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Research Letter

Placental mesenchymal dysplasia associated with antepartum hemorrhage, subchorionic hematoma, and intrauterine growth restriction

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A primigravid woman 38 years of age underwent amniocentesis at 17 weeks of gestation because of advanced maternal age, and the result revealed a karyotype of 46,XY. She was admitted to the hospital at 17 weeks of gestation because of antepartum hemorrhage, placenta previa, subchorionic hematoma, premature uterine contractions, and premature rupture of the membranes following amniocentesis. Level II ultrasonography revealed an amniotic fluid index of 6 cm, a singleton fetus with a biparietal diameter (BPD) of 3.35 cm (15.8 weeks), an abdominal circumference (AC) of 10.4 cm (16.3 weeks), a femur length (FL) of 1.63 cm (14.8 weeks), subchorionic hematoma, and a suspicion of placental abruption. At 20 weeks of gestation, the fetal biometry was equivalent to 18 weeks of gestation with a BPD of 4.5 cm (19.1 weeks), an AC of 12 cm (18 weeks), an FL of 2.28 cm (17.2 weeks), and an enlarged placenta with multiple hypoechoic spaces (Fig. 1). A diagnosis of placental mesenchymal dysplasia (PMD) was made. Chorionic villus sampling (CVS) of the bulky placenta was performed. Molecular analysis of the sampled placental tissue revealed no uniparental disomy (UPD) 11 and no genomic imbalance. The karyotype of CVS was 46,XY. Repeated amniocentesis revealed coffee-like brownish colored amniotic fluid. The karyotype of amniocentesis was 46,XY. Array comparative genomic hybridization (aCGH) analysis revealed no genomic imbalance in the amniocytes. At 22 weeks of gestation, the multiple hypoechoic spaces in the placenta persisted and intrauterine growth restriction (IUGR) was evident, and the fetal biometry was equivalent to 18 weeks of gestation. At 23 weeks of gestation, a dead 288-g male fetus was delivered with a bulky placenta weighing 300 g. The fetus was apparently normal. Gross examination of the maternal surface of the placenta showed multiple grape-like and dilated and tortuous sub-

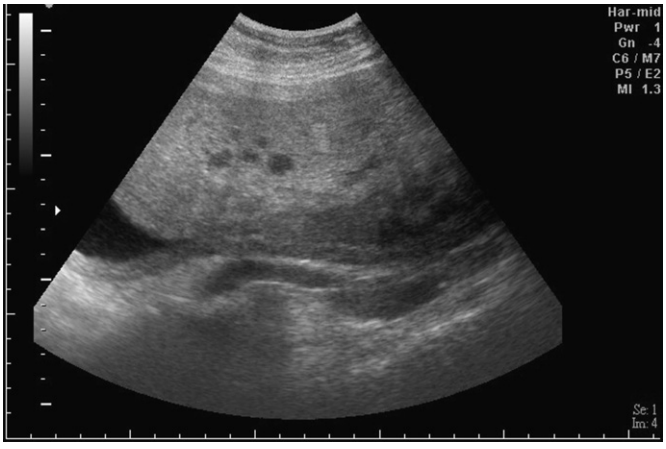

Fig. 1. Prenatal ultrasound at 20 weeks of gestation shows an enlarged placenta with multiple hypoechoic spaces.

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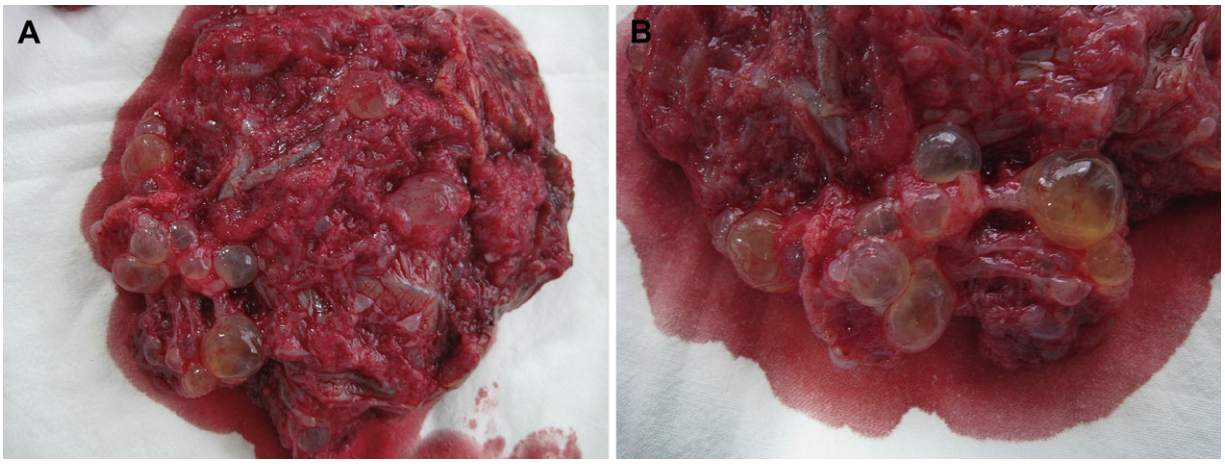

Fig. 2. Gross examination of the maternal surface shows multiple grape-like vesicles.

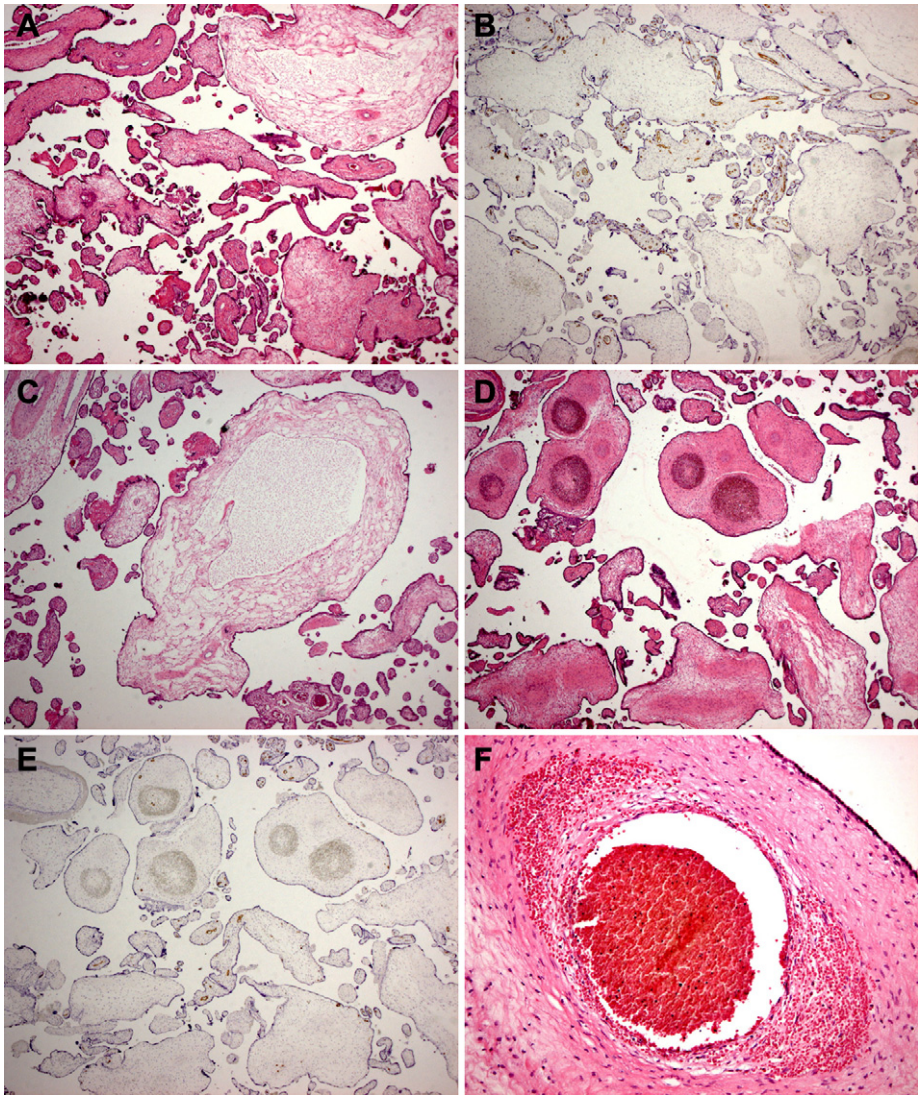

Fig. 3. Microscopic examination of the vesicles shows large dilated villi with the presence of obliterated vasculature, thrombosis and hemorrhage, and the absence of trophoblastic proliferation. (A) Hydropic stem villi with diminished blood vessels and no trophoblastic proliferation. H & E, original magnification ×20; (B) CD34 immunohistochemical staining shows decreased blood vessels within the affected hydropic villi, ×20; (C) Hydropic stem villi with a central cistern and the surrounding normal-appearing terminal villi (H & E, ×20); (D)–(F) stem villi with obliterated vasculature, thrombosis and hemorrhage; (D) H & E, ×20; (E) CD34, ×20; (F) H & E, ×100. H & E = hematoxylin-eosin.

chorionic vessels (Fig. 2). Microscopic examination showed large dilated villi with the presence of obliterated vasculature, thrombosis, and hemorrhage, and the absence of trophoblastic proliferation (Fig. 3). Postnatal genetic analysis of the dilated villi showed no methylation abnormality, a karyotype of 46,XY, and biparental inheritance with a 1:1 paternal:maternal dosage ratio in the microsatellite analysis of chromosomes 6, 7, 11, and 15.

PMD is a rare but benign condition that is characterized by placentomegaly with many grape-like vesicles resembling partial mole [1–6]. The incidence of PMD has been reported to be 0.02% [7]. There is a female preponderance in cases of PMD with a female:male ratio 3.6:1 [8]. PMD is different from partial mole by the absence of trophoblastic proliferation, the presence of a normal-appearing fetus, a fetus with IUGR or a fetus with overgrowth, and the diploid karyotype in majority of the cases [4]. PMD is associated with an increased risk of IUGR and fetal demise. In a review of 82 cases with PMD, of which 15 were associated with Beckwith-Wiedemann syndrome (BWS), Pham et al [9] found that, among all cases without BWS, 50% had IUGR, 43% had intrauterine fetal demise or neonatal death, and females represented 82% of cases.

There is an association between BWS and PMD. About 23% of the cases with PMD are associated with BWS [8]. In such cases, there may be fetal overgrowth, omphalocele, macroglossia, internal visceromegaly in addition to placentomegaly and an imbalance of imprinted gene expression of the genes *CDKN1C* ($P57^{KIP2}$), *H19*, *IGF-II,* and *KVLQT1* within 11p15.5 due to epigenetic errors and/or chromosomal abnormalities [10,11]. Aviram et al [12] additionally reported a case of transient neonatal diabetes mellitus and paternal UPD 6.

Recently, androgenetic/biparental whole genome mosaicism was observed in cases with PMD, and this androgenetic mosaicism may partially explain the PMD features of absence of trophoblastic hyperplasia, association with BWS, and the preponderance of females [10,13–19].

It has also been suggested that hypoxia or hypoperfusion can be associated with PMD [4]. Increased angiogenesis caused by increased expression of the vascular endothelial growth factor (VEGF) genes may explain the pathogenesis of PMD in cases of hypoxia or hypoperfusion [4]. X chromosome abnormalities have also been suggested to be associated with PMD because of abnormal expression of the *VEGF-D* gene on Xp22.31 [7].

The present case was a male, had a karyotype of 46,XY, and was associated with placental previa, placental hematoma, antepartum hemorrhage, and IUGR, but had neither UPD nor androgenic mosaicism or genomic imbalance. The underlying cause of PMD in this case is unknown. We speculate that enlarged stem villi along with chorionic vessel dilation may be a congenital malformation of the mesoderm. Our case provides evidence that PMD may present antepartum hemorrhage and subchorionic hematoma in early gestation.

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