COMPLETE HYDATIDIFORM MOLE IN A QUADRUPLET PREGNANCY WITH COEXISTING THREE VIABLE FETUSES: A CASE REPORT

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Abstract: We hereby report the occurrence of quadruplet pregnancy with delivery of three viable infants and a complete mole. This was an induced conception with clomiphene citrate. At 22 weeks molar change was noticed in one of the placenta. Case was discussed with oncologist and pregnancy was continued with close monitoring of β-hCG and ultrasound. Patient had no associated medical co-morbidity; she was given steroid cover at 32 weeks and delivery was planned at 34 weeks of pregnancy. Patient went into preterm labor at 33 weeks and three female infants were delivered followed by removal of three placentas along with copious molar tissue at the end. Babies were kept in nursery; none required assisted ventilation and were discharged in satisfactory condition. Histopathology and immunohistochemistry confirmed quadruplet pregnancy comprising of one complete mole with three normal placentas.

Keywords: Complete hydatidiform mole, quadruplet pregnancy, multiple pregnancy

Introduction
Cases of a hydatidiform mole (HM) coexisting with a fetus have recently become more common as a result of an increase in the incidence of multiple pregnancy arising from ovulation induction therapy and in vitro fertilization. HMs may be partial (PM) or complete mole (CM) depending on their gross appearance, immunohistochemistry and karyotype. PMs usually have a triploid karyotype, derived from maternal and paternal origins and they are positive for p57 antibody on immunohistochemistry, whereas CMs are diploid and have paternal origins only therefore they are negative for p57 stain.

Coexistence of a viable fetus with a hydatidiform mole is a rare condition with an estimated frequency of 1 in 22,000 to 100,000 pregnancies. Most cases suffer severe complications such as pre-eclampsia, abortion and preterm delivery or termination immediately after diagnosis. Delivery of viable infants from this condition is even rarer. Early diagnosis is very important because of the risk of developing severe complications in pregnancy. In most cases, termination of pregnancy is recommended when the diagnosis is made in early pregnancy. In the case of a normal fetal karyotype, it is justifiable to await developments in the absence of maternal complications.

Case report:
A 27 years old female in her second pregnancy, presented for booking after having her pregnancy confirmed by urine pregnancy test. Her present pregnancy was a result of treatment with clomiphene citrate 50 mg daily for five days owing to failure to conceive for four years. At 13 weeks, ultrasound showed Bichorionic Triamniotic pregnancy. Patient had severe nausea and vomiting throughout her first trimester for which she was given supportive treatment from time to time. Anomaly scan performed at 22nd week of gestation showed not only all the three alive and active fetuses but also showed cystic spaces in the left half of anteriorly lying placenta. Hydropic degeneration in one of the placentas was noted. Oncology consult was sought for the partial hydatidiform mole. Keeping in view normal development and growth of all three fetuses and absence of any maternal complications, pregnancy was decided to continue with close fetal surveillance and β-HCG levels. Patient's subsequent β-HCG continued to rise which peaked around 25th week of gestation to a level of 305881.68 mIU/ml and declined progressively thereafter. Pregnancy was not complicated by any medical disorder and she received routine prenatal care with iron and calcium supplements.

At 32 weeks +6 days she presented with complaint of severe abdominal pain and vaginal leakage. Examination confirmed triplet pregnancy with full dilatation. Hence an emergency cesarean section was planned.

First baby was a female weighing 1.6 kg with good APGAR score and delivered by cephalic presentation followed by its placenta. The second amniotic sac was ruptured and a female baby weighing 1.8 kg with good APGAR score was delivered by breech extraction; the
umbilical cord was edematous. The amniotic sac of the third female baby was then ruptured followed by breech extraction; its cord was also edematous and was followed by delivery of the placenta. Copious amount of trophoblastic vesicular tissue was also removed after the delivery of babies, placenta and membranes (Fig 3). All placentas along with the molar tissue placed in separate containers were sent for histopathology. Blood loss during surgery was 400 ml. No blood products were required. Patient was given prophylactic methotrexate at time of removal of placenta. Patient had a smooth post operative recovery. All the infants were transferred to neonatal Intensive Care Unit for observation and none required ventilator support. She was followed up with serial β-hCG monitoring for progression to invasive molar tissue/choriocarcinoma; β-hCG levels were normal within three months of delivery.

On gross examination it was a bichorionic triamniotic placenta with part of one placental disc showing numerous vesicular structures (Fig 3). Three well formed umbilical cords were visualized each showing three blood vessels. On microscopy, the normal appearing placenta showed mature chorionic villi with normal fetal membranes and umbilical cords. However, the vesicular structures reveal diffusely dilated chorionic villi with cistern formation and trophoblastic proliferation (Fig 4). Nucleated RBCs were not identified. The trophoblastic cells were negative for p57 immunostain (Fig 5-inset). Based on all these findings, a diagnosis of complete hydatidiform mole complicating a quadruplet pregnancy was made. The molar tissue was considered to be derived from the fourth fetus. The rest of placental tissue and umbilical cords belonging to three viable babies were unremarkable.
**Discussion**

CHM occurring with multiple living fetuses is very rare, and its prevalence is unknown. There are very few case reports of quadruplet pregnancy with complete molar; however all pregnancies ended up before 25 weeks either due to obstetric or maternal complications. Prenatal diagnosis of coexistent mole and fetus can depend upon the clinical symptoms and signs, physical examination, sonographic findings, and abnormal biochemical data. Clinically, the patient may present with hyperemesis, hyperthyroidism, vaginal spotting or even heavy bleeding, pregnancy-induced hypertension and larger-than-gestational age uterus. Although it is possible in most cases to diagnose CHM from 11-12 weeks of gestation (Jauniaux and Nicolaides, 1997; Lazarus et al, 1999), Amano T reported diagnosis of CHM coexisting with multiple fetuses at 18 weeks of gestation. Suspicion of molar change in our case was made at 22 weeks which is quite a late diagnosis however diagnosing multiple pregnancy using ultrasound, the focus is naturally on the fetuses, which may lead to other possible findings being overlooked. Although the present case resulted in a favorable outcome, a review of 14 reported cases suggests that the high fetal loss rate (90%) must be a consideration in the decision regarding management of such a pregnancy.

The β-hCG titer is generally higher than is seen in non molar gestations. Khazaeli et al. (1989) suggested that the excessive production of β-hCG may identify gestational trophoblastic disease as well as gestational trophoblastic disease. Monitoring serum concentrations of β-hCG is necessary to determine the early development of persistent trophoblastic disease, since up to 10% of moles develop into persistent or invasive moles.

Once the suspicion of molar change was made on ultrasound, serial β-hCG levels showed a rise from 748 mIU/ml at 23 weeks went up to 305881 mIU/ml at 29 weeks and a gradual decline thereafter to non-pregnancy level 12 weeks postpartum. In a study by Vaisbuch et al, they reported 130 cases of twins with CHMF (complete hydatidiform mole and coexistent fetus) pregnancy of which 41% were terminated because of the positive probability of serious maternal complications. Women with hydatidiform mole are at risk of preterm delivery (PTD). Some previous studies reported a greater risk of PTD in women who had a twin pregnancy with CHMF (50-60%) compared with a singleton molar pregnancy (15%). The recent study by Neumann in 2007 revealed that the risk of PTD after a diploid mole with a viable fetus is similar to that after a singleton molar pregnancy and elective early termination of such pregnancy because of the risk of PTD alone should not be recommended. Literature review of previously reported cases involving quadruplets or triplets with a complete hydatidiform mole revealed that all cases ended as premature non-viable fetuses; however our patient successfully completed 33 weeks of gestation. Selective feticide may be considered in order to improve the likelihood of attaining an advanced gestational age for a single fetus.

This is the first reported case of quadruplet pregnancy with complete mole to our knowledge in which pregnancy has completed 33 weeks of gestation and 3 live births without any feto-maternal morbidity. Intensive literature search, frequent discussion amongst multi-disciplinary team and timely administration of steroids for fetal maturity has led to a successful outcome. The pathological examination was also very interesting in this case. Initial interpretation, based on the presence of molar tissue co-existing with normal placenta, was that of a partial hydatidiform mole. However, there was diffuse enlargement of chorionic villi in the molar tissue with trophoblastic proliferation, cistern formation and absence of nucleated RBCs, suggesting complete hydatidiform mole. Histological distinction between partial and complete hydatidiform moles can be difficult due to a number of overlapping features. Therefore, for a more definitive diagnosis, immunohistochemical stain p57 was applied. p57 staining is helpful in differentiating a complete mole from a partial mole. It is a paternally imprinted protein and expressed predominantly from maternal allele in most tissues, not expressed in complete hydatidiform moles. In partial mole, maternal genes are present and expressed, therefore, p57 is immunoreactive in the cytotrophoblastic cells lining the chorionic villi. In our case p57 was negative confirming the morphological diagnosis of complete hydatidiform mole. In the current case, there were three well developed umbilical cords with bichorionic triamniotic placentas (three normal babies were delivered) with an associated complete mole. So, it was concluded that it was a quadruplet pregnancy to begin with and the fourth embryo transformed into a complete mole. The risk of persistent trophoblastic disease (PTD) is
the same as in the case of a singleton complete mole. Patient was followed up with serial $\beta$-hCG which became normal in three months.

**Conclusion**
Successful continuation of a molar pregnancy with co-existing viable fetuses under proper surveillance is possible, however literature review and the observations from our case are still limited for future management.

**References**


