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REVIEW ARTICLE

# Placental Mesenchymal Dysplasia

**Linda M. Ernst**[1]

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**Abstract** This is an updated review of the recently described entity, placental mesenchymal dysplasia, which has been shown to have recognizable antenatal characteristics, distinctive gross and microscopic pathologic findings, associated fetal and neonatal morbidity and mortality, and unique pathogenic mechanisms. Recent understanding of the frequently associated genotype, androgenetic biparental mosaicism, is reviewed and the spectrum of changes discussed.

**Keywords** Placental mesenchymal dysplasia · Androgenetic biparental mosaicism · Neonatal morbidity

## Introduction

Placental mesenchymal dysplasia (PMD) is a distinctive, rare placental lesion estimated to occur in 0.02 % of pregnancies, but with the recent increasing awareness of this placental lesion, it is possible the true incidence may be under-represented [1]. The features of PMD were not recognized as a distinct entity until the early 1990s. The first known description in the English medical literature is attributed to Moscoso [2] who described two cases of a placental vascular anomaly with diffuse mesenchymal stem villous hyperplasia, and suggested this represented a new clinic-pathologic entity. Later that year, Lage [3] reported four cases characterized by placentomegaly with massive hydrops of placental stem villi, diploid karyotype, and fetal omphalocele. The author suggested a possible association with Beckwith-Wiedemann syndrome. Several other reports of pseudo-partial mole [4, 5] described similar features. Initially, there was some debate about whether to call the lesion PMD or placental mesenchymal hyperplasia [4, 6–9], but to date PMD is the preferred terminology. More than 100 cases of PMD have been reported in the literature. However, discussion of this unique placental entity in contemporary surgical pathology textbooks is still inconsistent.

The characteristic features of PMD include placental enlargement, dilated and tortuous or cirsoid chorionic vessels which often show thrombosis, and a focal distribution of cystically enlarged villi, in a background of grossly normal-appearing villous tissue; hence, the similarity to partial hydatidiform mole (PHM). However, in contrast to PHM, the histology of PMD features clusters of enlarged, proximal, stem villi (not distal villi) with central cistern formation and absence of trophoblastic proliferation or hyperplasia.

The understanding of etiology and pathogenesis of PMD has advanced in recent years, and paternal uniparental disomy for the Beckwith–Wiedemann syndrome (BWS) locus on chromosome 11p15.5, often as a consequence of androgenetic biparental mosaicism (ABM), has been shown to underlie most cases of PMD. This review will discuss the clinical features, pathologic characteristics, and pathogenesis of PMD.

## Clinical Features and Associations

As PMD is a relatively newly described entity, the predominance of cases has been diagnosed after pathology examination; however, with increasing awareness of the

✉ Linda M. Ernst
linda-ernst@northwestern.edu

[1] Department of Pathology, Northwestern University Feinberg School of Medicine, Olson Pavilion 2-461, 710 N. Fairbanks Court, Chicago, IL 60611, USA

lesion, PMD is becoming recognized prenatally by antenatal imaging techniques. By conventional ultrasound methods, the placenta in PMD is typically described as large and thickened with multicystic, hypoechoic areas (Fig. 1a). The differential diagnosis for this ultrasonographic appearance includes PHM, complete hydatidiform mole (CHM) with co-existent fetus, chorangioma, intervillous hematoma, and infarct or nonspecific hydropic changes [10]. PHM is typically associated with elevated HCG levels and a triploid fetus and therefore, can be excluded by further genetic workup. Color Doppler has recently become a tool to help distinguish PMD from a molar gestation [11, 12]. PMD is reported to show a "stained-glass" appearance suggesting abundant blood flow in PMD while CHM shows little to no blood flow [12]. The large cystic parenchymal spaces in PMD are typically devoid of blood flow as they represent cystic change within the villous stroma (Fig. 1b). However, blood flow seen in PMD may be related to the dilated chorionic vessels and/or the thickened vessels within the dilated stem villi. The absence of color Doppler signal may not exclude PMD as the degree of flow may vary from patient to patient [13] and vary with gestational age [10]. Recently, magnetic resonance imaging (MRI) has also been described as a method to distinguish CHM with twin co-existent fetuses from PMD [11]. MRI may, more accurately, discern the location of the cystic placental tissue as within or outside the fetal "sac" (CHM outside, PMD within), and aid in the distinction of these two entities [11]. With continued recognition of cystic placental changes by advanced imaging techniques, it is likely that obstetricians will consider PMD in the differential diagnosis, more frequently.

One of the characteristic morphologic features distinguishing PMD from molar gestation is the lack of trophoblastic hyperplasia in the former, and accordingly, maternal serum βHCG levels are typically not elevated or only slightly elevated in PMD [14]. Additionally, there is no known risk of persistent gestational trophoblastic disease with PMD. While there are no other specific maternal serum markers of PMD, elevations in maternal serum alpha-fetoprotein (AFP) have been reported and may be associated with leakage or transfer of AFP across the hydropic villous stroma, malformed fetal vessels, or abnormal development of lymphatic structures in PMD [2, 15–17].

## Fetal Pathology

When PMD is diagnosed antenatally, it is generally thought to carry a better fetal prognosis than a molar gestation; however, fetal and neonatal mortality have been reported in association with PMD [18]. The rate of perinatal demise is not certain, but could be as high as 43 % of affected patients [18].Sudden intrauterine fetal death with massive fetal hemorrhage secondary to rupture of dilated periumbilical chorionic vessels has been reported [15, 19]. In addition, the cause of fetal death in many cases of PMD may be explained by longstanding, severe fetal hypoxia secondary to fetal vascular obstructive pathology characterized by chorionic vessel thrombosis. Fetoplacental vascular pathology and fetal thrombotic vasculopathy (FTV) may also account for the high rate of intrauterine growth restriction (IUGR) which is reported in up to 50 % of PMD cases [18]. Fetuses and newborns with PMD may also be at risk for fetomaternal hemorrhage [20].

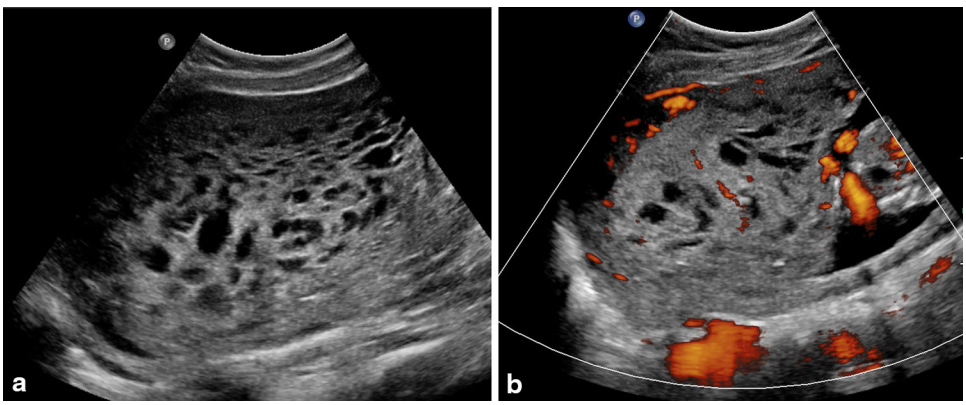


**Fig. 1** Two-dimensional ultrasonographic appearance of classic PMD in the placenta. **a** Two-dimensional ultrasonography of placenta with PMD. Note the multiple rounded echolucent foci within the more echogenic placental parenchyma. These represent cystic foci within the placental parenchyma. In this case, the cysts are more prominent near the chorionic plate (*top*) where stem villi predominate and are slightly compressed near the chorionic plate. **b** Two-dimensional ultrasonography with color Doppler flow of placenta with PMD. Note that the echolucent cysts are generally devoid of flow while some flow is noted in the adjacent more echogenic parenchyma. (Images kindly provided by Lynn Yee, M.D., Maternal-fetal Medicine division, Northwestern University Feinberg School of Medicine)

A structurally normal fetus/newborn is usually present; however, several congenital abnormalities have been associated with PMD including congenital hemangiomas [21–23], hepatic mesenchymal hamartoma [9, 22, 24–26], gastroschisis [27], pulmonary hamartoma [28], and BWS [29, 30]. BWS is a constellation of multiple congenital anomalies, characterized by macrosomia, omphalocele, and macroglossia [31]. Additional features include earlobe creases, adrenal cytomegaly, hyperplasia of the kidneys and pancreas, and neonatal hypoglycemia. Approximately one-third to one-fourth of cases of PMD are associated with BWS. Interestingly, BWS is a disease associated with imprinting and is caused by mutation or deletion of imprinted genes within the chromosome 11p15.5 region (OMIM #130650). Important genes involved in the region include CDKN1C, H19, and LIT1. In addition, hypermethylation of the H19/IGF2-imprinting control region on chromosome 11p15.5, which regulates imprinted expression of H19 and insulin-like growth factor 2 (IGF2) is associated with BWS. Paternal uniparental disomy (UPD) at 11p15.5 (involving IGF2 and CDKN1C), either as an isolated chromosomal defect or as part of pan-genomic paternal UPD in ABM, could be the genetic factor linking PMD and BWS [32]. In ABM, two lineages of diploid cells are present in the conceptus, one of which is abnormal in that, all 46 chromosomes are derived from the father and presumed to carry paternal epigenetic imprints.

## Placental Gross and Microscopic Features

The placenta in PMD is typically enlarged (placentomegaly) and shows strikingly dilated chorionic plate fetal vessels, which often show thrombosis (Fig. 2a). On cut section, the parenchyma shows patchy, cystically enlarged villi, in a background of grossly normal-appearing villous tissue (Fig. 2b). Histologically, this admixture of normal and abnormal-appearing villi is preserved at low power. Proximal stem villi are enlarged and show abnormal edematous/myxomatous stroma with cistern formation and

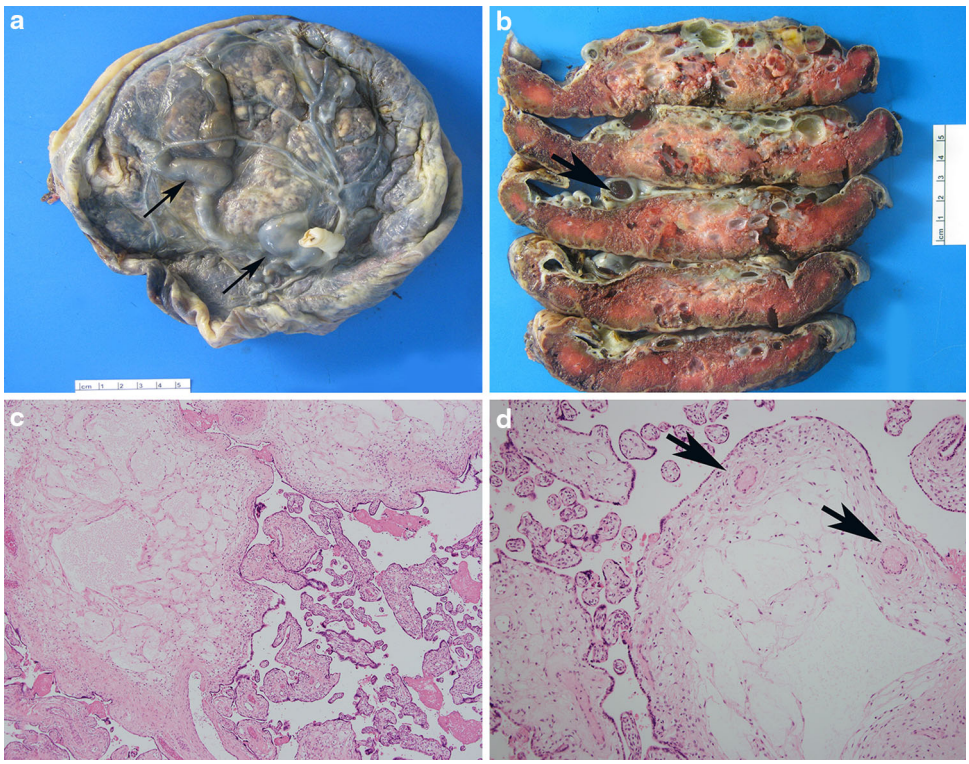


**Fig. 2** Gross and histologic appearance of PMD. **a** Gross photograph of the placenta from a classic case of PMD. The placental weight was >90th percentile for gestational age. This image of the fetal surface of the placenta shows dilated and tortuous chorionic vessels (*arrows*). **b** Gross photograph of the cut surface from a classic case of PMD. Note the numerous cystically dilated villous structures, particularly beneath the chorionic plate. Normal appearing villous parenchyma is featured near the basal surface and at the margins of the placenta. A dilated, thrombosed chorionic vessel is also visible (*arrow*). **c** Low-power photomicrograph of the villous parenchyma in PMD. Stem villous (*left*) is markedly enlarged and hydropic with myxoid stroma and development of a central cistern. Normal-sized chorionic villi are also present (*lower right*) demonstrating the admixture of hydropic and normal villi. Hematoxylin and eosin, original magnification 4×. **d** Medium-power photomicrograph of a hydropic stem villous in PMD. The large villous featured here shows hydropic change and a central cistern. However, the villous demonstrates thick-walled vessels (*arrows*) which distinguish it from most molar gestations. Also note there is no evidence of trophoblastic hyperplasia. Hematoxylin and eosin, original magnification 10×

thick-walled, peripheral blood vessels (Fig. 2c, d). The distal villi display increased capillaries with formation of chorangiomata and chorangiosis. There are frequently increased nucleated fetal erythrocytes in the capillaries of the distal villi. The villous cytotrophoblastic layer appears phenotypically normal without trophoblast proliferation or pseudoinclusions.

Because of the abnormal fetal vasculature in PMD, it is frequently accompanied by chronic fetal vascular obstructive changes in the placenta. Obstruction of fetal blood flow typically presents as thrombi within the large, dilated chorionic vessels, vaso-obliterative changes in stem villous vessels, and avascular villi or villous stromal-vascular karyorrhexis in the distal villi. Collectively, these fetal vascular changes are referred to as FTV when they involve a significant volume of the placenta [33]. As stated earlier, these changes can contribute to IUGR and fetal death [34, 35], often seen in PMD.

The immunohistochemical expression pattern of $p57^{KIP2}$ in PMD is abnormal. $p57^{KIP2}$ is a cyclin-dependent kinase inhibitor nuclear gene product (CDKN1C) encoded on 11p15.5 that is maternally expressed but paternally silenced, and therefore has become a useful indirect marker of an androgenetic genotype [36]. A normal staining pattern includes positive nuclear staining in both villous cytotrophoblast cells and villous stroma, while an androgenetic diploid conceptus shows loss of nuclear staining in both cell types, the typical staining pattern of CHM. However, abnormal villi in PMD demonstrate an intermediate pattern with loss of nuclear expression of $p57^{KIP2}$ in some or all villous stromal cells accompanied by retention of nuclear expression in villous cytotrophoblast cells (Fig. 3). A patchy distribution of villi with this pattern of $p57^{KIP2}$ immunostaining is observed with ABM, and suggests that biparental cells may have a selective advantage over the androgenetic cell lineage in the cytotrophoblast cells.

Since PMD is characterized by ABM, a variety of molecular diagnostic techniques can be used as an adjunct to demonstrate the presence of isolated 11p15.5 UPD or ABM, especially in cases with borderline or nonclassic morphology. PCR amplification of short tandem repeats or genomic single nucleotide polymorphism (SNP) array can be performed to assess for allelic imbalance by quantitative comparison of the maternal and paternal alleles at informative loci. Biparental tissue shows allelic ratios close to 1.0 (equal amounts of maternal and paternal chromosome material). Abnormal areas of the placenta, characterized by ABM show allelic ratios out of the normal range (excess paternal chromosomal material in androgenetic areas), compared with histologically normal (biparental) areas and known biparental control tissue. Although most cases of PMD may be due to AMB, a subset of cases is associated with selective paternal UPD at the BWS locus. Molecular diagnosis of the latter requires a SNP array or inclusion of 11p15.5 loci in an short tandem repeat analysis (STR).

## Pathogenesis

While PMD is known to be associated with a diploid karyotype, distinguishing it from the triploid karyotype of PHM, recent genotyping studies have shown the phenotypic and immunohistochemical features of PMD are associated with ABM [29, 37–40]. ABM in PMD is characterized by a mixture of two cells lines: an androgenetic

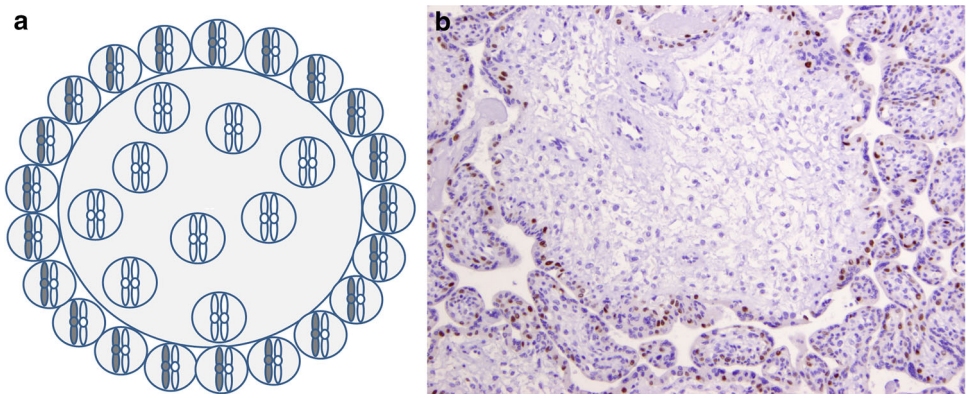


**Fig. 3** Androgenetic biparental mosaicism in PMD. **a** Diagrammatic representation of ABM in PMD. Villous cytotrophoblast cells circling the periphery of the villous have a normal biparental chromosomal complement (maternal component = dark chromosome; paternal component = white chromosome). Villous stromal cells are composed of a diploid paternal chromosome complement without any maternal component. This is the typical pattern of ABM seen in at least a subset of villi in PMD. **b** Classic pattern of $p57^{KIP2}$ staining in PMD. Note the nuclear expression in the villous cytotrophoblast around the periphery of the villous and loss of expression in the villous stromal cells. Loss of $p57^{KIP2}$ staining is used as an indirect assessment for androgenetic component and this pattern is characteristic of ABM in PMD. $p57^{KIP2}$ immunohistochemistry, original magnification 20×

cell line in the chorionic mesenchyme and a biparental cell line found in the villous cytotrophoblast and amnion [29]. ABM arises either from a single zygote (mosaicism) by a mitotic error or fusion of two zygotes (chimera). Possible mechanisms include: (1) normal fertilization with partial loss of the haploid maternal genome at cleavage and subsequent endoreduplication of haploid paternal genome (Fig. 4a); (2) fertilization of oocyte by two sperms resulting in a triploid conceptus, followed by unequal segregation to produce one diploid cell line and one with a haploid paternal genome which undergoes endoreduplication (Fig. 4b); (3) fusion of two fertilized oocytes, one biparental and one androgenetic to form a chimera (Fig. 4c).

While most PMD cases are diploid, there are reports of cases with PMD morphology and immunohistochemical staining pattern with lack of trophoblastic hyperplasia which show a hyperdiploid component (triploid/tetraploid) in the cytotrophoblast cells [29, 39, 41].

A fetus is nearly always present among PMD cases with strong fetal female predominance of up to 4:1 [20]. However, a recent case of PMD in a dichorionic twin gestation demonstrated that there may be early embryonic death and no recognizable fetal tissue later in gestation in PMD [41], stressing that there may be a spectrum of the phenotypic expression of ABM which depends on the quantity and distribution of the diploid androgenetic cell line. PMD may be considered to fall within the range of genetic possibilities between a completely biparental conceptus (normal) and a completely androgenetic conceptus (CHM). PMD placentas represent a mixture of these two types of cell lines, but the percentage of androgenetic cells within the villous stroma and/or fetus likely contributes to the phenotype. Therefore, not all PMD cases will have the same proportion of abnormal villi showing ABM and/or the same degree of fetal development or pathology. The reported cases of PMD range from ~30 % to 100 % involvement of the placenta [41–43]. It is possible that in some placentas with even smaller percentages of involvement, the cystic changes may be overlooked while those with 100 % involvement may not develop a fetus [41]. However, to date, no clear association has been made between percentage of ABM and fetal phenotype or outcome. PMD characterized by ABM can co-exist with CHM in the absence of twinning [39], and the proportion of CHM may range from morphologically-undetectable CHM (such as cases thought to represent PMD with elevated HCG) [4, 29] to frank areas with trophoblastic hyperplasia and loss of $p57^{KIP2}$ expression in villous cytotrophoblast and stromal cells [39].

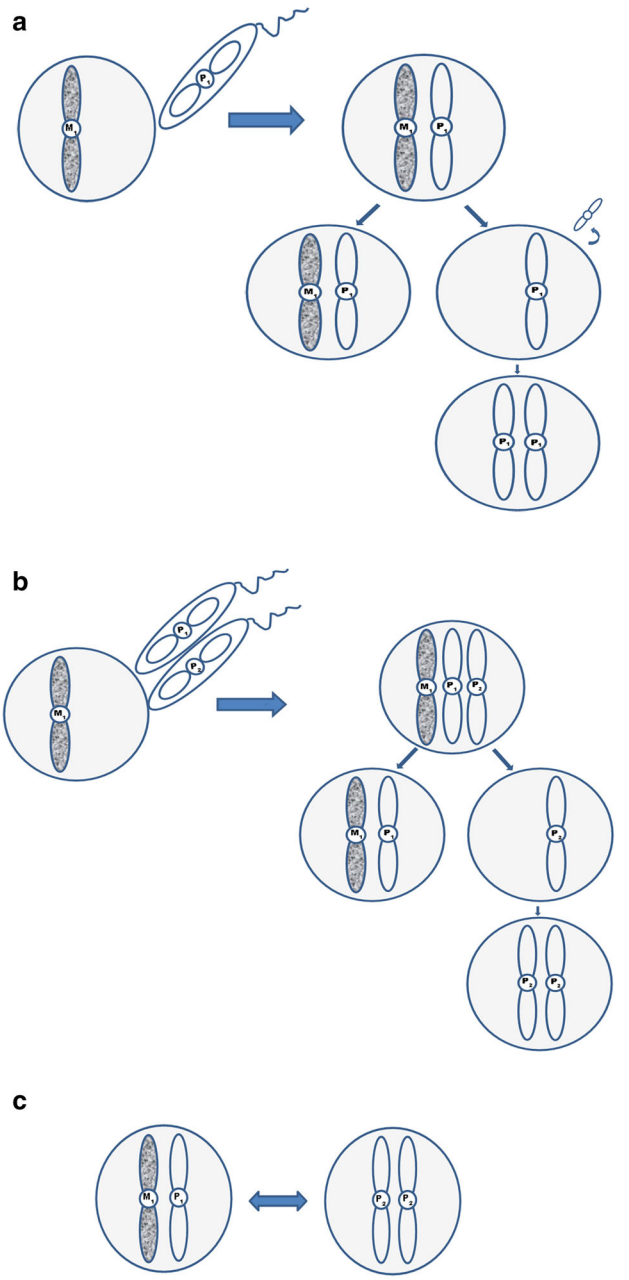


**Fig. 4** Diagrammatic representation of the mechanisms of pathogenesis of ABM. **a** Normal fertilization with partial loss of the haploid maternal genome (*dark chromosome*) at cleavage and subsequent endoreduplication of haploid paternal genome (*white chromosome*). Note that identical paternal alleles (isodisomy) will be present in every cell. **b** Fertilization of oocyte by two sperms resulting in a triploid conceptus, followed by unequal segregation to produce one diploid cell line and one with a haploid paternal genome which undergoes endoreduplication. Note that the biparental and androgenetic cells lines will have different sets of paternal alleles (heterodisomy). **c** Fusion of two fertilized oocytes, one biparental and one androgenetic to form a chimera. Note that the biparental and androgenetic cells lines will have distinct sets of paternal alleles

Rare cases with gross and histologic features of PMD have been found to be uniformly biparental without androgenetic allelic imbalance, suggesting that not all cases with PMD morphology are secondary to ABM [43]. Some of these cases may result from ABM below the threshold that can be detected by molecular genetic techniques. However, several case reports suggest that PMD occurs with mosaic paternal UPD or other forms of loss of heterozygosity confined to the 11p15.5 region [21, 43, 44], some cases associated with BWS [43, 44] and aberrant expression of genes CDKN1C and/or IGF2 located within this imprinted region of chromosome. Therefore, the villous stromal overgrowth seen in PMD is likely secondary to genes within this region alone, particularly, overexpression of the IGF2 gene, which is primarily expressed from the paternal allele [4, 43].

## Conclusions

PMD, a recently described entity, has a distinctive constellation of pathologic features that are important to recognize because PMD may have important implications for fetal and neonatal health, such as an increased risk for intrauterine fetal demise (IUFD), IUGR, and BWS. PMD has a complicated genotype characterized by a mixture of an androgenetic cell line and a biparental cell line, known as ABM. The androgenetic cell line is typically confined to the villous mesenchyme, while the villous trophoblast cells are biparental. To date, it is not fully understood why ABM in PMD is confined to villous stroma or how it leads to the villous and chorionic mesenchymal abnormalities characteristic of PMD. ABM within the mesenchymal cells of the fetus affected by PMD is also poorly understood, but may contribute to some of the associated fetal lesions, such as mesenchymal hamartoma of the liver. Further investigation is needed to answer these interesting and important questions about how the quantity and distribution of the androgenetic cell line affect pregnancy outcomes in PMD.

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**Compliance with ethical standards**

**Conflict of interest** None.

## References

1. Arizawa M, Nakayama M. Suspected involvement of the X chromosome in placental mesenchymal dysplasia. Congenit anom (Kyoto). 2002;42(4):309–17.
2. Moscoso G, Jauniaux E, Hustin J. Placental vascular anomaly with diffuse mesenchymal stem villous hyperplasia: a new clinico-pathological entity? Pathol Res Pract. 1991;187(2–3):324–8.
3. Lage JM. Placentomegaly with massive hydrops of placental stem villi, diploid DNA content, and fetal omphaloceles: possible association with Beckwith–Wiedemann syndrome. Hum Pathol. 1991;22(6):591–7.
4. Paradinas FJ, Sebire NJ, Fisher RA, Rees HC, Foskett M, Seckl MJ, et al. Pseudo-partial moles: placental stem vessel hydrops and the association with Beckwith–Wiedemann syndrome and complete moles. Histopathology. 2001;39(5):447–54.
5. Sander CM. Angiomatous malformation of placental chorionic stem vessels and pseudo-partial molar placentas: report of five cases. Pediatr Pathol. 1993;13(5):621–33.
6. Chen CP, Chern SR, Wang TY, Huang ZD, Huang MC, Chuang CY. Pregnancy with concomitant chorangioma and placental vascular malformation with mesenchymal hyperplasia. Hum Reprod. 1997;12(11):2553–6.
7. Hojberg KE, Aagaard J, Henriques U, Sunde L. Placental vascular malformation with mesenchymal hyperplasia and a localized chorioangioma: a rarity simulating partial mole. Pathol Res Pract. 1994;190(8):808–13 **(discussion 814)**.
8. Kuwabara Y, Shima Y, Araki T, Shin S. Mesenchymal stem villous hyperplasia of the placenta and fetal growth restriction. Obstet Gynecol. 2001;98(5 Pt 2):940–3.
9. Laberge JM, Patenaude Y, Desilets V, Cartier L, Khalife S, Jutras L, et al. Large hepatic mesenchymal hamartoma leading to mid-trimester fetal demise. Fetal Diagn Ther. 2005;20(2):141–5.
10. Vaisbuch E, Romero R, Kusanovic JP, Erez O, Mazaki-Tovi S, Gotsch F, Kim CJ, Kim JS, Yeo L, Hassan SS. Three-dimensional sonography of placental mesenchymal dysplasia and its differential diagnosis. J Ultrasound Med. 2009;28(3):359–68.
11. Himoto Y, Kido A, Minamiguchi S, Moribata Y, Okumura R, Mogami H, et al. Prenatal differential diagnosis of complete hydatidiform mole with a twin live fetus and placental mesenchymal dysplasia by magnetic resonance imaging. J Obstetr Gynaecol Res. 2014;40(7):1894–900.
12. Kuwata T, Takahashi H, Matsubara S. 'Stained-glass' sign for placental mesenchymal dysplasia. Ultrasound Obstet Gynecol. 2014;43(3):355.
13. Himoto Y, Kido A, Togashi K. Response to 'Diagnosis of placental mesenchymal dysplasia: magnetic resonance imaging or color Doppler?'. J Obstet Gynaecol Res. 2015;41(4):651.
14. Parveen Z, Tongson-Ignacio JE, Fraser CR, Killeen JL, Thompson KS. Placental mesenchymal dysplasia. Arch Pathol Lab Med. 2007;131(1):131–7.
15. Umazume T, Kataoka S, Kamamuta K, Tanuma F, Sumie A, Shirogane T, et al. Placental mesenchymal dysplasia, a case of intrauterine sudden death of fetus with rupture of cirsoid periumbilical chorionic vessels. Diagn Pathol. 2011;6:38.
16. Mulch AD, Stallings SP, Salafia CM. Elevated maternal serum alpha-fetoprotein, umbilical vein varix, and mesenchymal dysplasia: are they related? Prenat Diagn. 2006;26(8):659–61.
17. Heazell AE, Sahasrabudhe N, Grossmith AK, Martindale EA, Bhatia K. A case of intrauterine growth restriction in association with placental mesenchymal dysplasia with abnormal placental lymphatic development. Placenta. 2009;30(7):654–7.
18. Pham T, Steele J, Stayboldt C, Chan L, Benirschke K. Placental mesenchymal dysplasia is associated with high rates of intrauterine growth restriction and fetal demise: a report of 11 new cases and a review of the literature. Am J Clin Pathol. 2006;126(1):67–78.
19. Yamada A, Sakaida N, Okamura A, Yamada T, Ota T, Bo M. Placental mesenchymal dysplasia, a case of intrauterine sudden death. Kobe J Med Sci. 2014;60(1):E1–4.
20. Faye-Petersen OM, Kapur RP. Placental mesenchymal dysplasia. Surg Path Clin. 2013;6(1):127–51.

21. Robinson WP, Lauzon JL, Innes AM, Lim K, Arsovska S, McFadden DE. Origin and outcome of pregnancies affected by androgenetic/biparental chimerism. Hum Reprod. 2007;22(4):1114–22.
22. Lin J, Cole BL, Qin X, Zhang M, Kapur RP. Occult androgenetic-biparental mosaicism and sporadic hepatic mesenchymal hamartoma. Pediatr Dev Pathol. 2011;14(5):360–9.
23. Gibson BR, Muir-Padilla J, Champeaux A, Suarez ES. Mesenchymal dysplasia of the placenta. Placenta. 2004;25(7):671–2.
24. Francis B, Hallam L, Kecskes Z, Ellwood D, Croaker D, Kent A. Placental mesenchymal dysplasia associated with hepatic mesenchymal hamartoma in the newborn. Pediatr Dev Pathol. 2007;10(1):50–4.
25. Kitano Y, Ruchelli E, Weiner S, Adzick NS. Hepatic mesenchymal hamartoma associated with mesenchymal stem villous hyperplasia of the placenta. Fetal Diagn Ther. 2000;15(3):134–8.
26. Mack-Detlefsen B, Boemers TM, Groneck P, Bald R. Multiple hepatic mesenchymal hamartomas in a premature associated with placental mesenchymal dysplasia. J Pediatr Surg. 2011;46(8):e23–5.
27. Kim B, Hyeon J, Lee M, Hwang H, Shin Y, Choi SJ, Kim JS. Placental mesenchymal dysplasia with fetal gastroschisis. J Pathol Trans Med. 2015;49(1):71–4.
28. Tortoledo M, Galindo A, Ibarrola C. Placental mesenchymal dysplasia associated with hepatic and pulmonary hamartoma. Fetal Pediatr Pathol. 2010;29(4):261–70.
29. Kaiser-Rogers KA, McFadden DE, Livasy CA, Dansereau J, Jiang R, Knops JF, et al. Androgenetic/biparental mosaicism causes placental mesenchymal dysplasia. J Med Genet. 2006;43(2):187–92.
30. H'Mida D, Gribaa M, Yacoubi T, Chaieb A, Adala L, Elghezal H, et al. Placental mesenchymal dysplasia with Beckwith–Wiedemann syndrome fetus in the context of biparental and androgenic cell lines. Placenta. 2008;29(5):454–60.
31. Beckwith JB. Macroglossia, omphalocele, adrenal cytomegaly, gigantism, and hyperplastic visceromegaly. Birth Defects. 1969;5(2):188–96.
32. Kalish JM, Conlin LK, Bhatti TR, Dubbs HA, Harris MC, Izumi K, et al. Clinical features of three girls with mosaic genome-wide paternal uniparental isodisomy. Am J Med Genet A. 2013;161A(8):1929–39.
33. Redline RW, Ariel I, Baergen RN, Desa DJ, Kraus FT, Roberts DJ, et al. Fetal vascular obstructive lesions: nosology and reproducibility of placental reaction patterns. Pediatr Dev Pathol. 2004;7(5):443–52.
34. Redline RW, Pappin A. Fetal thrombotic vasculopathy: the clinical significance of extensive avascular villi. Hum Pathol. 1995;26(1):80–5.
35. Saleemuddin A, Tantbirojn P, Sirois K, Crum CP, Boyd TK, Tworoger S, et al. Obstetric and perinatal complications in placentas with fetal thrombotic vasculopathy. Pediatr Dev Pathol. 2010;13(6):459–64.
36. Castrillon DH, Sun D, Weremowicz S, Fisher RA, Crum CP, Genest DR. Discrimination of complete hydatidiform mole from its mimics by immunohistochemistry of the paternally imprinted gene product $p57^{KIP2}$. Am J Surg Pathol. 2001;25(10):1225–30.
37. Hoffner L, Dunn J, Esposito N, Macpherson T, Surti U. $p57^{KIP2}$ immunostaining and molecular cytogenetics: combined approach aids in diagnosis of morphologically challenging cases with molar phenotype and in detecting androgenetic cell lines in mosaic/chimeric conceptions. Hum Pathol. 2008;39(1):63–72.
38. Hoffner L, Parks WT, Swerdlow SH, Carson JC, Surti U. Simultaneous detection of imprinted gene expression (p57(KIP2)) and molecular cytogenetics (FICTION) in the evaluation of molar pregnancies. J Reprod Med. 2010;55(5–6):219–28.
39. Lewis GH, DeScipio C, Murphy KM, Haley L, Beierl K, Mosier S, Tandy S, Cohen DS, Lytwyn A, Elit L, et al. Characterization of androgenetic/biparental mosaic/chimeric conceptions, including those with a molar component: morphology, p57 immunohistochemistry, molecular genotyping, and risk of persistent gestational trophoblastic disease. Int J Gynecol Pathol. 2013;32(2):199–214.
40. Sunde L, Niemann I, Hansen ES, Hindkjaer J, Degn B, Jensen UB, et al. Mosaics and moles. Eur J Hum Genet. 2011;19(10):1026–31.
41. Linn RL, Minturn L, Yee LM, Maniar K, Zhang Y, Fritsch MK, et al. Placental mesenchymal dysplasia without fetal development in a twin gestation: a case report and review of the spectrum of androgenetic biparental mosaicism. Pediatr Dev Pathol. 2015;18(2):146–54.
42. Starikov R, Goldman R, Dizon DS, Kostadinov S, Carr S. Placental mesenchymal dysplasia presenting as a twin gestation with complete molar pregnancy. Obstet Gynecol. 2011;118(2 Pt 2):445–9.
43. Armes JE, McGown I, Williams M, Broomfield A, Gough K, Lehane F, et al. The placenta in Beckwith–Wiedemann syndrome: genotype-phenotype associations, excessive extravillous trophoblast and placental mesenchymal dysplasia. Pathology. 2012;44(6):519–27.
44. Reish O, Lerer I, Amiel A, Heyman E, Herman A, Dolfin T, et al. Wiedemann–Beckwith syndrome: further prenatal characterization of the condition. Am J Med Genet. 2002;107(3):209–13.