

Prenatal sonographic findings and management of placental mesenchymal dysplasia

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Placental mesenchymal dysplasia (PMD) is a rare disorder of the placenta characterized by placentomegaly with diffuse hydropic stem villous, aneurysmally dilated vessels, and lack of trophoblastic proliferation. *Case:* The prenatal ultrasound of a 34-year-old woman (G1P0) at 33 weeks of gestation showed an enlarged placenta with multiple cystic lesions, heterogeneous echoes with no active blood flow, and fetal growth restriction (FGR). The differential diagnosis involved partial mole, placental hemorrhage, and PMD. She developed preeclampsia at 38 weeks of gestation and gave birth to a normally formed, growth-restricted baby. The placenta, weighing 785 g, showed scattered cystic vesicles in the parenchyma. The histology shows enlarged edematous stem villi with occasional cistern formation and no area of chorioangioma or features of molar pregnancy. PMD associated fetal growth restriction was diagnosed. *Conclusion:* PMD has prenatal ultrasound result resembling those of partial mole, placental hemorrhage and chorioangioma, but the fetus is phenotypically normal. Nevertheless, fetal surveillance is essential.

Keywords

Placental mesenchymal dysplasia; Prenatal diagnosis; Ultrasound

1. Introduction

Placental mesenchymal dysplasia (PMD) is a rare disorder of the placenta, characterized by placentomegaly with diffuse hydropic stem villous, aneurysmally dilated vessels and lack of trophoblastic proliferation. Prenatally, a multiple cystic lesion appearance of the placenta should be differentiated among partial hydatidiform mole, complete hydatidiform mole with coexisting normal fetus, chorioangioma, subchorionic hematoma, intra-placental hemorrhage or placental lake, spontaneous abortion with hydropic change and placental mesenchymal dysplasia [1, 2]. Prenatal ultrasound might be useful for diagnosis however microscopic characteristics are required for definite diagnosis. Though cases of PMD have been occasionally published, the number of case reports is still limited, and more new cases are needed for further analysis of prenatal findings and management. Therefore, we report this case to describe the prenatal sonographic findings, management and postnatal pathological confirmation of a case of PMD. The main purpose of this report is to emphasize the importance of differential diagnosis of a multi-

ple cystic lesion appearance of the placenta, especially differentiating partial hydatidiform mole from PMD. This is clinically important since the two conditions have different prognosis and management. Partial hydatidiform mole is usually associated with fetal anomaly and termination of pregnancy is usually offered whereas PMD has a better prognosis and conservative management is preferred [3, 4]. Also, we want to underline the role of antenatal surveillance of a pregnancy complicated with PMD due to its potential adverse associations.

2. Case

A 34-year-old pregnant woman (G1P0) was referred for detailed ultrasound at 33 weeks of gestation due to placentomegaly. Her first antenatal care was at 12 weeks of gestation. The basic laboratory tests for antenatal care revealed normal results. Screening for fetal Down syndrome at 14.6 weeks of gestation (body weight: 53 Kg; BMI: 22.1) revealed as follows: AFP: 32.91 U/mL (0.96 MoM); b-hCG: 39.31 ng/mL (2.05 MoM); IHA: 377.28 pg/mL (1.47 MoM); uE3: 3.80 nmol/L (1.13 MoM), and the estimated risk of Down syndrome was 1 : 555. The first ultrasound scan at 21 weeks did not show evidence of fetal and placental abnormality. Antenatal course was uneventful, without any obstetric complications. The detailed ultrasound revealed normal anatomical scan, no hydropic sign and normal amniotic fluid volume. However, fetal biometry indicated fetal growth restriction, estimated fetal weight of less than 10th percentiles at 33 weeks of gestation. The Doppler studies of the umbilical artery and middle cerebral artery revealed normal results. The placenta was heterogeneous in echotexture with multiple small cystic lesions and homogeneous hypo echo density of fluid content; however, there was low internal blood flow, as shown in Fig. 1. The placental thickness was 7.5 cm. A provisional diagnosis was PMD or placental hemorrhage associated with fetal growth restriction. Based on the most important finding of multiple cystic lesion appearance of the thickened placenta, the differential diagnoses included partial mole, complete molar pregnancy with co-twin and chorioangioma. Though multiple cystic lesion appearance is typical

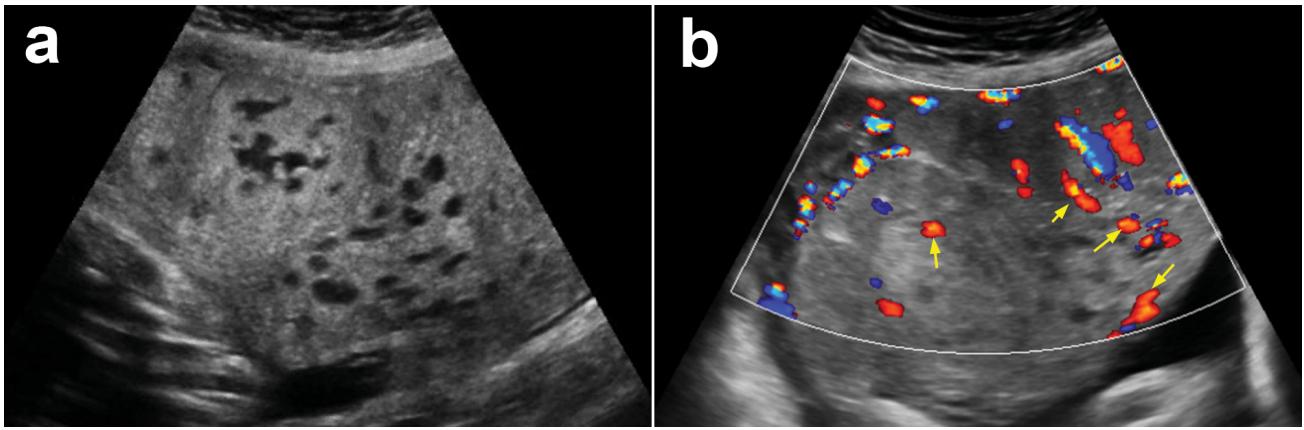


Fig. 1. 2D Ultrasound image at 33 weeks of gestation shows thickened placenta with heterogeneous in echo texture with multiple small cystic lesions (a) and color flow mapping shows low internal blood flow (arrows) (b).

for partial mole, it is usually associated with oligohydramnios, asymmetrical growth restriction, very scanty blood flow and fetal anomalies. Thus the case presented here, which had no anomalies and normal amniotic fluid volume, was unlikely to be partial mole, though definite diagnosis was based on pathological findings. Complete mole with co-twin is also listed in differential diagnoses. However, in such a condition, the normal fetus has its own separate normal placenta different from our cases which was a single globally enlarged placenta. Chorioangioma can also give the appearance of multiple cystic lesions. Nevertheless, the tumor is usually a well-defined mass, confined to an area separated from the rest of normal placenta, different from our cases which the abnormal area is globally distributed all over the placenta. Therefore, the provisional diagnosis of our case was PMD.

Serial ultrasound scans for fetal growth assessment and fetal surveillance were performed, revealing reactive non-stress test results. The results of the Doppler study and the amniotic fluid volume remained normal. On serial ultrasound scans at 35, 37 and 38 weeks of gestations, the placental appearances were relatively the same, with slow progressive increase in thickness from 7.5 cm at 33 weeks to 8.8 cm at 38 weeks and multiple cystic lesions became more prominent.

At 38 weeks and 6 days, she developed preeclampsia without severe features (blood pressure of 150/95 mmHg, 24-hour urine protein of 1.1 g, platelet count of $175,000 \text{ mm}^3$, aspartate aminotransferase of 52 IU/L, alanine aminotransferase of 60 IU/L, lactate dehydrogenase of 258 IU/L, creatinine of 1.0 mg/dL, and fibrinogen of 300 mg/dL). The female baby was delivered by cesarean section and weighed 2,450 g (10th percentile); it was small for its gestational age but appeared morphologically normal. The placenta was markedly enlarged, measuring $15.5 \times 15 \times 4 \text{ cm}$ and weighing 785 g (95th percentile) with marginal umbilical cord insertion. Dilated and tortuous subchorionic vessels with scattered cystic vesicles and spongy dark red appearance of the placental tissue were identified on the maternal surface of the placenta, as shown in Fig. 2. The microscopic examination showed

enlarged edematous stem villi with occasional cistern formation, whereas trophoblastic proliferation and stromal inclusion were absent. The subchorionic vessels were dilated and thick-walled with overgrowth of fibroblastic stroma (Fig. 3). The newborn was healthy and discharged within 3 days after delivery. Postnatal chromosome study revealed normal karyotype; 46; XX.

3. Discussion

Placental mesenchymal dysplasia (PMD) is a placental vascular abnormality that rarely occurs. It was first recognized by Moscoso *et al.* in 1991 [5]. Its incidence is about 0.02%, and it is more common in females [6]. Grossly, the large placenta shows dilated vesicles or cystic lesions and is microscopically characterized by dilated stem vessels with the absence of trophoblastic proliferation [1, 5, 7]. In this condition, adverse pregnancy outcomes such as preterm labor, preeclampsia and fetal growth restriction commonly occur. Such adverse outcomes may be associated with sub-amnion hemorrhage, infarct-like lesions and subchorial thromboses, as seen in our case. Preterm labor can occur in about 50% of cases, while intrauterine growth restriction and preeclampsia can occur in about 33% and 9% of cases, respectively. However, PMD is found in 9% of uncomplicated pregnancies [3]. Moreover, several studies also reported abnormal neonatal outcomes such as aneuploidy, Beck-Wiedemann syndrome, hepatic tumor, and hematologic disorders [8–13]. Accordingly, prenatal ultrasound indication of thickened placenta with suspicion of placental hemorrhage or PMD should be considered as a high risk pregnancy, which needs close surveillance and follow-up.

The differential diagnosis should be made based on gestational age. In early gestation, PMD is sonographically similar to complete mole, partial mole, and hydropic changes secondary to spontaneous abortion, whereas it must be differentiated from partial mole with a viable fetus, chorioangioma, and placental hematoma/hemorrhage in the second and third trimesters. The provisional diagnosis of our case in earlier

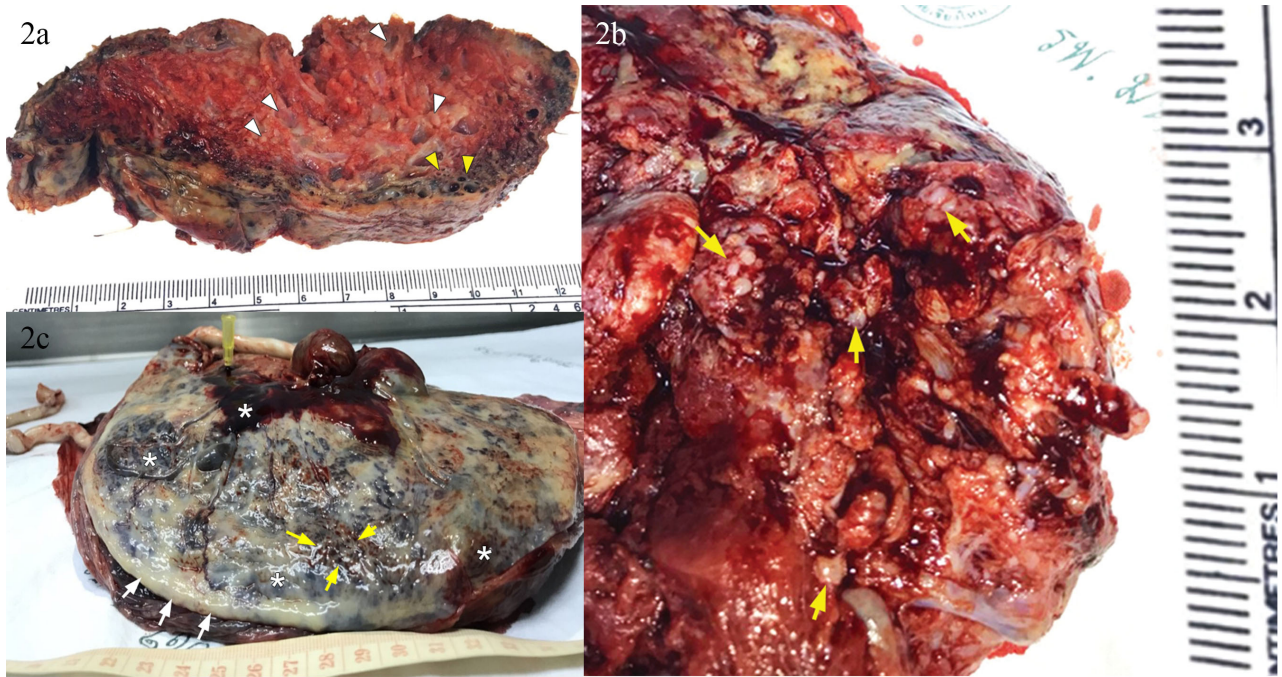


Fig. 2. Gross examination of the placenta. (2a) Cut surface of the placenta shows general thickening with multiple cystic vesicles (white arrow heads) and tortuous subchorionic vessels (yellow arrowhead). (2b) Maternal surface shows hydropic placenta with multiple cystic vesicles (arrows). (2c) Fetal surface of the placenta shows generalized necrotic ecchymosis (asterisk) with thickened fetal membranes (white arrows) and tortuous subchorionic vessels (yellow arrows).

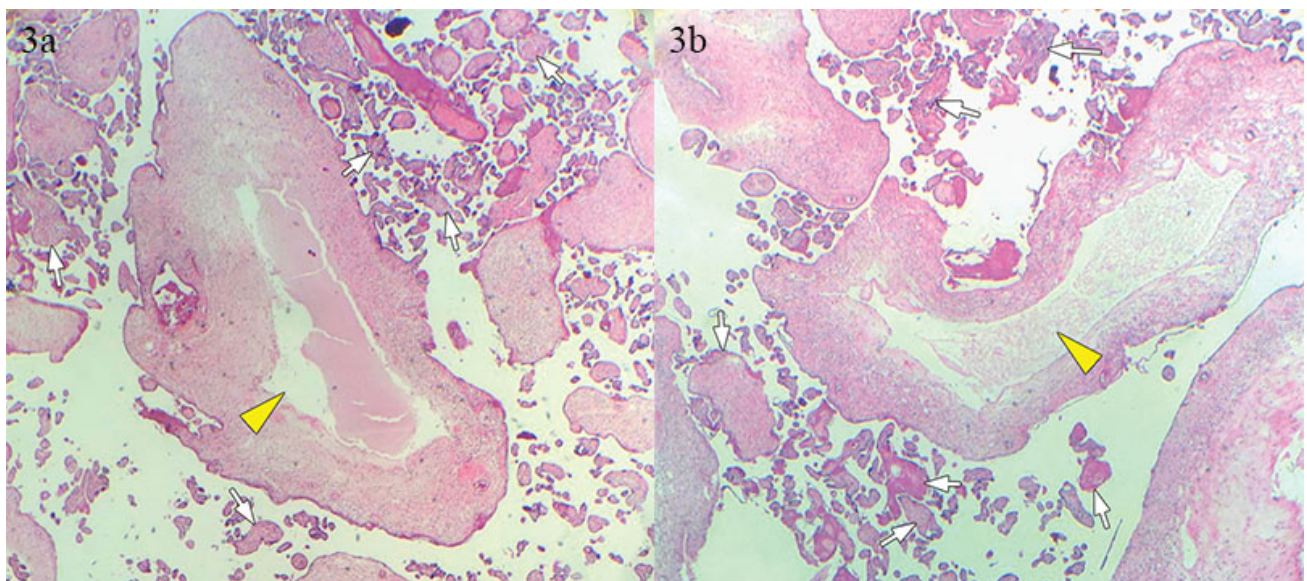


Fig. 3. Histopathology (hematoxylin and eosin staining; 100 ×) shows dilated stem villi with cystic change (arrowhead), and normal free villi (arrows).

gestation was placental hemorrhage, which is the most common cystic placenta in normal fetus, based on diffused heterogeneous echoes, thickened placenta and absence of multiple small vesicular patterns, typical of partial mole [14–16]. However, PMD was included in the differential diagnosis, though it is relatively rare. Because of the normal amniotic fluid volume and absence of fetal anomaly, partial mole was

unlikely. Since the pattern of cystic lesions, varying in size, became more obvious on the follow-up scans, PMD is more likely. Color flow may help differentiate PMD from mole. In partial mole, there is absence of blood flow in the hydropic villi, whereas in PMD Color Doppler shows various degrees of flow depending on the level of blood flow in a patient-by-patient manner and in some cases show a ‘stained-glass’ ap-

pearance, which indicates a varying degree of flow from dilated or aneurysmal like vessels of PMD [17]. In some cases as well as our case, PMD cysts may not have a sufficient flow for color Doppler to readily reveal the typical 'stained-glass' sign [18]. Because of thickened cystic placenta with a normal fetus, twins with coexisting mole might also be listed in differential diagnoses. Nevertheless, a twin pregnancy with coexisting mole usually has separate normal placenta of the normal fetus and abnormal placenta (mole) [19], whereas the case presented here had a single placenta with globally thickened cystic echoes. Thus, this case was not consistent with twins with coexisting mole.

Prenatal sonographic findings associated with PMD may vary. In the review by Nayeri *et al.*, the most common ultrasound finding of PMD was placental cyst or hypoechoic area (80%), followed by enlarged placenta (50%) [3]. Subchorionic hemorrhage might be the predominant finding of our first scan and some previous reports [20, 21]. Based on our findings and literature review, the prenatal aspects of PMD may be summarized as follows: Typical findings associated with PMD are cystic placental lesion and placentomegaly. Many reports often describe cystic finding as 'Swiss-cheese', 'moth-eaten' or molar. However, achieving the diagnosis in early gestation may be difficult since the typical cystic feature is not developed yet. In early gestation, ultrasound often shows thickened placenta and multiple cystic areas; the cystic spaces are often located deep in the placenta and move towards the chorionic plate in late gestation [22, 23].

Invasive prenatal diagnosis such as chorionic villus sampling or amniocentesis should be performed to confirm a normal karyotype, thereby excluding triploidy in partial mole and fetal aneuploidy [3]. Nevertheless, our case was encountered in late gestation, and though abnormal findings were identified, the fetus seemed normal, and change in management was unlikely regardless of chromosome study results. Thus, we performed chromosome study after birth. Abnormal rise of alpha fetoprotein (AFP) with normal or minimal rise of beta HCG levels are correlated with PMD [7]. Notably, our case was also associated with elevated b-hCG, but other biomarkers were normal. Advanced techniques such as magnetic resonance imaging and 3D ultrasound, especially inversion mode, showed a large multi-cystic area arising from the chorionic plate, which was adjacent to normal-appearing placenta [24]. In histopathology, the most important clue for the differential diagnosis of partial mole from PMD is the absence of abnormal trophoblastic proliferations [25].

Limitations of this study are as follows: (1) Because of no ultrasound study in early gestation, the natural history of disease progression could not be completely provided. (2) MRI, which might provide additional prenatal details, was not done, though ultrasound findings seemed to be adequate in this case.

4. Conclusions

Regarding cystic placenta with normal fetal anatomy, the common findings are partial mole, PMD and placental hemorrhage. Diffused heterogeneous echoes from the thickened placenta may give the first impression, as presented in our case. The combination of prenatal ultrasound of cystic echoes, normal karyotype is helpful in the diagnosis of PMD. Nevertheless, definite diagnosis is based on postnatal pathological study of the placenta. Finally, among pregnancies with PMD, awareness about adverse outcomes, such as preterm labor, FGR, preeclampsia and fetal death, should be promoted.

Author contributions

SL: Conceptualization, obstetric management of the patient, editing and approval of the manuscript. PC: Obstetric management of the patient, editing and approval of the manuscript. TP: Pathological examination and diagnosis, editing and approval of the manuscript. TT: Conceptualization, writing the first draft and approval of the manuscript. All authors contributed to the interpretation and writing of the paper and approved the final version.

Ethics approval and consent to participate

This case report was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of 4 (Study code: OBG-2561-05996). Informed consent was obtained from the patient.

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Conflict of interest

The authors declare no conflict of interest.

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