Prenatal diagnosis of a complete mole coexisting with a dichorionic twin pregnancy: Case report

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A complete mole coexisting with dichorionic twins was diagnosed by the combined use of sonography and chorionic villus sampling at 10 weeks gestation. The pregnancy resulted in the death of one fetus at 31 weeks from presumed feto-maternal haemorrhage, while the other fetus survived in good condition. A summary of the available literature, combined with this report, reveals a total of seven pregnancies with twins and a coexistent complete mole. Only two out of 14 fetuses survived. Maternal complications included one case of pre-eclampsia and one persistent trophoblastic tumour. Accurate diagnosis of complete mole is possible by genetic analysis of chorionic villi obtained with standard transabdominal sampling. Twins with a coexistent complete mole will usually undergo miscarriage. However, fetal survival is possible and the maternal risks seem limited. A concomitance between gestational trophoblastic disease and the occurrence of feto-maternal haemorrhage is observed.

Key words: complete mole/feto-maternal haemorrhage/multiple pregnancy/prenatal diagnosis/ultrasound

Introduction

The association of a complete mole with two viable twins is a rare condition that has only been reported in a handful of cases (Sauerbrei et al., 1980; Ohmichi et al., 1986; Azuma et al., 1992; van de Geijn et al., 1992; Amr et al., 2000; Rajesh et al., 2000). All but one of these pregnancies resulted in miscarriage.

We now report one case of a triplet trichorionic pregnancy, with two viable twins and one complete mole that was diagnosed by sonography and chorionic villus sampling at 10 weeks gestation and continued until 31 weeks, with survival of one of the two fetuses

Case report

The patient, a 32 year old primigravida, had undergone IVF with sperm microinjection of the oocytes, and replacement of three embryos in the uterus. A previous transvaginal sonogram performed elsewhere at 7 weeks gestation had demonstrated three gestational sacs, two with viable embryos and one empty (Figure 1). A triplet trichorionic pregnancy with early failure of one sac had been diagnosed at that time. At 9 weeks the patient was referred to our unit for a scan because of bleeding. Viable dichorionic twins were confirmed but the third sac was considerably changed in appearance and presented a thickened trophoblast containing a few microcysts that almost completely obliterated the cavity of the sac (Figure 2). A molar degeneration of the third placenta was suspected. At this time, free β-hCG was 80 000 IU/ml. The patient was already scheduled for chorionic villus sampling and at 11 weeks gestation all three trophoblasts were sampled with a transabdominal procedure using a 20G ultrasound-guided needle (Smidt-Jensen et al., 1993). The viable twins had normal karyotypes, 46,XX and 46,XY. The cells from the abnormal trophoblast were found to have a 46, XX karyotype. Molecular genotyping and segregation analysis of both parental and placenta alleles, by using several VNTR (D7S481, D7S500, D7S2439, D7S523, D7S640, D14S301, D14S288, D14S286, D14S283, D15S211, GABRB3, DXS206, DXS1214) as previously described (Gualandi et al., 2000), allowed us to establish a fully paternal origin of the genotype of the abnormal trophoblast leading to molecular confirmation of complete mole. The couple was counselled about the maternal and fetal risks derived from the coexistence of twins and a complete mole. The limited experience with such cases and the poor outcome derived from available reports was discussed. Eventually, the couple decided to continue the pregnancy. In the following weeks and for the rest of the pregnancy maternal blood pressure and thyroid function remained well within normal limits. β-hCG rose to 300 000 IU/ml at 24 weeks and then plateaued. A negative chest X-ray was obtained at 24 weeks. Serial sonography documented normal anatomy and growth of the living twins. The molar placenta decreased in echogenicity throughout the pregnancy with a typical multicystic appearance since 14 weeks of gestation (Figure 3). Although a
quantitative analysis of the molar placenta was not possible, the qualitative impression was that the placental disk grew similarly to the normal placentas.

Fetal surveillance with weekly biophysical profiles was initiated at 29 weeks gestation. At 31 weeks + 4 days the patient reported a reduction in fetal movements. A biophysical profile was immediately performed. The twins were of normal size and amniotic fluid volume, but the male fetus had no movements, absent tone and absent end diastolic velocities in the Doppler waveforms of the umbilical artery. Cardiotocography demonstrated a non-reactive tracing, with no heart rate accelerations and a severe reduction in variability. The female fetus demonstrated normal movements, tone, umbilical artery Doppler and had a reactive non-stress test. An emergency Caesarean section was performed. A female infant with an Apgar score of 8 and 9 and a stillborn male infant weighing respectively 1700 and 1640 g were delivered with their own placentas. A third placenta with a macroscopic molar appearance was removed (Figure 4). The female infant was admitted to intensive care unit due to prematurity but had an uneventful neonatal course and was eventually discharged in good condition. Pathology confirmed the presence of a complete mole (Figure 5). Examination of the dead fetus and his placenta was compatible with acute exsanguination as a cause of death. The skin of the fetus was extremely pale, and petechial lesions were present on the lung surface and gastric mucosa. The placenta of the dead twin, which was close to the molar placenta, also appeared pale and hypovascular (Figure 6). An acute feto-maternal haemorrhage affecting the male twin was suspected. The hypothesis of an acute materno-fetal transfusion was supported by a positive Kleihauer–Betke test on maternal blood. Furthermore, at 72 h after delivery a large amount of free DNA of fetal origin was retrieved in maternal plasma by quantitative PCR as described in the literature (Bianchi et al., 1997).

At 6 months of age, the female twin is thriving well and is following normal developmental milestones. Maternal serum β-hCG completely disappeared after 4 months.

**Discussion**

The case described here is unique for several reasons. The molecular diagnosis of complete mole with determination of...
paternal origin of the chromosomes on placental tissue obtained after miscarriage or delivery has been reported previously (Sauerbrei et al., 1980; Ohmichi et al., 1986; Azuma et al., 1992; van de Geijn et al., 1992; Amr et al., 2000; Rajesh et al., 2000). However, to our knowledge this is the first time that the diagnosis has been made antenatally in an ongoing pregnancy by the use of chorionic villus sampling.

The ability to diagnose a molar placenta in an ongoing pregnancy is clinically relevant. The ultrasound demonstration of a multicystic placenta coexisting with one or more viable fetuses is frequently a diagnostic dilemma. Differentiation between a complete mole, a partial mole and placental mesenchymal dysplasia may be difficult; the prognostic implications of these entities are quite different (Jauniaux, 1999), although obstetric management is similar as close fetomaternal surveillance is required. Excessive placental growth is associated with an increased risk of pre-eclampsia, vaginal bleeding, thyroid disorders, premature delivery, etc. In particular, partial mole is lethal for the fetus and carries a small risk of a persistent trophoblastic tumour to the mother. Placental mesenchymal dysplasia is in general a benign entity, although an association with fetal Beckwith–Wiedemann syndrome has been reported. A complete mole coexisting with one normal fetus carries significant risks to both mother and fetus and requires close surveillance. The fetal loss rate is ~60%, while severe maternal complications (pre-eclampsia, pulmonary embolism) occur in 10% of cases. The risk of tumour persistence is in the range of 20%, and does not seem to be influenced by the duration of the pregnancy (Sebire et al., 2002).

In our opinion, it is unlikely that fine needle biopsy would increase significantly the risk of spreading the tumour, particularly when one considers that molar pregnancies are commonly evacuated by dilatation and curettage, a procedure probably much more invasive than chorionic villus sampling. In a situation in which the nature of a multicystic placenta coexistent with a fetus is uncertain, we do believe that the clinical importance of a specific diagnosis outweighs by far the theoretical risks of the invasive procedure.

In our case, thanks to chorionic villus sampling, the cause of placental abnormality was available early. Other conditions which may cause placental overgrowth (see above) were excluded and couple could decide how to manage the pregnancy after being fully informed about the case and its prognostic implications.

Usually, complete mole appears sonographically as a multicystic placenta in the late first trimester. To the best of our knowledge, this is the first paper to report the appearance of a complete mole at 7 weeks gestation. At this time, the sonographic findings were aspecific and were compatible with a blighted ovum. In early pregnancy, a sonographic aspect suggestive of early missed abortion had been previously reported (Sebire et al., 2001).

The coexistence of a complete mole with a twin pregnancy has been reported previously in six cases (Sauerbrei et al., 1980; Ohmichi et al., 1986; Azuma et al., 1992; van de Geijn et al., 1992; Amr et al., 2000; Rajesh et al., 2000) (see Table I). In five pregnancies, miscarriage or labour occurred before 25 weeks. In the two remaining pregnancies, including the present case, delivery occurred prematurely and only one fetus from each survived. Maternal complications included one case of pre-eclampsia and one case of persistent trophoblastic tumour.

We speculate that the fetal death in our case was the consequence of a severe fetomaternal haemorrhage. The clinical data, the pathological examination and the presence of a large number of fetal blood cells and fetal DNA in the maternal circulation soon after delivery are all compatible with this hypothesis. Feto-maternal haemorrhage has been previously reported in association with gestational trophoblastic disease (Theunissen et al., 1992; Lee and Ho, 1999; Suh, 1999; Takai et al., 2000; Lam et al., 2002). The pathophysiological mechanism that favours haemorrhage from the fetal to the maternal circulation in the presence of a coexistent abnormal placenta remains obscure. It is of note that in our case the placenta of the dead fetus was in close proximity to the molar placenta.

In conclusion, our case and a summary of the literature suggest the following: at 7 weeks gestation a complete mole may appear sonographically as a blighted ovum; accurate prenatal diagnosis of complete mole may be achieved by genetic analysis of chorionic villus sampling; although most twins with a coexistent complete mole will undergo miscar-
riage, there is a slight chance of intact fetal survival (two of 14 fetuses thus far reported), and the maternal risks of continuing the pregnancy seem limited; there appears to be an association between trophoblastic disease coexisting with living fetuses and feto-maternal haemorrhage. The available experience is too limited to establish the optimal obstetric management in these cases. Serial ultrasound examinations and close clinical and laboratory surveillance of the mother are certainly indicated. We also suggest fetal monitoring in the third trimester and delivery as soon as fetal maturity is achieved.

References


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