Triplet Pregnancy with Partial Hydatidiform Mole Coexisting with Two Fetuses after Ovulation Induction and Intrauterine Insemination

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ABSTRACT

Partial hydatidiform mole with dichorionic twin fetuses is extremely rare condition, and only three cases have been reported before. Twenty- five years old primigravida having a trizygotic triplet pregnancy that has been conceived by ovulation induction and intrauterine insemination was referred to our department for threatened abortion. The fetus B with molar placenta has been selectively terminated at 11th weeks and the pregnancy was complicated with preeclampsia, hyperthyroidism, and culminated in spontaneous abortion at 20th weeks. After the abortion, the pathologic evaluation suggested partial mole, and genetic evaluation confirmed the diagnosis. The postpartum course complicated with persistent trophoblastic disease that well responded to four course of methotrexate therapy. The optimal management of partial hydatidiform mole coexistent with two fetuses is currently uncertain. The choice of continuing the pregnancy must be individualized, depending on the patient condition. These patients should be carefully followed after the pregnancy for persistent trophoblastic disease.

Keywords: Triplet pregnancy, Partial hydatidiform mole, Ovulation induction, Intrauterine insemination

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Introduction

Partial hydatidiform mole coexistent with two or more fetuses (PHM-TCF) is an extremely rare condition. Since only single case reports or series reported in the literature, the prevalence of this condition is unknown. With the widespread use of ovulation induction, and increasing availability of ultrasonography (US) in the follow- up for pregnancy, the incidence of PHM-CF will likely to increase. There have been several reports of a triplet or higher order pregnancy with a partial hydatidiform mole co-existent with two or more fetus.[1-3] To the best of our knowledge, three cases of triplet pregnancy with partial hydatidiform mole and coexistent fetuses were reported before. Moreover, partial hydatidiform moles are rarely associated with persistent gestational trophoblastic disease, with an estimated risk ranging 2-4%.[2]

With this background, we report on a case of triplet pregnancy with partial hydatidiform mole coexisting with two fetus, and review the related literature.

Case Report

25 years old, G1P0 women was admitted to the emergency department with the complaint of premature contraction. Her history revealed that she conceived by means of ovulation induction with 75U gonadotropin, and intrauterine insemination. She had had trichorionic, triamniotic pregnancy and multifetal pregnancy reduction was performed at 12 4/7 week by terminating fetus B which was smaller than fetus A and C, and had slightly vacuolar placenta. The pregnancy subsequently carried on as dichorionic diamniotic twin. She had undergone prophylactic Mc Donald cerclage operation due to short cervix at 14 weeks'. Initial US evaluation showed 20 weeks old dichorionic diamniotic twin pregnancies. The placentas were seen to be fused distally at the lateral uterine wall. The third placenta having molar appearance intersected two normal looking placentas at the fundal region (Figure 1). Her blood pressure was 160/100 mmHg, pulse rate 112/beat per minute, and dipstick urine analysis revealed (+++) proteinuria, and thus she was diagnosed as preeclampsia. She had severe hyperemesis gravidarum since 6 weeks'. Laboratory evaluation showed high Beta Human Chorionic Gonadotropin (β-hCG), 120903mIU/mL, Free Thyroxin (1.65 pg/mL, 0.88-1.72 ng/dL), and Free triiodothyronine (4.37ng/dL, range: 2.3- 4.2 ng/dL) levels with severely suppressed Thyroid Stimulating Hormone (0.006 mIU/L, range: 0.57- 5.6 mIU/L). She was ad-

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mitted to the obstetrics ward. Gynaecological examination revealed dilated cervix with a prolapsed membranes. The fetuses were expulsed shortly after the admittance. Pathological evaluation of the gestational products confirmed our antenatal diagnosis (Figure 2). Fluorescence in-situ hybridization analysis (Leica Cytovision, Imaging System, Heidelberger) of the paraffin embedded and thawed placental samples revealed three sets of 21,13 and X chromosomes which is consistent with triploidY (Cytocell, Cambridge).

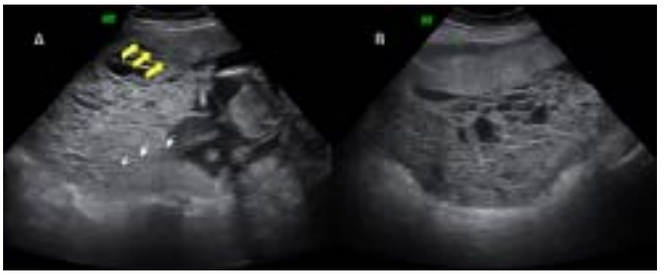

Figure 1: Transabdominal ultrasonography at 20 gestational weeks' showing demarcation lines between molar and two normal placentas. Yellow arrows indicates border between fetus 1 and fetus 2, and white arrows demarcates the border between fetus 2 and fetus 3 (A) Slight angulation of the probe superiorly shows the relation between placenta 2 and placenta 1 in full view (B).

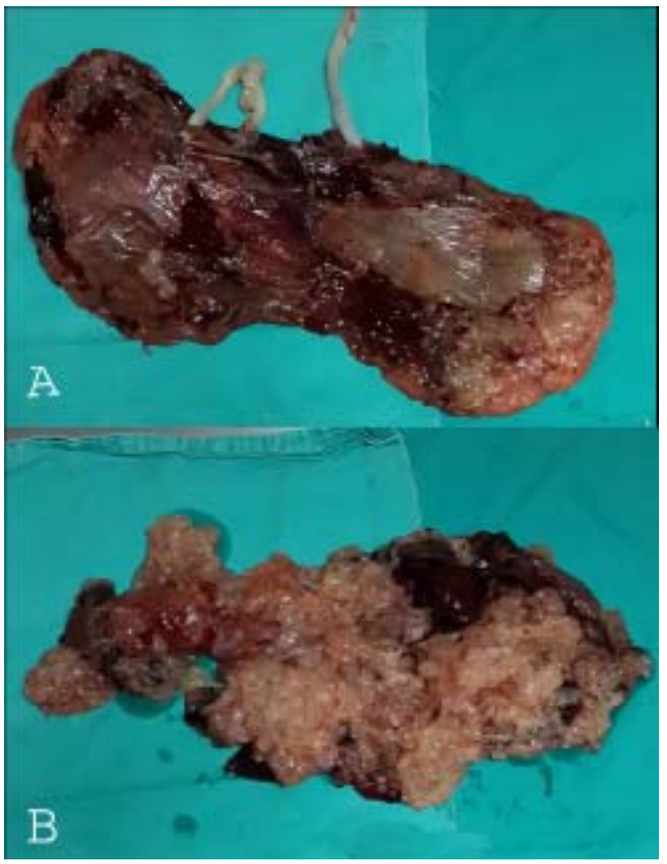

Figure 2: Postpartum view of the sligtly fusioned two normal placentas. Note the vacuolar appearance around the placentas, probably representing molar invasion of the amniotic membranes (A). Molar placenta (B)

After the initial decline, β-hCG levels increased weekly between 4 and 6 weeks after the abortion at the follow-up. Transvaginal US showed irregular endometrial echo measuring 8 mm, and pathological result of the re- curettage was partial mole and retained placenta. She was treated with four course of methotrexate and folinic acid. β-hCG titters then fell to a normal level.

Discussion

Hydatiform moles are classified as complete or partial based on histopathological examination and karyotype. Partial moles generally have a triploid karyotype, resulting from fertilization of a normal ovum by two sperms (69, XXX or 69, XXY).[4] Though clinical experience with complete hydatidiform with coexistent fetus (CHMCF) has been accumulated recently, little is known about multiple pregnancies with partial molar component.

Ultrasound is the modality of choice for the initial diagnosis of molar pregnancy with a sensitivity of 44% [5,6] for isolated molar growth, and 68% for molar pregnancy with coexisting fetus. The partial hydatidiform mole is optimally diagnosed histopathologically when the strict histopathological criteria defined by Chew et al. are demonstrated.[7] Because, partial hydatidiform mole results from diandric triploidy, flow cytometry can be utilized for supporting diagnosis.[8] Additionally, p57 ^{kip2} immunohistochemistry staining is a very useful tool for the differential diagnosis of CHM and PHM in difficult cases.[2] In our case, the sonographic demonstration of fetus which is almost always absent in molar gestation and histopathological examination strongly suggested PHM- TCF. The demonstration of triploidy by FISH analysis of paraffin section of the placental sample confirmed the diagnosis.

PHM-TCF pregnancies present a management dilemma for both the parent and the physician as to whether to continue or terminate the pregnancy, and especially for patients desiring a baby. Since the presence of partial molar pregnancy with twin is extremely rare condition, the principles of prenatal counselling are based on the data derived from CHM and coexistent two fetuses. In general, pre and perinatal outcome is dismal for triplet and higher order pregnancies with complete mole. Takagi K et al's[9] literature review showed that neonatal survival rate was 10% in CHM and coexistent twin. The PHM-TCF was first described by Marinoff et al. in a quadruplet pregnancy yielding two live- born infant after the expulsion of partial molar placenta.[1] Kim HC et al.[2] described a case of triploid pregnancy consisting of partial mole and twin pregnancy. In their case, the pregnancy was terminated because of families' request, and subsequently complicated with persistent gestational trophoblastic disease (pGTD), pulmonary metastasis that well responded to MTX therapy. Very recently, Sundari et al. reported an another case yielding two healthy-preterm infants.[3] After an isolated partial molar pregnancy, only approximately 2-4% of these pregnancies have pGTD.[2] However, our literature search showed that (Table 1), three of

Table 1: Summary of the cases of partial hydatidiform mole, and coexistent triple or more fetuses in the literature

Case	References	Number of Fetuses	Complication	Outcome	pGTD
Marinoff et al.	1	Quadriple	Hyperemesis, Preeclampsia	Two healthy, live- born infant at 32 6/7 weeks.	No
Kim et al.	2	Triple	None	TOP at 14 weeks	Yes
Sundari et al.	3	Triple	Preeclampsia	Two healthy, live- born twin at 32 weeks	Yes

pGTD: Persistent trophoblastic disease, TOP: Termination of pregnancy

the four cases (75%) of PHM- TCF, including ours, were complicated with pGTD, and it may occur irrespective of whether the pregnancy undergone early TOP, or conservative management.[3] Based on the aforementioned limited data, it can be surmised that achieving surviving infant is possible in PHM-TCF (50%). Hence, the close follow-up for women with PHM-TC for both gestational complications such as preeclampsia, hyperthyroidism, and determining the presence of pGTD after termination is necessary.

In conclusion, the optimal management of hydatidiform mole with coexistent fetuses is currently uncertain. The choice of continuing the pregnancy must be individualized, depending on the patient condition, the fetal viability, and the patients desire to continue the pregnancy. Clinicians are recommended to present their individual cases for the establishment of guidelines for the management and prenatal counselling for PHM- TCF.

Ovülasyon İndüksiyonu ve İntrauterin İnseminasyon Sonucu Oluşan Parsiyel Molar ve İkiz Gebelik Kombinasyonu

ÖZET

Dikoryonik ikiz gebelikle birlikte parsiyel mol hidatiform oldukça nadir görülür ve bu vakadan önce yalnızca üç vaka bildirilmiştir. Yirmi beş yaşında primigravid hasta ovulasyon indüksiyonu ve intrauterin inseminasyon ile elde edilmiş trizigotik üçüz gebelik ve düşük tehdidi tanılarıyla kliniğimize kabul edildi. Molar plasentaya sahip fetus B gebeliğin 11. haftasında selektif sonlandırıldı ve arkasından gebelik preeklampsi, hipertiroidizm ile komplike olarak 20. gebelik haftasında spontane düşükle sonlandı. Düşük sonrası patolojik inceleme parsiyel molü destekleyince genetik inceleme ile tanı doğrulandı. Doğum sonrası dönem dört doz metotreksat tedavisine iyi cevap alınan persistan trofoblastik hastalık ile komplike oldu. İki fetus ile birlikte gelişen parsiyel mol hidatiform olgularına yaklaşım henüz net değildir. Gebeliğin devam seçeneği hastanın durumu gözetilerek bireyselleştirilebilir. Gebelik sonrası hastalar persistan trofoblastik hastalık açısından mutlaka yakın takip edilmelidir.

Anahtar Kelimeler: Üçüz gebelik, Parsiyel mol hidatiform, Ovulasyon indüksiyonu, İntrauterine inseminasyon

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