Honore´(4)	1988	26	4, 1, 1, 1	2 Partial	Evacuation	—	12, ?
		39	5, 3, 2, 3	2 Partial	Evacuation	—	10, 9
Rice et al.(5)	1989	26	3, 1, 0, 1	2 Partial	Evacuation	—	NR
Narayan et al.(6)	1992	27	4, 0, 0, 0	4 Partial	Evacuation	—	13, 8, 8, 7
Helwani et al.(7)	1999	NR	6, 2, 0, 2	4 Partial	Evacuation	—	NR
		27	4, 0, 0, 0	2 Partial	Evacuation	—	NR
S Koc et al(8)	2006	28	3, 0, 0, 0	3 Partial	Evacuation	MTX	9, 8, 11
Present case 1	2012	25	0, 1, 3, 2	3 partial	Evacuation	-	9-10
Present case 2	2012	27	0, 1, 2, 1	2 partial	Medical method	-	9-10
G-gravidity, P-parity, L-living children, A-abortion, NR- not reported, MTX-methotrexate, Evacuation - surgical							

Recurrent partial hydatiform molar pregnancies are a very rare clinical entity. Following simple methods like consumption of food rich in antioxidants, vitamins, minerals and carotene, avoiding use of caffeinated drinks and alcohol for at least 6 months prior to conception, may help to improve the quality of oocytes and sperms. Prompt counselling regarding the possibility of a higher recurrence compared to previous non molar pregnancies and need for a strict follow up as they stand a risk for worsening of histology and possibility of persistence of disease and if so need be, for prompt intervention, is called for. It is possible to have normal healthy living children following recurrent partial molar pregnancies.

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