# Twin Conception of a Hydatidiform Mole and a Co-Existing Viable Fetus

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## ABSTRACT

**Multiple pregnancy with a normal live fetus and concurrent gestational trophoblastic disease is associated with obstetric complications and potential adverse outcomes. Diagnosis with appropriate imaging, counselling and a systematic approach are the mainstay of the management of these exceptional cases.**

**24 years old in her second pregnancy was diagnosed as twin gestation. Early gestational imaging showed twin gestation with one live fetus and the other sac with possible missed miscarriage. Subsequent imaging at 10 weeks showed one live fetus and the other sac with molar changes. Pregnancy was monitored up to 14 weeks but had to be terminated due to thyrotoxicosis, hypertension and vaginal bleeding. At 14 weeks abdominal assessment revealed a uterus of more than 25 gestational weeks. Ultrasound assessment showed the placenta to be covering the cervix with increased vascularity. A multidisciplinary approach was undertaken and in view of thyrotoxicosis associated with molar changes and vaginal bleeding, the pregnancy was terminated by hysterotomy. The postpartum period was complicated with preeclampsia which necessitated admission to the intensive care unit. Post-delivery the client received six cycles of methotrexate as chemotherapy. After 8 months from initiation of chemotherapy, the client attained complete recovery.**

**Keywords: Molar pregnancy, Thyrotoxicosis, Hysterotomy, Methotrexate, Multiple pregnancies**

## INTRODUCTION

Gestational trophoblastic disease manifests with premalignant and malignant potential. It is a rare type of tumour associated with pregnancy, which originates from the abnormal proliferation of placental trophoblast. Premalignant conditions incorporate complete and partial molar pregnancy also known as hydatidiform mole[1]. Malignant conditions incorporate Invasive mole, choriocarcinoma, placental-site trophoblastic tumor and epithelioid trophoblastic tumor[2]. The incidence of developing a molar pregnancy with a co-existing viable fetus of twin gestation is extremely rare at approximately 1: 20,000-100,000 pregnancies[3]. This very rare presentation poses significant adverse outcomes to both the mother and the developing fetus. The complications include miscarriages, preterm labour, placental abruption, intrauterine death, preeclampsia, thyrotoxicosis, massive bleeding, mortality and persistent trophoblastic disease[4,5]. Such cases are mentioned infrequently in the literature. The management of these pregnancies need well-experienced obstetricians. Follow up in a trophoblast centre is crucial and essential for the optimal recovery in these individuals.

We report a case from Bahrain Defence Force hospital of a twin conception with a viable fetus and a co-existing hydatidiform mole who developed antenatal complications and hence termination of the pregnancy was executed based on multidisciplinary team discussion to save the life of the mother.

## CASE REPORT

A 24-year-old Syrian lady, who was G2P0A1 with no significant medical and surgical history was receiving fertility treatment in the form of ovulation induction with clomiphene citrate due to anovulation. She had one previous miscarriage at 6 weeks one year prior to presentation. During the present pregnancy, an early scan at 6 weeks of gestation showed two intrauterine gestational sacs, identified as dichorionic diamniotic with one viable pregnancy. Into the 10th week of pregnancy, the patient was admitted as she had episodes of vaginal bleeding. An ultrasound showed dichorionic diamniotic twin conception with one viable fetus with CRL corresponding to 10 gestational weeks and a normal placenta. The other twin was seen as collapsed sac with molar changes in the second placenta. The level of β-hCG was elevated at (956900 mUI/ml) and thyroid function tests reported low TSH level of 0.03ulU/ml, high FT4 and FT3 levels of 36.04 and 10.51pmol/l respectively. She was started on propylthiouracil. The findings were discussed with the oncology team and the couple. The decision was made to continue with the pregnancy.

Further on in pregnancy, at 14 weeks of gestation, she was admitted again with hyperemesis gravidarum and vaginal spotting. Upon examination the fundal height was corresponding to 25 weeks of gestation. Ultrasound was performed which showed molar tissue increased in size to 22 X 25 cm and occupied most of the uterine cavity. The live fetus was 14 weeks and pushed to the upper left part of the uterus. MRI showed partial mole pregnancy with no sign of myometrial invasion and coexisting viable twin. The molar tissues were seen covering the cervical os with increased vascularity. The ovaries were mildly prominent and showing few follicular cysts. Termination of pregnancy was discussed with the couple. Given the enlarged uterus at 25 weeks gestation with potential increased bleeding from the cervix, possibilities of complications were explained in detail. ICU admission, hysterectomy, the need for blood transfusion and repeated procedure was discussed with the couple. After discussion with the tumour board, a combined decision was taken to terminate the pregnancy via the

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abdominal route to control the bleeding quickly and reduce the risk of retained product of conception. The chest X-ray was normal, liver function tests and renal functions tests were within normal limits.

Haemoglobin was 8mg/dl, thus blood transfusion was started. Hysterotomy was performed which was complicated with intraoperative bleeding with estimated blood loss of approximately +/-2000mL. She received 3 units of PRBC and 4 units of FFP. Post-operatively patient's haemoglobin level increased to 9.1g/dL. She was transferred to ICU due to uncontrolled high blood pressure and difficulties in maintaining normal O2 saturation. As the patient had difficulty in breathing, chest x-ray was done which showed bilateral pulmonary congestion. Heart echo was normal. Patient was managed with anti-hypertensive treatment and fluid management with strict input and output assessment. Two days later, BHCG level was 840219mlU/ml then dropped to 464200mlU/ml the following day. She was followed up with weekly BHCG levels abroad, which showed a decreasing trend but not to the expected level.

Due to slow decrease in HCG levels, MRI was performed five weeks later which showed a bulky uterus with increased vascularity, there was no focal endometrial mass however there were few thin discrete nodules within the uterine cavity measuring approximately 1 cm in diameter with faint peripheral enhancement, there was no retained product of conception. There was no irregularity of the uterine serosa. There was no ascites or adnexal masses.
Histopathology examination confirmed a twin placenta with one disc within normal limits and the other disc had a complete mole. The case was discussed at the local tumour board meeting and advised referral to a specialized centre in trophoblastic diseases. Further follow up was done in a trophoblastic disease centre in Syria where she had a single agent chemotherapy for six cycles. The drug used was methotrexate. Her treatment was successful and BHCG was normalised four months after initiation of chemotherapy. She was advised barrier method of contraception.

Later on, two years after surgery, the patient was seen in clinic pregnant with a single intrauterine viable pregnancy.

## DISCUSSION

A twin conception where a hydatidiform mole co-exists with a live fetus is a rare presentation with complex management demand. In recent years, an increasing trend of molar pregnancy concurrent with a fetus have been reported after ovulation induction methods[6,7]. Our case too had to go for induced ovulation preconception. Verda group reported a case of complete hydatidiform mole with co-existing live fetus after intra cytoplasmic sperm injection in 2020. She was delivered at 26 weeks due to severe pre-eclampsia[8].

This unique entity known as the Sad fetus syndrome is a subclass of gestational trophoblastic disease which consists of gestational trophoblastic disease with a living fetus or fetuses[9]. There are three types described; The first is a twin pregnancy with one normal fetus along with a normal placenta and the other sac with complete mole[10]. The second type is a twin conception with one normal fetus with normal placenta and the other sac with a partial mole. The third variety is a singleton normal fetus with a partial molar placenta[11]. The case we are reporting belong to the first type. The incidence of a twin pregnancy consisting of a hydatidiform mole co-existing with a fetus is 1 in 22,000-100,000 pregnancies, with the majority being complete hydatidiform mole[12]. The reported prevalence of a partial mole with co-existing fetus is 0.005-0.01% of pregnancies[13]. Niemann and colleagues studied the number of gametes involved in twin conception consisting of a hydatidiform mole and a normal fetus and concluded that a diploid mole and a normal co- fetus are mostly derived from one single oocyte fertilised with one or more spermatozoa[14]. A case of monochorionic mono amniotic twin with aneuploidy and cystic placenta consistent with molar changes have been reported by Ray A et al after inducing ovulation with clomiphene citrate[15]. Interestingly, Rajasekharan group reported the sad fetus syndrome with triplets[16]. This emphasises the wide range of presentation of this condition.

The clinical portrayal of gestational trophoblastic disease may include vaginal bleeding, increased uterine size to gestational age and hyperemesis[17]. The case reported had these signs along with elevated Beta HCG. Spontaneous miscarriage, intra-uterine foetal death, pre-eclampsia and hyperthyroidism are obstetric complications which are potentially life threatening[18,12,] Our case was challenging as the patient had intermittent vaginal bleeding, pre-eclampsia and hyperthyroidism. Anti-thyroid drugs were started to avert a thyrotoxic crisis. She was also admitted to the ICU for blood pressure control.

Elective pregnancy interruptions and post molar gestational neoplasia are more common when the maternal complications occur less than 20 weeks of gestation[19,12]. This occurred with our case as maternal complications started early in pregnancy and hysterotomy had to be done to evacuate the uterus. K.Dolapcioglu and colleagues reported 2 cases in 2009, in which one of them was terminated due to vaginal haemorrhage and concluded that the estimated live birth was between 30-35% with the risk of persistent trophoblastic disease similar to complete molar singleton pregnancy[20].Similarly Steller MA and group investigated the natural history of a twin conception which included a complete hydatidiform mole and co-existing fetus and came to a conclusion that they are prone for developing persistent gestational trophoblastic disease[21].In contrast, Edi Vaisbuch et al reported 2 cases in 2005 and found no evidence of persistence or metastases during the follow up period[22].

The potential survival of the coexisting twin needs to be addressed when this devastating diagnosis is confirmed. Bristow and colleagues inferred after studying 26 cases, that the survival of the fetus was associated with features of less molar growth[23]. The patient in our reported case presented with extensive growth of the molar tissue and the fetus was pushed to the upper left uterine quadrant. At 10 weeks of gestation, molar tissue was identified by ultrasound in the second sac. However, the decision was taken to continue with the pregnancy on the grounds of the couples wishes. In the event of continuing pregnancy, monitoring a twin pregnancy with sad fetus syndrome is mandatory to identify potential maternal and foetal complications. Between 1966 and 1997, seven women with this condition were treated at John I. Brewer Trophoblastic Disease Centre of Northwestern University Medical School. The team looking after those cases found an increased risk of haemorrhage and development of persistent gestational trophoblastic disease[24].

It was inferred by J.Massardier et al that even if a healthy child was born, the possibility of persistent gestational trophoblastic disease is higher than in a case of complete hydatidiform mole alone[25]. In Japan, 72 cases were identified by gross appearances and histopathological examinations. Hideo Matsui group deduced that the risk of development of persistent trophoblastic disease is higher in complete hydatidiform mole with co-existing fetus than in a singleton complete mole (50% and 12.5% respectively)[26]. Continuation of pregnancy may be considered as the risk of malignancy is not altered with increasing gestational age. However maternal complications should be controlled and foetal karyotype as well as growth must be normal[26]. In contrast, Pascale Marcorelles and colleagues found the risk of persistent

gestational trophoblastic disease in complete hydatidiform mole co-existing with live fetus to be the same as that of singleton complete mole. They however agreed with the opinion that if the fetus was of normal karyotype, it was justifiable to continue with the pregnancy in the absence of maternal complications and diligent antenatal and postpartum follow up is warranted[27]. In our case we did not perform foetal karyotype assessment as she was apprehensive regarding the procedure. MRI is considered a helpful tool for the diagnosis of complete hydatidiform mole with co-existing fetus[28]. In our case the MRI reported a partial mole.

Subtle pathological changes are found in the early diagnosis of a complete mole when compared to a later molar pregnancy opined EIO Garner et al. Hence the use of immunohistochemical methods as ancillary testing in differentiating complete from partial mole is on the rise[29]. RA Fisher highlighted p57 immunostaining use in the diagnosis of complete mole and genotyping use for differentiating partial hydatidiform mole, familial recurrent hydatidiform mole, mosaic conceptions with molar change and aneuploid conceptions[30]. The histopathological report of the conceptus in the reported case showed a twin placenta with one disc being within normal limits and the other disc, a complete mole.
As there was a discrepancy between the diagnosis from imaging and histopathology a multidisciplinary team decided to go with the histopathological diagnosis as it is the definitive diagnosis.

Advances have been made in the management of patients with this condition and hence normal reproductive function can be anticipated[31]. Soper group too made the same observation, along with minimizing acute complications and identifying malignant potential after reviewing the management and surveillance of molar pregnancies. Individualisation of cases for treatment and using less toxic drugs for low risk disease and multi-agent drugs for high risk disease was also advised[32]. The FIGO prognostic score assessment of parameters provides an estimate of the risk category and patients are offered the initial treatment with either single agent or multi agent chemotherapy. The risk factors include age, antecedent pregnancy, months from index pregnancy, pre- treatment HCG levels, largest tumour size, site of metastases, number of metastases and previous chemotherapy[33]. Single agent chemotherapy was used in our case as the FIGO score was less than 6. A retrospective descriptive study over 11 years from Oman royal hospital highlighted the significance of patient assessment, histopathology findings and follow up[34]. As the cure rate for low-risk gestational trophoblastic disease is nearly 100%, this provides significant assurance to stressed patient with this diagnosis. However, follow up of HCG levels is essential to assess the regression of the disease. A multidisciplinary team approach and a specialized centre treatment led to the complete recovery of our patient.

## CONCLUSION

**Due to the unique biology and comparative rarity of the sad fetus syndrome, this case highlights the need for termination of the pregnancy, should antenatal complications arise in order to prevent a fatal outcome.**

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