Pregnancy outcome with coexisting mole after intracytoplasmic sperm injection: A case series

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Received: 21.03.2015
Review completed: 21.03.2015
Accepted: 10.07.2015

Access this article online
Quick Response Code:

Website:
www.jhrsonline.org

DOI:
10.4103/0974-1208.165149

ABSTRACT

Partial/complete hydatidiform mole with coexisting fetus is a rare condition. Optimal management is a challenge that remains a dilemma since these pregnancies are associated with maternal as well as fetal complications including hemorrhage, preeclampsia, thromboembolic disease, intra uterine demise and increased risk of persistent trophoblastic disease. Here we report 2 cases of partial mole with live fetus after ICSI and a case of complete mole with coexisting fetus after ICSI in a turner mosaic that resulted in a live birth.

KEY WORDS: Complete hydatidiform mole, intracytoplasmic sperm injection, partial mole, twin pregnancy

INTRODUCTION

Gestational trophoblastic disease encompasses a diverse group of lesions with specific pathogenesis, morphological characteristics, and clinical features.[1] The modified world health organization classification of the gestational trophoblastic disease includes complete, and partial mole, invasive mole, choriocarcinoma, placental site trophoblastic tumor, epitheloid trophoblastic tumor, exaggerated placental site and placental site nodules.[2] Molar pregnancy is significantly more common in extremes of age.[3] The usual management of the gestational trophoblastic disease is the evacuation of the uterus and follow-up because of the higher chances of patients developing choriocarcinoma.[1] But sometimes when molar change is there in the placenta along with a live fetus, expectant management can be performed under strict surveillance.[4,5] Although triploidy is the most frequent association, a fetus with normal karyotype can survive in cases of partial molar pregnancy. No difference was seen in the risk of developing persistent gestational trophoblastic disease (PGTD) and gestational trophoblastic neoplasia (GTN) in patients undergoing termination of pregnancy as well as the patients allowed to continue pregnancy; this observation has permitted the clinician to delay intervention till after delivery, while successfully managing the complications associated with the trophoblastic disease. We report such a series in which pregnancy with coexisting moles were managed successfully.

CASE REPORT

Case 1: Partial mole with live fetus after intracytoplasmic sperm injection

A 24-years-old, G2A1, K/C/O Turners Mosaic, Menarche at 13 years, induced with HRT, not a known diabetic/hypertensive, married for 2 years, husband is oligospermic. She conceived after intracytoplasmic sperm injection (ICSI) and ovum donation. Ultrasound revealed single live intrauterine fetus (SLIUF) of 6 weeks. At 10 weeks, SLIUF of 10 weeks 1-day with multiple small cystic spaces was seen in the placenta. Beta-human chorionic gonadotrophin (β-HCG) 194,300 mIU/ml (normal range). At 12–13 weeks scan revealed SLIUF 12–13 weeks, NT 1.3 mm. The placenta was anterior with the multiple cystic spaces, a partial mole with a normal

How to cite this article: Rao AR, Dafle K, Padmashri G, Rao DR, Sivakumar NC. Pregnancy outcome with coexisting mole after intracytoplasmic sperm injection: A case series. J Hum Reprod Sci 2015;8:178-81.

fetus diagnosed are shown in Figure 1a and b. β-HCG same day 375,000 mIU/ml which was abnormally high, for the gestational age (GA), (N β-HCG 13,300–254,000 mIU/ml). Five days later (14 weeks) β-HCG - 603,360 mIU/ml. At no point, in a singleton pregnancy does β-HCG go beyond 3 lakh mIU/ml. No symptoms of hyperemesis or vaginal bleeding were present. The Thyroid Stimulating Hormone (TSH) was normal. A second opinion was sought. The patient was sent to the higher center at 16–17 weeks GA where they confirmed a structurally normal fetus with the partial mole. Chorionic villus sampling and Amniocentesis revealed the normal karyotype, and hence we decided to continue with the pregnancy after explaining the risks to the patient. At 23 weeks GA, ultra sonography SLIUF with 23 ± 2 weeks, placentomegaly (6.6 cm) thick placenta – only a few cystic spaces (regression of molar tissue), decreased liquor 8.5 cm Doppler – normal. Low dose heparin was started with 0.3 ml s/c daily. Follow-up scans showed decreased liquor with mild Doppler abnormality, and Placentomegaly with few cystic spaces. At 30–32 weeks, the patient developed mild PIH, controlled with alpha dopa, AFI was only 4. Umbilical artery-high resistance flow, middle cerebral artery-normal, placentomegaly, intrauterine growth restriction, and no fetal movements seen, LSCS done at 32 weeks. Delivered a girl baby weighing 1.5 kg with Apgar score of 9. The baby was in NICU for 10 days after which she was discharged. β-HCG followed-up postnatally showed a declining trend as in a normal pregnancy. The placenta on gross examination weighed 480 gm, soft, and friable with irregular whitish areas, and a short cord. The histopathology revealed the edematous villi, and the placenta had extensive hemorrhage and infarcts.

Case 2: Partial mole with intrauterine fetal death after intracytoplasmic sperm injection

A 27-year-old, G2A1 married for 6 years, husband is severe oligoasthenospermic, and conceived with ICSI. SLIUF of 6 weeks on ultrasound are shown in Figure 2a. SLIUF of 10 weeks with multiple small cystic spaces are seen in the placenta anteriorly. β-HCG – 6844 mIU/ml (5 weeks) and 192,640 IU (10 weeks) TSH – 1.89 USG – SLIUF of 12 weeks 2d, placenta shows changes consistent with the partial molar degeneration shown in Figure 2b. Amniocentesis (17–18 weeks) – normal karyotype. Anomaly scan revealed – normal fetus, partial molar degeneration, and adequate liquor. Intrauterine fetal death at 27 weeks with co-existent mole, and spontaneous expulsion of deadborn male fetus HPE – Hydatidiform mole with necrotic villi, necrotic decidua, and absent fetal capillaries. Postnatally β-HCG titers declined followed by the rise after 15 days. The USG revealed-enlarged uterus with thick endometrium. Check curettage done. Two injections of methotrexate given. The patient was followed for 1-year postnatally.

Case 3: Complete mole and coexisting fetus with live birth after intracytoplasmic sperm injection

Mrs. X, 29-year-old married for 2 years primary infertility, Turner's syndrome with hormone induced menstrual cycles. The ultrasound revealed hypoplastic uterus and both ovaries were not imaged. Karyotype 45X/46XX Turners mosaic. FSH, LH high suggesting the premature ovarian failure, and hypothyroid, on treatment. Normal renal scan, and the echocardiogram. She was put on hormone replacement therapy for 11 months. Her husband had OATS, underwent an excision of the right intraabdominal testis and we planned for ICSI with the ovum donation. She had 2 × 8 cells grade1 embryos transferred. At 6 weeks of gestation single fetal pole, with cardiac activity was seen on TVS. By the 12 weeks gestation, multiple cystic spaces where seen near fundal aspect of placenta. An elevated serum βHCG level of (190,090 mIU/ml) was noted on second-trimester serum screening. The patient was referred for further evaluation in the higher center, at 16th week ultrasound demonstrated a viable, structurally normal 16 weeks fetus with a normal-looking placenta. The fundus of the uterus was occupied by a large cystic mass shown in Figure 3a. The appearance was in keeping with a molar pregnancy.

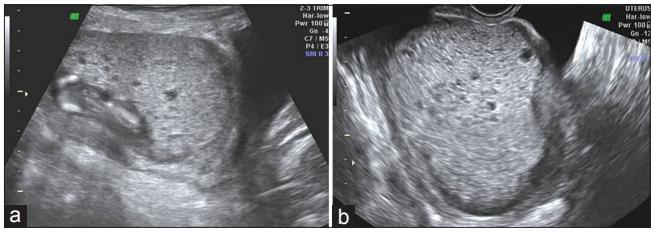

Figure 1: (a) Sonographic image is showing partial mole with a fetus at 12 weeks. (b) Sonographic image showing placenta with the multiple cystic spaces

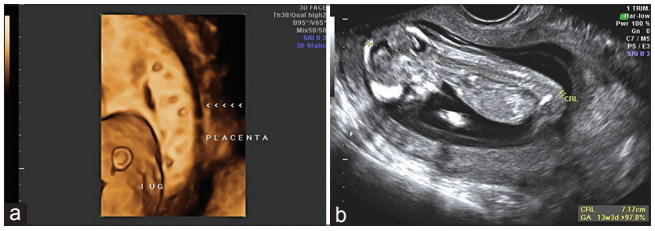

Figure 2: (a) Sonographic image is showing partial mole with a fetus at 7 weeks. (b) Sonographic image showing partial mole with a fetus at 12 weeks

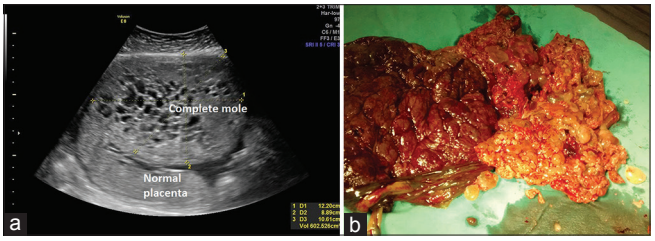

Figure 3: (a) Normal looking placenta and complete mole at 29 weeks. (b) Complete Mole and normal placenta after delivery at 31 weeks

During the following 10 weeks, the patient had a few episodes of vaginal bleed, of small quantity all of which settled spontaneously. The fetal anomaly scans at 21 and 24 weeks were unremarkable. She developed a gross hydronephrosis in the second trimester and had recurrent urinary infections. She had impaired GTT and was put on a diabetic diet. The `mole' continued to grow in size with advancing gestation, and the uterus remained large for dates. Betamethasone was administered to promote fetal lung maturity at 28 weeks gestation.

She had no preeclampsia and related complications. She went into preterm labor at 31 weeks and emergency LSCS was performed, a live female infant 1.67 kg with Apgar-8/10.9/10, and normal placenta (500 g) were delivered. Thereafter more than 400 gm of cystic, vesicular tissue was extracted, and the uterus completely evacuated, shown in Figure 3b. The uterus contracted well. The histological examination confirmed the clinical impression of one normal placenta, and a second complete hydatidiform mole. The baby was in NICU for prematurity and low birth weight for 19 days and was discharged with a birth weight of 2.0 kg. Postoperatively, serial serum βHCG concentrations showed a steady fall and at 4 weeks post-delivery was 16 mIU/ml and normal up to 1-year follow-up. The infant up todate has achieved normal milestones of development and has a normal karyotype.

DISCUSSION

Partial mole and coexisting fotus

The incidence of a normal live fetus with a partial molar placenta after ICSI is extremely rare; although triploidy is the most frequent association, a fetus with normal karyotype can survive in case of partial molar pregnancy. One case reported by Zhang *et al*. University of California San Diego where the female fetus died in utero at 26 weeks.[6] Another study was reported by Bruchim *et al*. in Israel,[7] they delivered one woman at 41 weeks of gestation with partial mole and another at 26 weeks but those cases were of complete hydatidiform mole along with a normal fetus which was a twin pregnancy. Any pregnancy along with a molar change in the placenta has a definite risk of preterm delivery as obvious from many case reports.

The follow-up of a patient with partial hydatidiform mole has been questioned by some authors that whether they need follow-up by serum β-HCG. Such patient can develop choriocarcinoma, and one death has been reported in the study conducted by Seckl *et al*.[8] However partial hydatidiform mole rarely requires chemotherapy.

Fetal survival depends on partial molar pregnancy with a normal karyotype of the fetus; smaller molar area compared to the normal placenta, the onset of the molar degeneration, speed of degeneration, the absence of anemia in the fetus, the absence of maternal complications such as preeclampsia, thyrotoxicosis, and vaginal bleeding.

In our first case of partial mole in turner mosaic, the molar tissue regressed after 23 weeks of gestation, she had mild PIH and oligohydramnios resulting in a live birth at 32 weeks. In our second case of partial mole after ICSI the molar tissue was of large size resulting in an IUD at 27 weeks.

Complete mole and coexisting fetus

Twin gestations consisting of complete molar changes and coexisting normal fetus are rare, with an estimated incidence of 1 in 22,000–100,000 pregnancy and may be increasing due to the greater use of Assisted Reproductive Techniques.[9] The management of complete hydatidiform mole with coexisting twin fetus (CHMCTF) is more complex, and challenging and has still not been standardized. Only 40% of these pregnancies result in a live birth, while others normally aborting by the second trimester.[10] Since the fetus is viable, and many of these patients have conceived late in age after many IVF attempts, the pregnancy is extremely precious. Counseling the patients of the risk involved, and close monitoring till delivery is crucial for the management of CHM. The babies, thus born, have been reported to be normal.

In a large series of 77 CHMCTF patients, Sebire *et al*.[10] reported a successful delivery of 31 live babies. In contrast, in a recent study by Lee[11] in 2010, only one out of six patients delivered a live baby while five ended in pregnancy termination. A large number (50%) of these patients of CHMCTF develop PGTD.[12] This risk is higher than in CHM patients (20%)[13] or PHM patients (4–11%).[14,8] It has now been demonstrated that the risk of PGTD is not reduced, even if pregnancy terminated early instead of being allowed to continue to term. Under careful surveillance and multidisciplinary management, it is possible for the woman to give birth to a normal child and to be cured of the mole.

Our third case who is a turner mosaic with CHMCTF, was hospitalized and observed; she had uneventful pregnancy resulting in a live birth at 31 weeks. She did not develop complications like PAH and PGTD.

CONCLUSION

Although the rate of adverse perinatal outcome is high in partial mole, if amniocentesis or fetal blood sampling reveals a normal karyotype, continuing the pregnancy with the close follow-up in a tertiary center is most rewarding.

It is possible to achieve a live birth in case of complete mole and coexisting fetus under careful surveillance and

multidisciplinary management. The patients should be carefully monitored and thorough informed consent obtained. The risk of complications such as GTN and PTD are not increased, when the intervention is delayed till after delivery.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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