

Original Article

Placental mesenchymal dysplasia in a normal female infant: a rare case report with follow-up

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Abstract: Placental mesenchymal dysplasia (PMD) is a rare disorder of unknown etiology, which is often misdiagnosed as partial hydatidiform mole because of their similarity in ultrasonographic, gross, and histologic presentations. However, the treatment and prognosis of these two conditions are different. Patients with PMD often have intrauterine growth restriction, intrauterine fetal death, and Beckwith-Wiedemann syndrome, but there may also be a normal fetus. PMD with a normal female infant is extremely rare, and only a few cases have been reported. We report a case of PMD in a normal female infant and its follow-up results.

Keywords: Placenta, P57, hydatidiform mole, placental mesenchymal dysplasia (PMD)

Introduction

Placental mesenchymal dysplasia (PMD) was first reported in 1991 by Moscoso and colleagues [1]. Previous reports declare PMD is a rare, benign entity that is characterized by placentomegaly and an abnormal chorionic villus with vesicle formation resembling molar pregnancy on ultrasonography, as well as macrography, fibroblastic hyperplasia, and vascular abnormalities [2]. This condition can be misdiagnosed as partial hydatidiform mole. The majority of PMD cases are associated with intrauterine growth restriction (IUGR), intrauterine fetal death (IUFD), and Beckwith-Wiedemann Syndrome (BWS), which includes macrosomia, exomphalos, macroglossia, omphalocele, internal visceromegaly, and placentomegaly. However, PMD can also occur in a normal fetus [3-5]. We report a case of PMD in a healthy female infant who was misdiagnosed with partial hydatidiform mole. We also review the literature on PMD.

Case report

A previously healthy, 26-year-old woman, gravida 2, para 1, underwent a first trimester screen-

ing scan at 13 weeks' gestation. The sonographer reported a single live fetus with a normal nuchal thickness (1.7 mm). Abnormalities of the head, spine, hands, and feet were excluded. A following scan at 24 weeks showed normal fetal growth, amniotic fluid, and fetal morphology. The placenta was unclear, but an inhomogeneous and cystic area without vascular flow, measuring 55×12 mm, was first detected in the placenta. As the pregnancy progressed, the area gradually enlarged to 55×15 mm at 26 weeks' gestation. Close follow-up ultrasonic inspection showed a normal amniotic fluid index, fetal anatomy, and a gradual increase in size in placental vesicular lesions at 28, 30, and 32 weeks' gestation. The size of the fetus was consistent with the gestational age. At 35 weeks, ultrasound showed that the vesicular lesion had grown to 69×29 mm with thrombosis (**Figure 1**), but the size of the fetus was equivalent to 33 gestational weeks. This finding implied that growth of the fetus was approximately 2 weeks delayed from normal. When IUGR was confirmed, the patient was referred to our hospital and had cesarean delivery of a 2290-g, live-born, female infant at 37 weeks of gestation. The newborn had no malformations at birth and the Apgar score was 10 at 1 minute

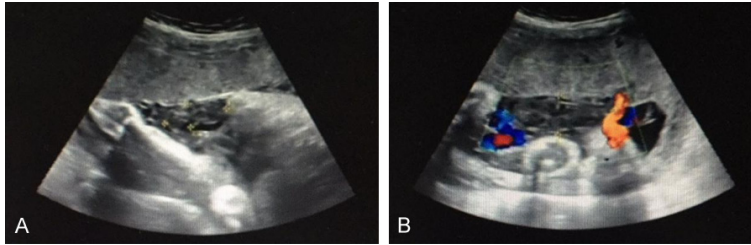


Figure 1. Ultrasonography: (A) A large cystic placenta, (B) Thrombosis in the large cystic placenta.

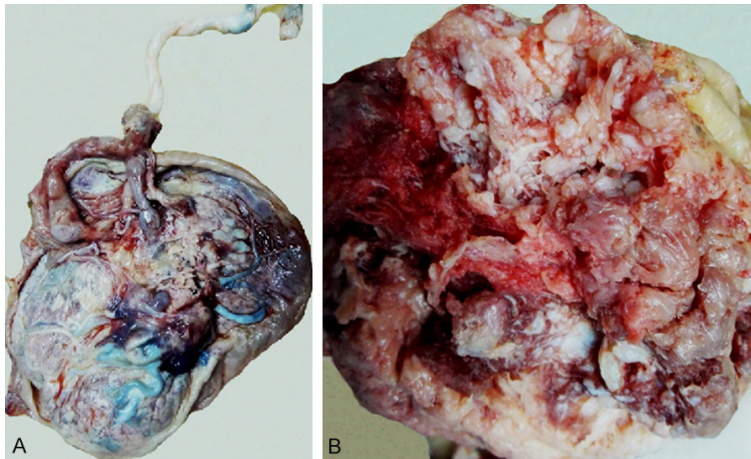


Figure 2. Gross findings (A) Abnormal blood vessels on the fetal plate, (B) Grape-like vesicles involving the whole maternal plate.

and 10 at 5 minutes. After birth, the neonate presented with jaundice and underwent phototherapy. An echocardiogram, cranial ultrasound, and urinary tract ultrasound were normal. The neonate and her mother were discharged in a good condition from the hospital 1 week later.

The placenta measured 16×14×5 cm and weighed 520 g. The gross features were suggestive of partial hydatidiform mole. Abnormal blood vessels with dilation, congestion, and a radial arrangement from the cord to the edge of the placenta were visible on the placental fetal plate. The umbilical cord was 25 cm long and 1 cm in diameter. At a distance of 6 cm from the placenta, the umbilical cord was divided into three blood vessels that were inserted into the placenta (**Figure 2A**). The maternal plate showed bulky, grape-like vesicles ranging from 0.2-0.8 cm in diameter. These vesicles were interspersed among normal-appearing villous tissue involving the whole placenta with no border (**Figure 2B**). The cut surface of the placenta

also showed a mixture of normal-appearing areas and numerous clusters of grape-like, fluid-filled vesicles.

A microscopic examination showed mesenchymal stem villous hyperplasia with hydropic changes and thick-walled vessels at the periphery, and these were surrounded by tertiary villi with a normal appearance (**Figure 3A** and **3B**). Occlusive vascular thrombosis and hemorrhagic endovascularitis were observed (**Figure 3C**). Large hydropic stem villi with a reduction in small vessels, loose myxoid stroma with overgrowth of fibroblastoid cells, and a lack of trophoblast proliferation were observed (**Figure 4**). These findings suggested PMD. An immunohistochemical examination showed positive expression of p57 in all villous cytotrophoblast cells of PMD, including normal and enlarged villi. In contrast, p57

expression was absent in partial hydatidiform mole (**Figure 5**). There was low detectable Ki-67 expression in PMD, while high expression was observed in partial hydatidiform mole (**Figure 6**).

Follow-up results showed that trophoblastic dysplasia appeared in the smooth muscle of the uterine scar 5 months after cesarean section, and the morphology was consistent with choriocarcinoma. A single metastatic nodule appeared in the left lung 7 months after cesarean section. The lung nodule gradually narrowed and disappeared after six courses of chemotherapy. Currently, the patient is in good condition.

Discussion

Previous studies have shown that PMD is a rare, benign condition characterized by placentomegaly and abnormal chorionic villi with vesicle formation, fibroblastic hyperplasia, and vascular abnormalities [2]. However, follow-up

Placental mesenchymal dysplasia in a normal female infant

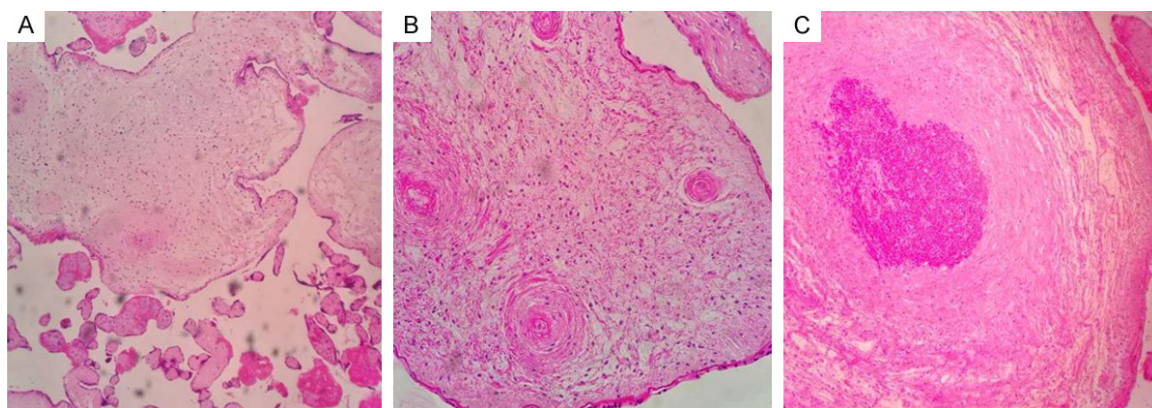


Figure 3. Hematoxylin and eosin stain: (A) Enlarged stem villus with myxomatous stroma in a mixed background of small normal and dysmature villi, (B) Villous thick-walled vessels are located in the periphery, (C) Occlusive vascular thrombosis and hemorrhagic endovascularitis.

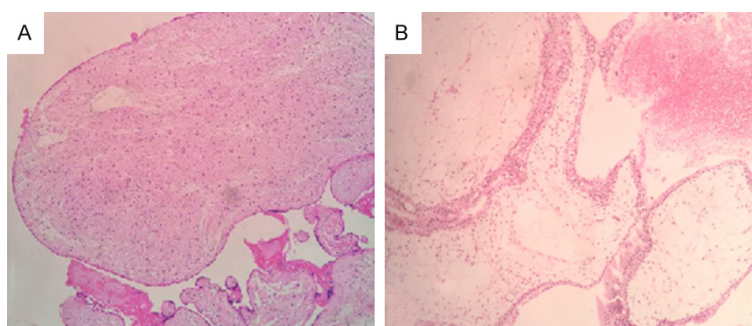


Figure 4. Hematoxylin and eosin stain: (A) Enlarged stem villus with fibrous interstitial dysplasia, but this is not accompanied by trophoblast proliferation, (B) Villous interstitial edema with trophoblast proliferation suggesting partial hydatidiform mole.

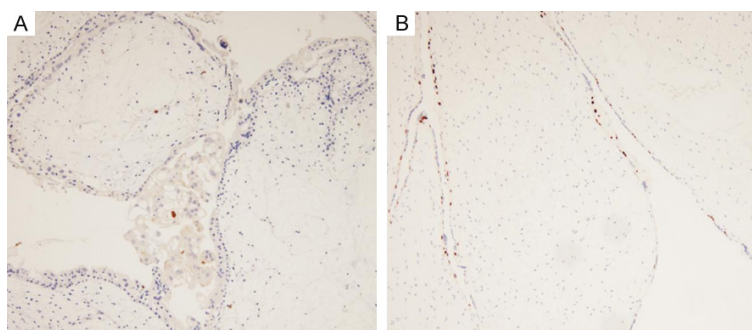


Figure 5. Immunohistochemical staining of p57: (A) Negative expression of p57 in partial hydatidiform mole (IHC×200); (B) Positive expression of p57 in PMD (IHC×200).

results in our patient showed that PMD is not a pure benign disease, and it can convert into choriocarcinoma and metastasize. PMD is found in approximately 0.02% of pregnancies, with 129 cases of PMD described to date [6].

There is a female preponderance in PMD, with a female: male ratio of 3.6-4:1 [7]. Recently, androgenetic/biparental mosaicism has been suggested as the underlying cause of PMD. PMD has distinct clinicopathological complications, including IUGR, IUFD, and BWS, with rates of 50%, 43%, and 25%-33%, respectively. A total of 40% of PMD can result in fetal demise or neonatal death. However, none of these lesions was apparent at birth in our case. In our case, the neonate had a normal genotype and phenotype.

Development of PMD is a slow and gradual process. Recent studies have shown that approximately 70% of PMD is diagnosed as multicystic placenta at 13-20 weeks of gestation [8]. None of the reported PMD cases were detected before 13 weeks of gestation. This finding indicates that placental cystic changes begin at the 13th week of pregnancy. In our

case, ultrasound showed that placental cystic changes began to appear at 13 weeks of gestation and cystic changes progressively enlarged with progression of pregnancy. Enlarged chorionic vessels are usually found in third-trimester

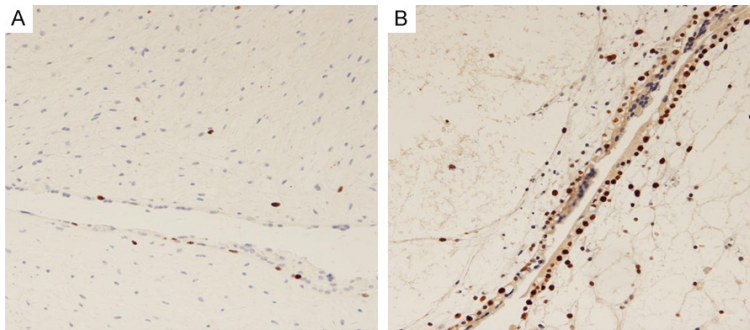


Figure 6. Immunohistochemical staining of Ki-67: (A) Low Ki-67 expression in PMD (IHC×200), (B) High Ki-67 expression in partial hydatidiform mole (IHC×200).

PMD placentas [9]. Prominent chorionic vessels may not be able to be identified grossly during the early stages, as found in our case.

The diagnosis of PMD requires comprehensive analysis of ultrasound, and gross and histopathologic findings, especially histomorphological changes [10, 11]. PMD is often misdiagnosed as partial hydatidiform mole because of their similarity in ultrasonographic, gross and histologic presentations [12, 13]. Differential diagnosis between these two conditions is important because of their different treatment and outcomes, and treatment of these two conditions can be achieved by different methods. Ultrasonographic assessment and maternal serum beta-human chorionic gonadotrophin measurement can be obtained prenatally [14]. We also found bulky, grape-like vesicles that ranged from 0.2-0.8 cm in diameter and they were interspersed in villous tissue with a normal appearance. These vesicles are easily misdiagnosed as partial hydatidiform mole in the clinic. While a histologic examination is critical for PMD, unlike hydatidiform mole, PMD shows villous thick-walled vessels located in the periphery, stem villus edema expansion, villus interstitial cell proliferation, and the absence of trophoblastic hyperplasia. Immunohistochemical staining for p57 and Ki-67 in our case was helpful for excluding the possibility of partial hydatidiform mole. Positive p57 expression and low Ki-67 expression in cytotrophoblast cells are found in PMD, but expression of Ki-67 and p57 are opposite in partial hydatidiform mole. A karyotype examination is also effective to separate these diseases. Partial hydatidiform mole presents as triploid, while most PMD cases are diploid. A triploid fetus usually has several mor-

phological anomalies and tends to die in the first trimester. Therefore, partial molar pregnancy is usually accompanied by an abnormal triploid fetus [15]. Most patients with PMD can have a normal diploid fetus if PMD is found in a timely manner and properly managed, such as in our case.

At present, the incidence of partial hydatidiform mole is significantly higher than that of PMD. When attempting to diag-

nose partial hydatidiform mole in a pregnancy test, the possibility of PMD should be excluded first. Because early diagnosis and differential diagnosis of PMD are important, once PMD is diagnosed, the patient should be closely followed up and hospitalized if necessary. Our follow-up results suggest that patients should be closely monitored for human chorionic gonadotrophin after delivery. More cases are required to determine whether the uterus should be resected in PMD.

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Disclosure of conflict of interest

None.

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