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# Placental Mesenchymal Dysplasia – a case report

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## ABSTRACT

Placental mesenchymal dysplasia (PMD) is a very rare vascular placenta anomaly, characterized by an enlarged placenta with grape-like vesicles. Initially, the disease can be mistaken for a molar pregnancy on ultrasound, but the condition is not a trophoblastic disorder, and presents with unique diagnostic and clinical features. Genetically, there is an association with androgenic/biparental mosaicism which can be confined to the placenta but also can be present in the fetus, and there is an increased risk of imprinting disorders such as Beckwith-Wiedemann syndrome. Obstetrically, PMD is associated with fetal growth restriction, preeclampsia, preterm delivery, and increased risk of intrauterine fetal demise. Thus, PMD is often associated with severe maternal and/or fetal complications, and this case illustrates the challenge in the diagnosis and prenatal counseling.

**Keywords:** Placental mesenchymal dysplasia, androgenetic/biparental mosaicism, genome wide paternal UPD, placenta abnormalities, hypertensive disorders of pregnancy

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## INTRODUCTION

Placental mesenchymal dysplasia (PMD) is a rare condition characterized by placental enlargement with grape-like vesicles and is often misdiagnosed as a hydatiform mole due to the similar ultrasonographic appearance (1).

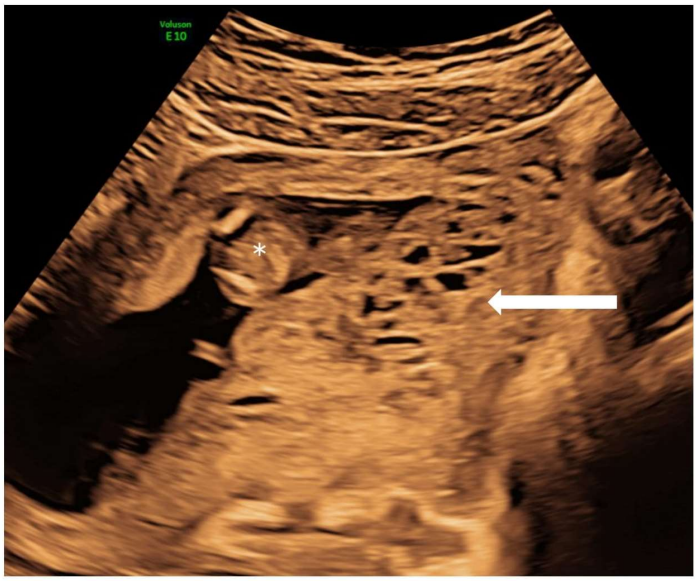
Unlike molar pregnancies, PMD has no potential for malignancy, and usually presents with a normal fetus. However, it is associated with severe maternal and fetal complications such as fetal growth restriction, preeclampsia, preterm delivery, increased risk of intrauterine fetal demise and imprinting disorders such as Beckwith-Wiedemann syndrome (2-4). This case demonstrates early diagnosis due to ultrasonographic appearance as well as increased risk for trisomy 21 in the combined first trimester screening. Early diagnosis in this case might have been missed since sampling from the placenta was extremely difficult.

## CASE REPORT

A 28-year-old woman, gravida 1, was referred to a chorionic villus sampling (CVS) due to increased risk for trisomy 21 in the combined first trimester screening (1:278). The level of β-HCG was 1.261 MoM and PAPP-A was 0.325 MoM. No abnormalities of the fetus were detected, and the nuchal translucency was 1.3 mm. The sampling was conducted at 13 weeks and 1 day of gestation and sent to chromosomal microarray analysis.

The ultrasound during the CVS revealed a hypertrophic placenta with a multicystic molar-like appearance. The sampling was taken from these pathological areas, but it was extremely difficult to obtain tissue, and two separate attempts were necessary to get a small amount of tissue out for genetic analysis. A follow up ultrasound a week later detected no ultrasonic abnormalities of the fetus but confirmed the enlarged placenta with multiple anechoic cysts (Figure 1).

Figure 1




Ultrasound at 14 weeks and 1 day of gestation; showing the enlarged, multicystic placenta (arrow) and fetus (*).

Chromosomal microarray analysis of DNA from the CVS was without apparent chromosomal imbalances for a female fetus, however single nucleotide polymorphism data indicated signs of uniparental disomy. Subsequent quantitative fluorescent PCR (QF-PCR) (analyzing polymorphic microsatellite markers on chromosomes) of the DNA from the CVS compared with DNA from the couple revealed a mosaicism in the placenta with two different cell lines; a large cell line with paternal UPD - all two sets of chromosomes originating from the father - and a smaller cell line with a normal biallelic pattern, with chromosomes from both the father and the mother, indicating mosaic genome-wide paternal uniparental disomy (GWpUPD) also known as androgenic/biparental mosaicism (ABM).

From the combined genetic analyses and ultrasound appearance of the placental tissue, the diagnosis of PMD was assessed to be the most likely. The couple was informed of the increased morbidity and mortality in fetuses associated with PMD, as well as increased obstetrical risks. The couple decided to apply for an abortion, and the pregnancy was terminated at 15 weeks and 5 days of gestation.

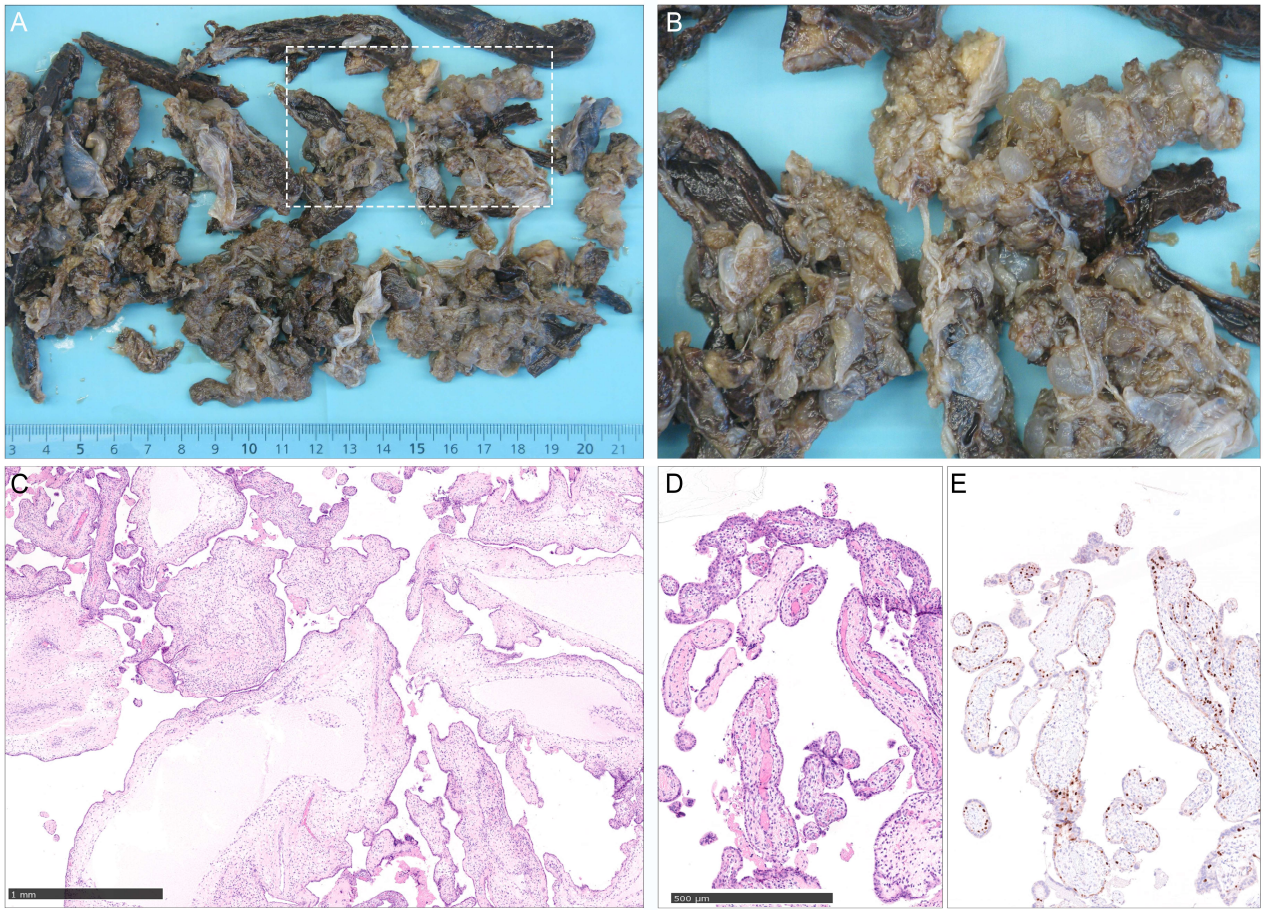



**Figure 2:** Gross and histological appearance from the placental examination. A) Gross photograph of the placenta. It was received fragmented, with a total area of 11 x 9 x 1 cm and was found with grape-like clear cysts/vesicles of varying size, up to 0,8 x 0,5 x 0,4 cm, in areas as clusters of grapes. In between the placental tissue was frayed, light brown in color and with occasional blood clots. The maternal and fetal surfaces were difficult to assess. There were numerous cystic blebs and dilations (insert in B) admixed with more normal appearing placental tissue. C) Low-power view of villous parenchyma. Many villi were abnormally large, irregular in shape and size, some with edema and some were acellular and cystically dilated corresponding to the gross appearance. D) Higher-power view of an area with a more cellular stroma, immunostained for p57 (E). There was no abnormal trophoblastic hyperplasia or proliferation. The immunostaining showed discordant expression with p57-positive cytotrophoblast and p57-negative stroma. Only focal areas showed normal p57 reaction of both cytotrophoblast and stroma. There were no morphological or immunohistochemical signs of a component of complete mole. Ki-67 was low in all areas (not shown). C, D: Hematoxylin and eosin, original magnification 2.5X and 5X, respectively. E: p57 immunostaining, original magnification 5X.

The fetal autopsy showed a female fetus with biometries corresponding to 15 weeks of gestation. There were no malformations, signs of fetal growth restriction, or Beckwith-Wiedemann syndrome.

The gross features of the placenta confirmed the presence of grape-like vesicles. The microscopic investigation showed abnormal placental tissue with fetal vascular malperfusion, stem villous cystic dilation, and vesicle formation. There was no atypical trophoblastic proliferation. Immunohistochemical staining for p57 showed retained expression of the cytotrophoblast and no expression of the villous stroma, compatible with PMD with ABM (Figure 2).

Genetic analysis of fetal tissues showed biallelic pattern why it is most likely that the abnormal uniparental cell line was confined to the placenta (confined placenta mosaicism), but low level mosaicism in the fetus could not be ruled out.

The macroscopic, microscopic, and genetic data were consistent with the diagnosis of PMD.

## DISCUSSION

Serologically, PMD often presents β-HCG within normal limits (2,3) and usually a normal fetus is seen on ultrasound. Genetically, PMD is most often associated with ABM in the placenta. However, the fetus can present with a normal biallelic pattern. The diagnosis of PMD can be confirmed with placental gross features of enlarged grape-like vesicles and histologic features of hydropic cystic stem villi, no trophoblastic proliferation and preserved expression of p57 in cytotrophoblast. In this case, chorionic villus sampling was very difficult, most likely due to the pathological placenta tissue, and the diagnosis would have been delayed and the diagnosis of ABM likely missed prenatally, if an amniotic fluid sample had been performed instead. Of note, the distribution of the mosaicism in the CVS only represents the small sample, and not the distribution of the mosaicism in the placenta as a whole. Nevertheless, it is crucial to obtain tissue from the pathological areas of the placenta, since mosaicism can be present scattered in fetal tissue once ABM is found in the placenta – no matter the percentage of cell-lines. This genetic information radically influenced the decision of the couple to opt for termination of the pregnancy. To our knowledge, it has not been previously described that CVS can be extremely difficult with PMD.

PMD with fetal ABM mosaicism is associated with risk of Beckwith-Wiedemann syndrome (approximately 20% of fetuses with PMD); a syndrome involving overgrowth of organs, omphalocele, hypoglycemia, and risk of tumors in the liver or kidneys (4). Other imprinting diseases such as Angelman syndrome can be seen as well.

There is a substantially increased risk of fetal growth restriction (33%), intrauterine fetal demise (29%) and preterm delivery < 37 weeks of gestation (52%) associated with PMD (5-7). As it is a vascular abnormality, there are also markedly increased maternal risks, approximately 13% will develop hypertensive disorders, including preeclampsia and/or HELLP syndrome (5-7).

## CONCLUSION

The diagnosis of PMD is difficult as it can be mistaken for the more common hydatidiform mole. Even though a normal fetus is often seen, it is not possible to rule out a mosaicism in the fetus prenatally, in the case of ABM in the placenta. In our case, the PMD/ABM diagnosis might have been missed prenatally, since CVS was extremely difficult to perform. The pregnant woman should be counselled about the high risk of fetal and maternal complications during a pregnancy with PMD, including the risk of fetal mosaicism associated with a diagnosis of AMB, and should be monitored closely if the pregnancy is continued.

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