CASE REPORT

Placental mesenchymal dysplasia associated with spontaneous ovarian hyperstimulation syndrome

Payam Davoudian

Department of Obs & Gynae,
South West Acute Hospital,
Enniskillen, UK

Correspondence to
Dr Payam Davoudian,
payamdavoudian@yahoo.com

Accepted 3 April 2015

SUMMARY

Placental mesenchymal dysplasia (PMD) is a rare disorder of unknown aetiology characterised by placentomegaly, serpiginous surface blood vessels and large cystic villi. Although a mimic of molar pregnancies and other entities, it can be distinguished from them by its association with intrauterine growth restriction or death of a relatively normal fetus and its characteristic histopathology. We report the case of a 20-year-old primigravida who presented at 16 weeks with heavy clotty vaginal bleeding and subsequent miscarriage. The placenta was grossly abnormal and resembled a partial molar pregnancy. PMD was confirmed by microscopic examination. Postmiscarriage, ultrasound revealed enlarged and multicystic ovaries similar to those seen in ovarian hyperstimulation syndrome (OHSS), which returned to normal a few weeks after miscarriage. This is the first report of PMD associated with OHSS, and we hypothesise that the most likely pathogenesis is ovarian stimulation from PMD-derived vascular endothelial growth factor.

BACKGROUND

Placental mesenchymal dysplasia (PMD) is a rare placental disorder of unknown aetiology characterised by placentomegaly, serpiginous surface blood vessels and large cystic villi. Macroscopically, PMD often resembles a partial mole.¹

Clinically, PMD is associated with intrauterine growth restriction and fetal death. Unlike molar pregnancies, in which the fetus is absent or malformed, fetal scans in women with PMD are normal during early pregnancy, which often advances to the third trimester. PMD is most commonly associated with Beckwith-Wiedemann syndrome (BWS), which is present in around 50% of cases.²

PMD was initially described in 1991 as 'stem villous hyperplasia' by Moscoso *et al*,³ who described the unique pathology of two cases of women presenting with elevated serum α fetoprotein levels and enlarged placentas with corresponding ultrasonographic features suggestive of a partial mole.⁴

PMD needs to be included in the differential diagnosis of a cystic-appearing placenta with a normal fetus.⁵ We report the case of PMD associated with spontaneous ovarian hyperstimulation, its differential diagnoses, sonographic features and a review of the literature.

CASE PRESENTATION

A 20-year-old primigravida presented at 16 weeks to accident and emergency with heavy clotty vaginal bleeding. Her 7-week booking scan was

normal (blood pressure 140/64, body mass index 25, urinalysis negative), her menstrual cycle unremarkable (6/26) and she had no significant medical history. There was no history of alcohol excess, cigarette smoking, or prescribed or illicit drug use, except for PregnaCare once daily during the pregnancy. The booking blood tests and infection screen were normal. At her 12-week antenatal clinic appointment, the patient was clinically well and asymptomatic with a normal blood pressure of 117/77; her ultrasound scan showed the presence of a 12+3 week fetus with heartbeat and an anterior placenta. No biochemical aneuploidy screening was undertaken. She miscarried following admission to the gynaecology ward.

INVESTIGATIONS

On pathological examination, the placenta was grossly abnormal, measured approximately 12×10×4.5 cm, weighed 518 g and resembled a partial molar pregnancy. The cord was 14 cm in length, 0.4 cm in diameter and was not oedematous or discoloured. Histological examination confirmed placental abnormalities. Some villi showed 'fjord-like', irregular outlines and trophoblastic pseudoinclusions in the stroma, some were enlarged and oedematous with central cysternae, and others had a lobulated outline with marked hypervascularity and numerous small fetal capillaries in a myxoid stroma. However, there was no trophoblastic proliferation to indicate partial molar change and the histological appearances were consistent with PMD.

Following miscarriage, the endometrium was 1.3 cm thick on ultrasound and the ovaries looked hyperstimulated (right ovary 10 cm in diameter and left ovary 9 cm in diameter) containing multiple small cysts measuring 1–3 cm in diameter (figure 1). There was no ascites. The patient's full blood count and electrolytes were normal and thyroid function tests were negative.

OUTCOME AND FOLLOW-UP

Postnatally, she was reporting mild abdominal pain but she was nausea free. Her β -human chorionic gonadotropin (hCG) was 24 890 (normal value: 0–5) following miscarriage, which dropped significantly on weekly follow-up. Her ovaries gradually returned to normal after a few weeks and she remains alive and well.

DISCUSSION

PMD is a benign condition with an estimated incidence of 0.02% of all pregnancies.⁶ Grossly, PMD placentas are large for gestational age with

CrossMark

To cite: Davoudian P. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-207420

Figure 1 Ultrasound scans of polycystic ovaries. (A) A 9 cm left ovary and (B) 10 cm right ovary. Cysts measured between 1 and 3 cm in diameter.

aneurysmally dilated chorionic plate vessels and fibromuscular hyperplasia. Cystically dilated vesicles, similar to those seen in molar pregnancies, are present, which represent dilated stem vessels with thickened vasculature surrounded by normal villi. Pathologically, PMD can be distinguished from molar pregnancies by the presence of dilated stem vessels and a lack of trophoblastic proliferation.^{4 5}

The fetus is usually normal in PMD and the pregnancy often advances to the third trimester, in contrast to molar pregnancies, which are characterised by absent or malformed fetuses. In 20% of cases, PMD is associated with BWS, a condition characterised by macrosomia, visceromegaly, hemihyperplasia (hemihypertrophy), macroglossia, omphalocele and adrenal cytomegaly, which is recognisable prenatally or in infancy.² The typical sonographic features of PMD are a thickened placenta with hypoechoic areas that can resemble a complete mole with a co-twin, a partial molar pregnancy or a chorioangioma.⁵

The pathogenesis of PMD is unclear. There are multiple competing theories, including congenital malformation of the mesoderm, molecular disruption of the imprinting genes of chromosome 11p15.5 associated with BWS and androgenetic/biparental mosaicism.^{2 4 7 8} Hypoxia and hypoperfusion of unknown cause may lead to the vascular abnormalities seen in PMD due to production of vascular endothelial growth factor (VEGF) by villous macrophages. A putative causative gene for PMD is VEGF-D, located on chromosome Xp22.31.⁷

The differential diagnosis of PMD is broad and includes partial molar pregnancy, complete mole with coexisting normal fetus, chorangioma, subchorionic haematoma, confined placental mosaicism and spontaneous abortion with hydropic changes. PMD is most often mistaken for molar pregnancy due to their similar sonographic findings.⁸

Although PMD may present with increased hCG levels (although not in this case), to the best of our knowledge there have been no reports of PMD occurring with ovarian hyperstimulation syndrome (OHSS). Spontaneous OHSS is extremely rare in normal pregnancies, and only a few cases of OHSS have been reported in association with hypothyroidism, hydatidiform mole and multiple pregnancies.

The pathophysiology of spontaneous OHSS is also poorly understood. According to the De Leener classification, three types of spontaneous OHSS exist: type I is associated with mutations in the follicle stimulating hormone (FSH) receptor and may result in recurrent spontaneous OHSS; type II is secondary to high levels of hCG, such as in hydatidiform mole and multiple gestation pregnancies, and is most frequent; and type III is related to hypothyroidism.⁹ In our case, type II OHSS was ruled out and there was no clinical or biochemical evidence of hypothyroidism.

We therefore explored possible explanations for the coexistence of PMD and OHSS. With respect to mutated FSH

receptors and OHSS, normal expression of the FSH receptor decreases drastically in the corpus luteum but remains constant in the granulosa cells of developing follicles.¹⁰ FSH receptors are usually not, or only very weakly, stimulated during pregnancy, since pituitary gonadotrophins fall to very low or undetectable levels. However, mutated FSH receptors expressed in the developing follicles may be hyperstimulated by pregnancy-derived hCG and result in enlarged follicles. In addition, luteinising hormone receptors expressed by granulosa cells may also be stimulated by hCG to induce follicular luteinisation and the secretion of vasoactive molecules such as VEGF, angiotensin II and various interleukins that are responsible for the development of the syndrome.^{10 12} In one case report, a woman presented in the 15th week of pregnancy with a partial (triploid) hydatidiform mole, and ongoing and severe OHSS even after termination of pregnancy. VEGF levels were very high despite low levels of hCG, supporting the hypothesis that VEGF might cause OHSS.^{11 12} In our case, since VEGF can be produced by PMD macrophages and has been associated with OHSS, we postulate that PMD-derived VEGF was responsible for the spontaneous OHSS.

Learning points

- ▶ Placental mesenchymal dysplasia (PMD) is characterised by placentomegaly and aneurysmal and dilated chorionic vessels.
- ▶ PMD is associated with adverse outcomes in pregnancy, and with Beckwith-Wiedemann syndrome in about half of cases.
- ▶ PMD is in the differential diagnosis when faced with sonographic features of molar pregnancy, with definitive diagnosis dependent on pathological evaluation.
- ▶ We report the first case of PMD associated with spontaneous ovarian hyperstimulation syndrome (OHSS), and hypothesise that OHSS can arise as a result of PMD-associated vascular endothelial growth factor secretion.

Acknowledgements The authors gratefully acknowledge editorial assistance from Nextgenediting (<http://www.nextgenediting.com>).

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Kaplan CG. *Color atlas of gross placental pathology*. New York: Springer, 2007.
- 2 Pham T, Steele J, Stayboldt C, et al. 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;126:67–78.
- 3 Moscoso G, Jauniaux E, Hustin J. Placental vascular anomaly with diffuse mesenchymal stromal villous hyperplasia: a new clinico-pathological entity? *Pathol Res Pract* 1991;187:324–8.
 - 4 Parveen Z, Tongson-Ignacio JE, Fraser CR, *et al.* Placental mesenchymal dysplasia. *Arch Pathol Lab Med* 2007;131:131–7.
 - 5 Woo GW, Rocha FG, Gaspar-Oishi M, *et al.* Placental mesenchymal dysplasia. *Am J Obstet Gynecol* 2011;205:e3–5.
 - 6 Arizawa M, Nakayama M. Suspected involvement of the X chromosome in placental mesenchymal dysplasia. *Congenit Anom (Kyoto)* 2002;42:309–17.
 - 7 Akbarzadeh-Jahromi M, Sari Aslani F, Parvari S. Placental mesenchymal dysplasia complicated by hydrops fetalis and fetal death: a case report. *Arch Iran Med* 2013;16:551–4.
 - 8 Nayeri UA, West AB, Grossetta Nardini HK, *et al.* Systematic review of sonographic findings of placental mesenchymal dysplasia and subsequent pregnancy outcome. *Ultrasound Obstet Gynecol* 2013;41:366–74.
 - 9 Sridev S, Barathan S. Case report on spontaneous ovarian hyperstimulation syndrome following natural conception associated with primary hypothyroidism. *J Hum Reprod Sci* 2013;6:158–61.
 - 10 Delbaere A, Smits G, Olatunbosun O, *et al.* New insights into the pathophysiology of ovarian hyperstimulation syndrome. What makes the difference between spontaneous and iatrogenic syndrome? *Hum Reprod* 2004;19:486–9.
 - 11 Ludwig M, Gembruch U, Bauer O, *et al.* Ovarian hyperstimulation syndrome (OHSS) in a spontaneous pregnancy with fetal and placental triploidy: information about the general pathophysiology of OHSS. *Hum Reprod* 1998;13:2082–7.
 - 12 Suzuki H, Matsubara S, Uchida S, *et al.* Ovarian hyperstimulation syndrome accompanying molar pregnancy: case report and review of the literature. *Arch Gynecol Obstet* 2014;290:803–6.

Copyright 2015 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow