Placentomegaly and placental mesenchymal dysplasia

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SUMMARY

A 23-year-old primigravida presented to the labour ward at 37 weeks gestation referred with intrauterine growth restriction, oligohydramnios and placentomegaly. Differential diagnoses of placentomegaly were considered. Her antenatal blood screening tests were normal. There were no fetal malformations. However, triple screen and fetal karyotype were not done as patient presented late in pregnancy. The patient soon went into spontaneous labour and delivered a girl weighing 2.15 kg with a normal Apgar score. The cord was long and twisted; placenta was bulky, 1.7 kg, with prominent grape-like vesicles involving whole placenta with a rim of normal placenta at the periphery. Microscopy showed some areas of multiple villi with marked hydropic changes and myxoid degeneration, preserved vasculature and no trophoblastic proliferation. Placental mesenchymal dysplasia was thus diagnosed. The baby had no evidence of Beckwith-Wiedemann syndrome. The child is now 3 years old with normal development and is doing well.

BACKGROUND

Placentomegaly is an important ultrasound finding in pregnancy. It has been associated with normal fetal outcome, polyhydramnios, fetal hydrops, diabetes, partial mole and even fetal growth restriction as in placental mesenchymal dysplasia (PMD).¹ This case of PMD emphasises careful assessment in a case of a patient with a large placenta with cystic spaces to prognosticate the course of the pregnancy.

CASE PRESENTATION

A 23-year-old primigravida presented to the labour and delivery ward at 37 weeks 3 days period of gestation referred with intrauterine growth restriction, mild oligohydramnios, term rupture of membranes and possibility of a partial mole. The index pregnancy was a spontaneous conception, supervised irregularly in a local hospital. A second trimester ultrasound at 17 weeks 3 days reported corresponding fetal parameters. However, a subsequent ultrasound done at 31 weeks was significant for restricted fetal parameters corresponding to 28–30 weeks gestation, estimated fetal weight of 1.4 kg, mild oligohydramnios and a bulky placenta with small cystic spaces in a heterogeneous soft tissue. Fetal movements were good. There was no significant medical and family history. A differential diagnosis of partial mole or chorioangioma of placenta was made. Subsequently, the patient followed up only at 37 weeks and was referred to our tertiary care hospital in view of intrauterine growth retardation. On examination, the patient was febrile with a temperature of 38.5°C, maternal

pulse rate 94/min and fetal tachycardia of 180 beats/min. Pelvic examination revealed that membranes were absent and liquor was clear. Cervical bishop's score was 8.

INVESTIGATIONS

Her blood work including haemogram, electrophoresis, thyroid function tests and blood sugars were normal and her blood group was B positive. Ultrasound was noted to show a single live fetus with cephalic presentation, intrauterine growth restriction, an estimated fetal weight of 2.2 kg and mild oligohydramnios. Placenta was bulky. There were no fetal malformations. However, no fetal karyotype was done as patient presented late in pregnancy.

DIFFERENTIAL DIAGNOSIS

PMD is characterised by ultrasound and clinical features of gross placentomegaly with grape-like vesicles and vascular anomalies.¹ Reported in the literature as 'placentomegaly with massive hydrops of placental stem villi' and 'pseudopartial mole', PMD is often misdiagnosed as partial mole, dichorionic twin pregnancy with normal fetus and coexisting complete hydatidiform mole, placental mosaicism and placental chorioangiomas.^{1–4}

However, while partial hydatiform mole is almost never associated with a structurally normal fetus and has trophoblastic proliferation and stromal trophoblastic inclusions on pathological analysis, the fetus may be normal in majority of cases of PMD, with no trophoblastic proliferation or evidence of trophoblastic disease or recurrence.^{1–4} In complete mole with coexistent fetus, the abnormal fetal vessels in the stem villi characteristic of PMD are absent even though the fetus has a diploid karyotype.^{1–5} An early ultrasound with two gestational sacs and high-velocity low-impedance flow in the molar placental tissue may support this diagnosis of complete mole with coexistent fetus.⁴

Cystic villi on ultrasound have also been reported with confined placental mosaicism with trisomy 16 and can be diagnosed by karyotype of placenta and newborn.¹ Placental chorioangioma, subchorionic haematoma, infarcts and spontaneous abortion with hydropic changes are other conditions that simulate PMD on ultrasound.⁴ Spontaneous abortion is characterised by degenerative changes on histology and small vesicles that are focal rather than diffuse in contrast to PMD.⁴ Placental chorioangioma has a well-circumscribed echogenic area with increased vascularity which may be seen as a protrusion on the fetal placental surface.⁶ This increased flow may lead to fetal congestive heart

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failure. In contrast to chorioangioma and molar pregnancy, PMD has absent or low venous signals inside the placenta, in the first and second trimesters.⁴ Jauniaux *et al*⁷ showed that there was no association between size of placenta and fetal salvagability in PMD.

A careful ultrasound assessment of fetal structure, growth and karyotype is warranted. The fetus may be normal in karyotype and phenotype in most cases of PMD.¹ Though growth restriction may be associated with 50% of cases of PMD, macrosomia may suggest Beckwith-Wiedemann syndrome (BWS). Various characteristics of placenta and Doppler flow, as mentioned above, may differentiate PMD from causes of placentomegaly with cystic spaces in the placenta. Postnatally, clinical examination of the placenta and baby, histopathology of the placenta and karyotype of the fetus and placenta is helpful to confirm the diagnosis.

OUTCOME AND FOLLOW-UP

At presentation, our patient was admitted to the labour ward and received antipyretics and antibiotics. Subsequently, she went into spontaneous labour and delivered a live-born girl of 2.15 kg with an Apgar score of 8 and 9. The cord was long and twisted; placenta was bulky, 1.7 kg, with prominent grape-like vesicles involving whole placenta with a rim of normal placenta at the periphery (figure 1). Microscopy showed some areas of multiple villi with marked hydropic changes and myxoid degeneration, relatively preserved vasculature and no trophoblastic proliferation (figure 2). Other areas of placenta were normal. A diagnosis of PMD was made. The patient became afebrile on day 2 postpartum and was discharged on day 3 in satisfactory condition. Serum human chorionic gonadotropin (HCG) after 3 weeks was 0.01 IU/dl and follow-up. A chest x-ray performed at 4 weeks postpartum was normal. The child is now 3 years old with normal development and is doing well.

DISCUSSION

Since the time PMD was first described by Moscoso *et al* in 1991, about 100 cases have been reported. It is rare with a reported incidence of 0.02% with a female preponderance of 3.6:1.¹ Androgenic/biparental mosaicism is the most important pathogenesis implicated though other debated mechanisms include abnormal expression/imprinting of genes on chromosome 11.¹⁻⁸ PMD is associated with elevated maternal serum α -fetoprotein (AFP) and normal or slightly elevated serum HCG (40%).¹ In our patient, serum AFP levels were not done. However, HCG normalised soon after delivery. Ultrasound and karyotype can help differentiate PMD from other causes of

Figure 1 Macroscopic view of the placenta showing multiple grape-like vesicles.

Figure 2 High power of the hydropic villi (H&E stain, original magnification $\times 200$).

large placenta with cystic spaces. Examination and histopathology of the placenta confirm the diagnosis postdelivery.

PMD is associated with normal fetal outcomes as in our case, fetal growth restriction, prematurity, preeclampsia or BWS.⁹ In 20% of cases, PMD is associated with BWS which is characterised by macrosomia, exomphalos, hemi hyperplasia, macroglossia, visceromegaly, increased susceptibility childhood tumours, neonatal hyperinsulinemic hypoglycaemia and has female preponderance.¹⁻⁹⁻¹⁰ However, 15% cases of BWS are familial.¹ Even without BWS, Pham *et al*⁹ analysed that 50% fetus had intrauterine growth restriction and 43% suffered an intrauterine or neonatal death. The growth restriction or intrauterine death has been thought to be due to chronic hypoxia secondary to thrombosis of the chorionic vessels, umbilical cord abnormalities or even reduced exchange surface in the abnormal pathology of placenta.⁹ Delayed language skills have also been reported in surviving children.⁹

Parents should be counselled in a non-judgemental yet empathetic manner regarding the risks of growth restriction, intrauterine death and BWS associated with PMD. However, as the fetuses are phenotypically and morphologically normal in majority of cases, especially with normal karyotype, so unnecessary termination of pregnancy should be avoided. Finally, the baby should be assessed for BWS and growth restriction and placenta sent for histopathology.⁹⁻¹⁰

Learning points

- Placental mesenchymal dysplasia is an important differential for placentomegaly, especially when present with growth restriction.
- Careful evaluation of causes of placentomegaly helps to prognosticate and manage the pregnancy.
- Though there may be association with intrauterine growth retardation, intrauterine growth restriction, prematurity and Beckwith-Wiedemann syndrome, majority of children may be normal.

Competing interests None.

Patient consent Obtained.

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