Severe fetal anaemia resulting from a widely metastatic antenatal choriocarcinoma

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Introduction:

Molar pregnancies belong to a group of diseases classified as gestational trophoblastic diseases, which result from an altered fertilization (1, 2). Partial molar pregnancy with a live fetus is a very rare condition, occurring in 0.005 to 0.01% of all pregnancies (1). it presents a challenging diagnosis, especially when clinical signs are nearly absent (5, 13).

Case presentation:

This is a rare case of molar pregnancy complicated by metastatic choriocarcinoma during pregnancy, in which a normal-appearing male fetus with diploid karyotype was delivered at 35 weeks gestation by emergency

caesarean in a 42-year-old Chinese woman. This was a spontaneous first pregnancy with a background history of subfertility. The dating ultrasound scan (US) raised concerns of the associated molar changes at the placental site, however; a review with fetal medicine consultant assured that it is likely due to vanished second twin or degenerated subchorionic hematoma. This lady was booked in the high-risk maternal medicine clinic following blood investigations indicating elevated thyroid function tests and was started on Carbimazole 20 mg once daily. The pregnancy progressed smoothly with regular antenatal visits and follow up by the maternal medicine consultant with normal growth ultrasound scan finings. At 33 weeks gestation, she was admitted to the respiratory ward with un-explained cough & shortness of breath (SOB), and a CT chest indicated some pulmonary infiltrates and was treated as pneumonia with antibiotics, fetal monitoring was normal. She was readmitted 2 weeks later to the respiratory ward with increasing cough and SOB, with a low O2 saturation. A repeat CT scan of the chest indicated some lung changes suggesting the possibility of vasculitis and pulmonary embolism was ruled out. Next day she complained of increasing shortness of breath, she continued to be hypoxic with reduced fetal movement. Cardiotocography (CTG) indicated a pathological trace. She was delivered by an emergency caesarean section (LSCS), delivering a 2.235 kg male baby severely pale handed to the neonatologists. Severe fetal anaemia (Hb 35 mg/dl) was immediately confirmed, and the baby was transfer to the neonatal unit (NNU) where he made a full recovery following blood transfusion. Bilateral enlarged haemorrhagic cystic ovaries were noticed during the CS with the right around 12 cm size, which was biopsied. Histology confirmed theca lutein cysts. Pathological analysis of the removed placenta confirmed choriocarcinoma. She made a good post operative recovery but remained hypoxic with PO2 ranging between 90-92%. Choriocarcinoma was confirmed following receiving the result of a very high B-HCG of 2622500 IU/L which was followed by full maternal body imaging indicating widespread metastasis to the lungs, liver, kidneys and brain. The patient was transferred to the regional Trophoblastic centre where she started her systemic and intrathecal chemotherapy after scoring which indicated high score. She is making good response and the trophoblastic team is hoping for full cure.

Conclusion: Molar pregnancy with an alive fetus is a very rare condition that presents a challenging diagnosis especially when BhCG is within normal. High index of suspicion is paramount when the US in early pregnancy suspects this possibility and follow up with repeated BhCG in pregnancy together with checking the placental history at birth are vital. Severe fetal anaemia secondary to metastatic Choriocarcinoma was never reported before which could follow the same mechanism of severe fetal anaemia secondary to an associated partial hydatidiform mole.

Introduction:

Hydatidiform mole belongs to a group of diseases classified as gestational trophoblastic disease which results from an impaired fertilization (1, 2). Hydatidiform moles have been divided into complete or partial moles on the basis of distinctive histopathological features and genetic abnormalities (3). Partial molar pregnancy with coexisting fetus is a rare complication with an incidence of 0.005– 0.01% of all the pregnancies (1). It usually develops from dispermic fertilization of a haploid normal oocyte and produces a triploid set of chromosomes (69 XXX, 69 XXY, or 69 XYY) and is most commonly associated with the presence of a malformed fetus (1, 2). The most relevant symptom of a molar pregnancy is heavy vaginal bleeding in early pregnancy. Other symptoms can be severe nausea, hyperemesis, hyperthyroidism, hypertension, and proteinuria, and the occurrence of fetal anaemia. Human chorionic gonadotropin (hCG) levels are generally lower than in complete molar pregnancy (3, 4). A diagnosis can be achieved with US and sensitive measurement of serum BhCG. However, partial moles are often misdiagnosed as an incomplete or missed miscarriage during the first trimester. In less than 25% of cases, pregnancy with a partial mole and a single normal fetus evolves to a viable fetus: in such cases the diagnosis can be suspected but the management can be challenging due to the potential maternal and fetal complications (5). We report a rare case of a misdiagnosed partial molar pregnancy in which a severely anaemic but normal-appearing male fetus with a diploid karyotype was delivered at 35 weeks gestation.

Fetal anaemia caused by fetomaternal transfusion in a case of partial mole has been previously reported before (20). Although the neonatal anaemia was effectively treated by exchange transfusion, the infant died

from respiratory distress syndrome 67 days after birth.

A 42-year-old Chinese woman was booked at 7 weeks gestation. Her pregnancy was deemed high risk due to maternal age of 42 and thyrotoxicosis. Dating scan at 11 weeks gestation raised a concern of an echo free area measuring 25mm x 11mm posterior to the gestation sac which could represent a small amount of fluid or possibly a second early gestation sac (Figure 1). Combined maternal serum screening indicated a low risk for triploidy. A repeat scan at 13 weeks revealed a mixed echo structure with cystic spaces measuring 66.4 X 27.8 X 56.6 mm between the gestational sac and the cervix raising a differential diagnosis of co-eisting partial mole versus atypical fibroid or an atypical hematoma (patient mentioned that she had a scan while being in china with suspicion of fibroid uterus). (Figure 2)

She developed gestational diabetes (GDM) confirmed by oral glucose tolerance test. The GDM was managed by diet control and Modified release Metformin. Although she had been feeling well in herself, blood tests revealed a high T4 of 31.1 with low TSH < 0.2 with no signs or symptoms of Grave's disease. She was started on carbimazole 20mg OD by the maternal medicine and endocrinology teams.

She was admitted through the emergency department at 33 weeks gestation following a one-week history of intermittent pleuritic chest pain and haemoptysis with SOB. With pregnancy being a risk factor for pulmonary embolism, a CTPA (computerised tomography perfusion scan) was done. Although it showed no pulmonary embolism, a widespread peripheral tree in bud appearance with multifocal peripheral consolidation was seen suspicious of an atypical pneumonia. Screening for tuberculosis (TB) confirmed negative results. She was started on amoxicillin for a week and was discharge home aiming for bronchoscopy in 4 weeks.

She was readmitted two weeks later with persistent cough and pain radiating to her kidneys with increasing SOB and hypoxia (PO2 90-92%). A repeat CXR showed multifocal opacities which were more extensive than previously. A rare carbamazepine induced vasculitis was suggested due to negative cultures, so carbimazole was stopped.

Two days later, the patient complained of diminished fetal movement & had a CTG which confirmed a pathological antenatal pattern necessitating delivery. She was delivered by an emergency CS delivering a male fetus weighing 2.235 kg who looked very pale at birth. Severe fetal anaemia confirmed Hb 35 mg/dl. The baby was transferred to the NNU and recovered well following blood transfusion. Bilateral enlarged haemorrhagic cystic ovaries were noticed, largest on right ovary around 10-12 cm. A wedge biopsy of the right ovary was taken. Thea placenta looked normal with some difficulty to remove it, was sent for histology. Tumour Markers were collected.

Alfa fetoprotein (AFP) was high (7126 ng/mL) and dropped to 1982 ng/mL next day and B-HCG was 2622500 IU/L. Placental histology confirmed choriocarcinoma and the ovarian wedge biopsy confirmed theca leutin cysts (thecoma).

The patient continued to be hypoxic and breathless with haemoptysis. A repeat CT Angiography on day 7 postpartum, ruled out pulmonary embolism but showed multiple scattered lesions throughout both lungs which were concerning of malignancy. There was a few ill-defined low-density lesions located within the liver (Figure 3 and 4). Once the BhCG was received, the diagnosis of antenatal metastatic choriocarcinoma was made.

The regional Trophoblastic Centre was informed, and the patient was transferred there following imaging for staging. This has confirmed widespread metastasis of choriocarcinoma to both lungs, liver, kidneys, and brain.

Scoring system indicated high risk gestational trophoblastic disease and multiple potent systemic chemotherapeutic agents were commenced low dose Etoposide and cisplatin along with intrathecal Methottrexate for 2 weeks. Thereafter she received EP/EMA which consists of the drugs Etoposide, Cisplatin, Methotrexate and Dactomycin. This regimen is administered weekly alternating with EP and EMA along with intrathecal

Methotrexate on the week given EP. The chemotherapy was given till the B-HCG reached normal levels and continued for 8 weeks after.

Discussion

Partial molar pregnancy with coexisting fetus is an extremely rare variation of gestational trophoblastic disease. It accounts for 0.005 to 0.01% of all pregnancies and usually derives from dispermic fertilization of a haploid normal oocyte and produces a triploid set of chromosomes (1, 6). An increased incidence could be explained by the greater use of assisted reproductive techniques (7).

There are three types of molar pregnancy with coexisting normal live fetus: the most frequent case is a twin pregnancy with one normal fetus having a normal placenta and another complete mole; the second type is a twin pregnancy with regular fetus and placenta coexisting with a partial mole (8); the third and most uncommon occurrence reported only 19 times in the literature is a singleton normal fetus with partial molar placenta, which has some similarity to our case (5).

The diagnosis of molar pregnancy with coexisting fetus is difficult. In fact, the diagnosis can be achieved with ultrasonography and sensitive measurement of serum B-HCG usually during the first trimester (9). Moreover, in molar pregnancy, symptoms are hyperemesis, heavy vaginal bleeding, increased blood pressure with possible proteinuria that can lead to preeclampsia (6, 9, 10). Women with hydatidiform mole may experience symptoms typical of hyperthyroidism because of extremely high levels of B-HCG which can mimic the action of TSH (11, 12). High concentrations of B-HCG and suppressed levels of TSH can help to confirm the diagnosis.

Many of these pregnancies don't continue due to triploidy of the fetuses and severe intrauterine growth restriction and limited normal functional placental circulation. If the pregnancy continues, management of molar pregnancies with an apparently normal fetus remains challenging (5, 13).

In our patient, severe fetal anaemia was probably due to Malfunction cancerous placenta. There is no fetal bleeding into the abnormal hydatidiform molar placenta evidenced by a negative Kleihauer-Betke test.

The woman must be counselled regarding the maternal and fetal complications of this condition which include late miscarriage, vaginal bleeding, malpresentations, preterm labour, persistent gestational trophoblastic disease, severe fetal anaemia, hyperthyroidism, hypertensive disorders of pregnancy, pulmonary oedema, and thromboembolic phenomena (14, 15).

Hence following such pregnancy with regular ultrasound assessment of fetal anatomy and growth is important. A chorionic villous biopsy could be done if a live fetus is present, to confirm the diagnosis and to differentiate between a partial mole and complete mole: it has been reported that the latter has approximately 20% tendency to become an invasive mole or even a choriocarcinoma, while the risk was lower for partial moles (14, 16). Follow-up BhCG during and following pregnancy in order to early identify cases of persistent trophoblastic disease, invasive mole and choriocarcinoma is necessary (17-19).

Conclusion

High index of suspicion of coexistent molar pregnancy with a normal fetus is paramount considering BhCG follow up in pregnancy and postnatally. Severe fetal anaemia secondary to widely metastatic antenatal choriocarcinoma was never reported. However, the aetiology of fetal anaemia can be similar to coexistent partial molar pregnancy where the trophoblastic changes result in dysfunctional placental unit. Confirming the diagnosis by post-natal B-HCG and placental histology are important.

Disclosure of interest

There is no financial, personal, political, intellectual, or religious interests associated with the case reported.

Patient's consent

Patient was consented and permission from her personally was granted for publication of the case reported.

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Details of ethics approval

There is no need for ethical approval for publication of this case report.

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Figures

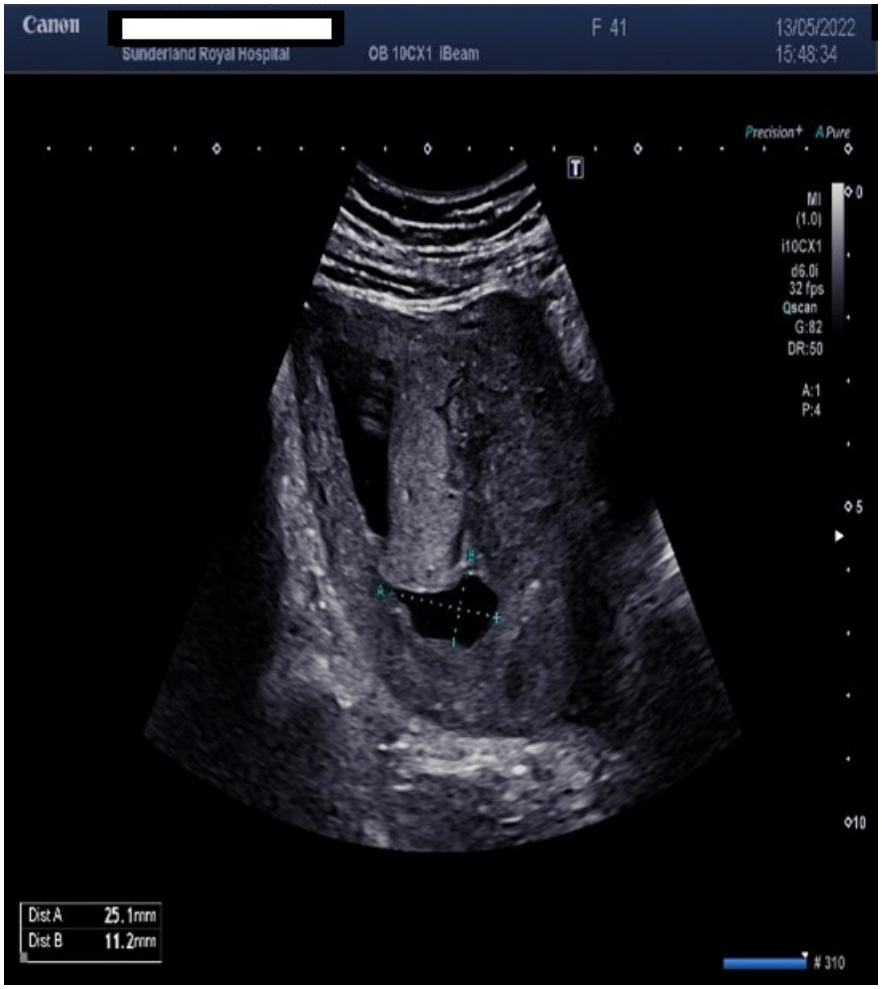

Figure - booking US scan 11 weeks

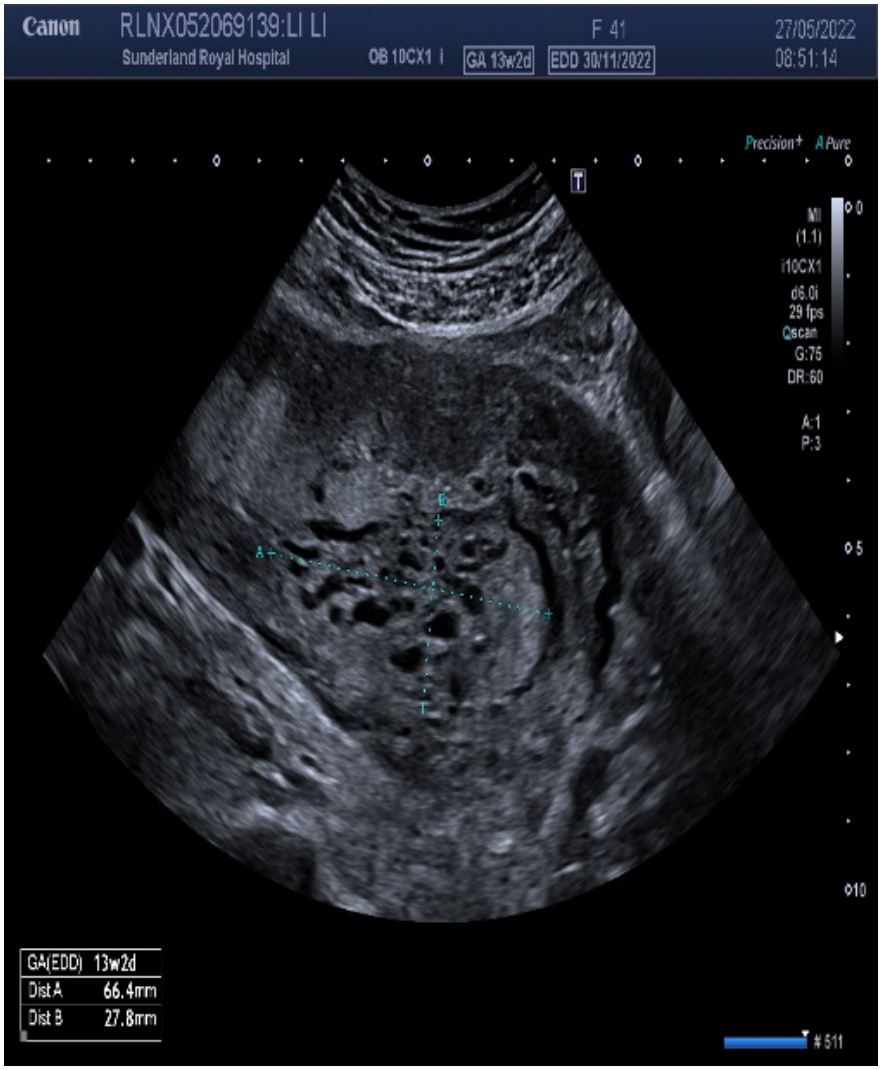

Figure - US scan 13 weeks

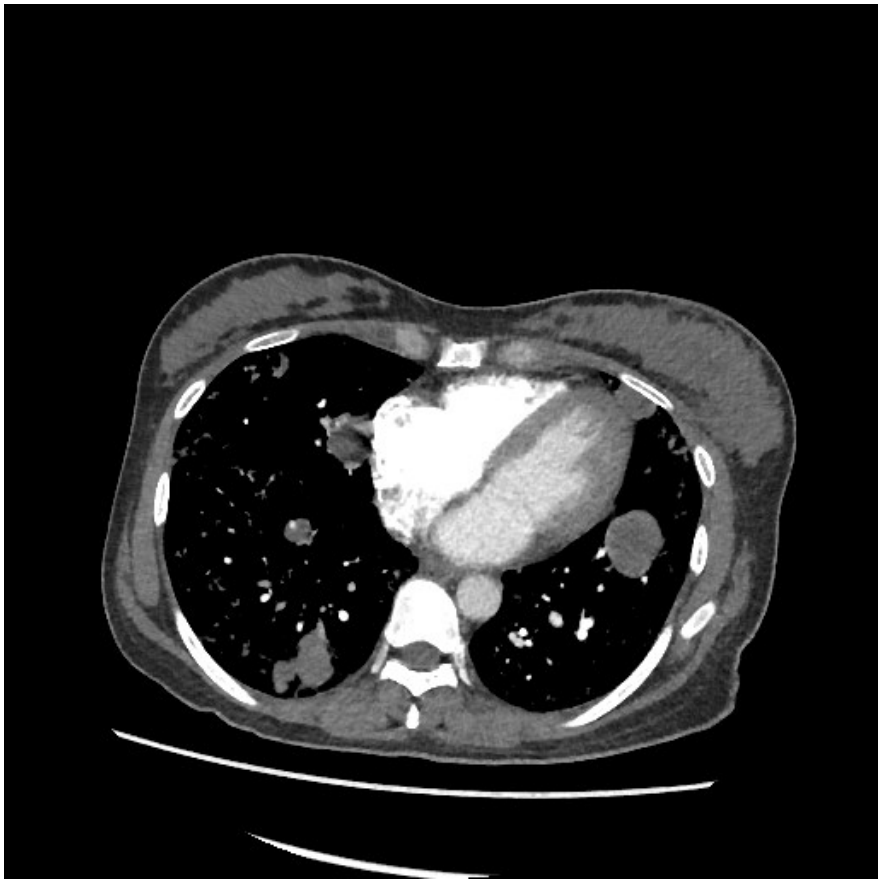

Figure CT scan findings day 7

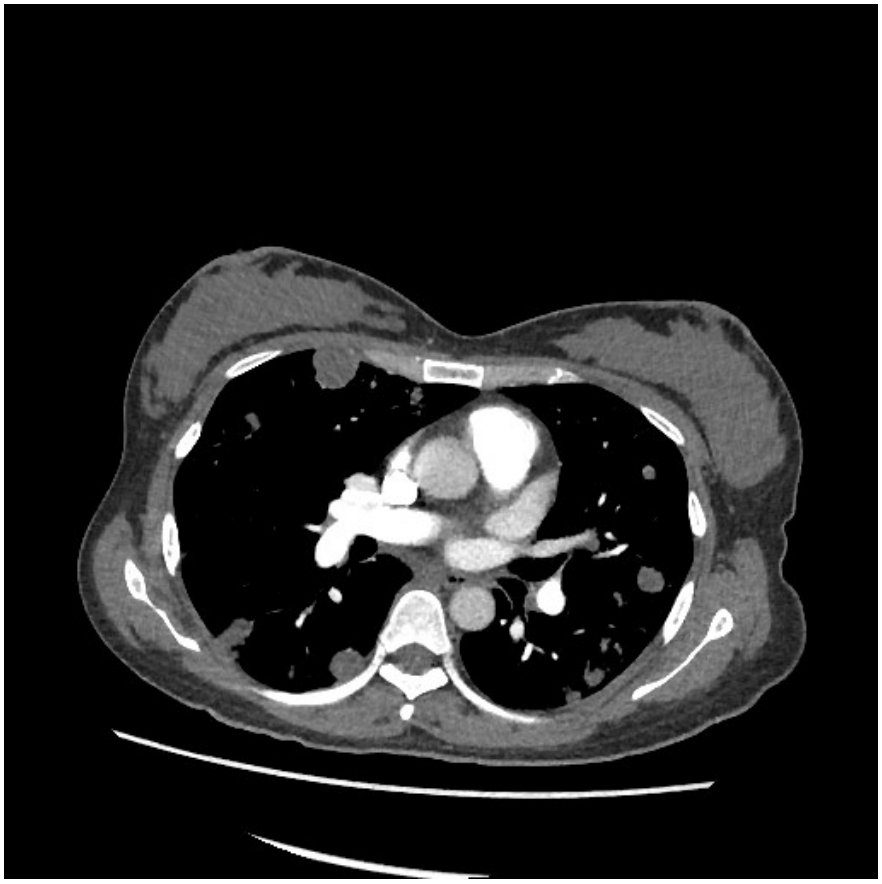

Figure - CT scan finding Day 7