Narrative Reviews

Placental Mesenchymal Dysplasia: Chronological Observation of Placental Images during Gestation and Review of the Literature

Satoshi Ohira [a], Nao Ookubo [a], Kyoko Tanaka [a], Akiko Takatsu [a], Hisanori Kobara [a], Norihiko Kikuchi [a], Ayumi Ohya [b], Makoto Kanai [a], Tanri Shiozawa [a]

Department of [a]Obstetrics and Gynecology, [b]Radiology, Shinshu University School of Medicine, Matsumoto, Japan

3-1-1 Asahi, Matsumoto 390-8621, Japan

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Address correspondence and reprint requests to:

Tanri Shiozawa, M.D. Department of Obstetrics and Gynecology, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto 390-8621, Japan

FAX: +81-263-34-0944; TEL: +81-263-37-2719

e-mail: tanri@shinshu-u.ac.jp

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Abstract

Placental mesenchymal dysplasia (PMD) is characterized by multiple hypoechoic vesicles, which are similar to molar changes in the placenta; however, the process of such morphological changes of PMD during pregnancy has not been fully understood. We performed a review of all PMD cases published in English, identified 49 articles including 110 cases. With regard to the gestational age at which the multi-cystic pattern was seen, approximately 70 % of cases were diagnosed at 13-20 weeks of gestation. Another characteristic feature of PMD is varicose dilation of fetal chorionic vessels. Ninety % of cases were diagnosed as placenta with dilated fetal chorionic vessels in the third-trimester. We also report a case of PMD which was found at 10 weeks of gestation according to ultrasonic molar patterns. Serial observations of the placenta using ultrasound and magnetic resonance imaging revealed that multi-cystic lesions became smaller after 23 weeks. In contrast, dilated placental vessels on the fetal side became apparent at 38 weeks. The present review highlights that PMD's placental vesicular lesions may precede dilation of fetal chorionic vessels during pregnancy. We also indicated that the potential of a gradual reduction in size of PMD's placental vesicular lesions by serial study of placental images.

Introduction

Placental mesenchymal dysplasia (PMD) is a rare condition of pregnancy that presents as multiple hypoechoic vesicles, which are similar to molar changes in the placenta. It is estimated to occur in 0.02 % of pregnancies [1]. These cases are often misdiagnosed as partial mole or twin pregnancy with complete mole and coexistent fetus. Most cases of PMD show multi-cystic area in ultrasonography at 13 weeks or later of gestation [2]. Another characteristic feature of PMD is varicose dilation of fetal chorionic vessels. Although approximately one hundred cases of PMD have been reported, serial course of PMD's placental appearance during pregnancy have not been elucidated. We review previously reported cases of PMD in relation to presented gestational age of multi-cystic pattern and dilated chorionic vessels of the placenta.

Literature

We performed a review of all PMD cases published in English between 1986 and April 2012. All studies were derived from Medline using the terms 'placental mesenchymal dysplasia' and references of articles. All articles without an abstract or with unavailable full text were excluded. We identified 49 articles including 110 cases of PMD [1-49].

Clinical Case

We recently observed a 32-year-old, primigravida woman who referred to our hospital at 12 weeks of gestation because of multi-cystic patterns in ultrasonography detected at 10 weeks of gestation. Ultrasound identified a large area of chorionic tissue consistent with a molar tissue pattern (Fig. 1); normal chorionic tissue was unclear. Fetal growth and amniotic fluid volume were normal. Partial mole or twin pregnancy with complete mole and coexistent fetus, or PMD was initially suspected. Serum human chorionic gonadotropin (hCG) was 241,270 mIU/mL at 12 weeks of gestation, and the titer gradually decreased. Amniocytes were collected at 17 weeks of gestation, and the

karyotype was 46,XX. Because the fetal karyotype was normal diploid and serum hCG levels were not elevated as complete mole, PMD was finally suspected. Magnetic resonance imaging (MRI) at 17 weeks of gestation showed that the whole area of the placenta was occupied by small cysts 2-15 mm in diameter (Fig. 2a). After 23 weeks of gestation, serial ultrasonic evaluation revealed a gradual reduction of size in placental vesicular lesions (Fig. 3a, 3b). After 29 weeks of gestation, placental multi-cystic pattern was indistinct (Fig. 3c), but the placenta was thick in ultrasonography. MRI at 34 weeks of gestation showed almost normal appearance of the placental parenchyma (Fig. 2b). In ultrasonography, the fetus demonstrated reduced growth parameters from 34 weeks of gestation, and dilated superficial placental vessels were observed on the fetal side at 38 weeks of gestation (Fig. 4a). Because non-reassuring fetal status including prolonged decelerations in fetal heart rate monitoring was observed at 39 weeks of gestation, cesarean section was performed. The newborn was a 1998 g female (< 3 percentile) with Apgar scores of 8 and 9 at 1 min and 5 min, respectively. The placenta weighed 1200 g. Fetal plate of the placenta showed aneurismal and varicose dilations of chorionic vessels (Fig. 4b). Microscopically, stem villi contained some dilated vessels with thrombosis. Some terminal villi contained increased density of fibroblastic cells (Fig. 4c). Stem villi occasionally showed hydropic swelling with cistern formation. Abnormal trophoblastic proliferation and inclusion were not observed. These pathological findings were compatible with PMD. The patient’s puerperal course was uneventful.

Results

PMD has a high incidence of fetal growth restriction and intrauterine fetal death, and is associated with Beckwith-Wiedemann syndrome (BWS), a condition characterized by macrosomia, visceromegaly, macroglossia, and omphalocele [18]. Of the 110 cases reviewed, 16 (14.5 %) were associated with BWS [2-10], 33 (30.0 %) had evidence of

fetal growth restriction [4, 11-24, 41, 46, 48] as the current case, and 28 (25.5 %) ended in intrauterine fetal death [4, 6-8, 12, 13, 15-18, 25, 26, 45, 47]. There is a female preponderance in cases of PMD; 78 females and 19 males of which presented the data of infants were reviewed.

Of the 110 cases reviewed, 44 cases of PMD showed multi-cystic placenta in antenatal ultrasound scan [1-3, 5, 7, 9-13, 16, 18-20, 22, 23, 26-34, 41-48]. Figure 5 represents the gestational age that the multi-cystic pattern was identified in 44 cases and the current case. Approximately 70 % of cases were diagnosed as multi-cystic placenta at 13-20 weeks of gestation. Another characteristic feature of PMD is aneurismal and varicose dilation of fetal chorionic vessels. Of the 110 cases reviewed, 48 cases of PMD presented the data of dilation of fetal chorionic vessels [2, 3, 9, 11-15, 17, 18, 20-24, 26, 34-36, 40, 41, 44-48]. Figure 6 represents the gestational age when aneurismal and varicose dilation of chorionic vessels were identified in 48 cases and the current case. Ninety % of cases were diagnosed as placenta with dilated fetal chorionic vessels in the third-trimester, and 55 % of cases showed this feature after 36 weeks of gestation.

Discussion

PMD is a rare disorder. The increased propensity of PMD in BWS and female infants has led to speculation that genes important for the development of PMD may be related to the BWS complex (11p15.5) or the X chromosome [1], but the genetic constituency and pathogenesis of PMD is unclear.

Prenatal differential diagnosis of PMD is partial mole or twin pregnancy with complete mole and coexistent fetus. It is important to distinguish PMD from molar pregnancy because it may avoid unnecessary termination of pregnancy, especially if prenatal ultrasonographic examination shows features suggestive of molar pregnancy in the presence of a normally appearing fetus. Fetal karyotype is an important initial factor in distinguishing PMD from partial mole. While partial mole is usually triploid, fetus

with PMD is almost always diploid [23]. Although it is difficult to distinguish PMD from twin pregnancy with complete mole and coexistent fetus in terms of prenatal imaging of the placenta, serum hCG levels with PMD are reportedly lower than that of complete mole [23]; the peak of serum hCG levels with PMD may be up to 500,000 mIU/mL as normal pregnancies.

Serial course of PMD's placental image during pregnancy have not been elucidated. Our review showed approximately 70 % of cases was diagnosed as multi-cystic placenta at 13-20 weeks of gestation. Meanwhile, in the several cases, the multi-cystic pattern in ultrasonography was detected prior to 13 weeks of gestation as the current case. Thus, the morphological changes in the villi appear to begin early during gestation. Our review also showed that no previous report of PMD had detected aneurismal and varicose dilation of fetal chorionic vessels prior to 25 weeks of gestation. These findings suggest that vascular malformation develops progressively after the late second-trimester. Macroscopic features of aneurismal and varicose dilation of fetal chorionic vessels may be secondary changes in circulatory disorders in PMD's multicystic placenta.

Serial change of the size of PMD's vesicular lesions during pregnancy has not been also elucidated. Only two reports stated that sonographic evaluation of a case of PMD revealed a reduction in size of placental vesicular lesions as the pregnancy advanced [23, 45]. Our case also revealed a gradual reduction in size of placental vesicular lesions by serial study of placental images including ultrasound and MRI; therefore, PMD's placental vesicular lesions may have the potential of a gradual reduction in size. Although ultrasonography is suitable for observation of the placenta, MRI is more fitting to understand whole intrauterine structures using 3-dimensional observations. Moreover, there have been no reports of PMD's imaging using MRI. Therefore, we consider that the use of MRI in combination with ultrasonography can be a potent strategy in chronological observation of PMD during pregnancy. In the current

case, we could certainly see that vesicular lesions occupied not partial but whole area of the placenta due to the wider field of view and excellent tissue contrast of MRI.

With regard to the pathogenesis of PMD, Heazell et al. [1] described that cells lining the cistern in PMD were labeled with D2-40, an established lymphatic marker immunohistochemically. Therefore, vesicular lesions in PMD's placenta may be caused by abnormal lymphangiogenesis. Although the reason for the gradual reduction in size of placental vesicular lesions is unclear, we speculate that lymph vessel-like structures in PMD's placenta may be reduced rather than increased.

In summary, the present review highlights that PMD's placental vesicular lesions may precede dilation of fetal chorionic vessels during pregnancy. We also indicated that the potential of a gradual reduction in size of PMD's placental vesicular lesions by serial study of placental images including ultrasound and MRI. Further studies are needed to clarify the etiology and pathogenesis of PMD.

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Figure legends

Figure 1. Ultrasonographic image at 12 weeks of gestation. The multi-cystic pattern existed within the parenchyma of chorionic tissue (surrounded by arrows).

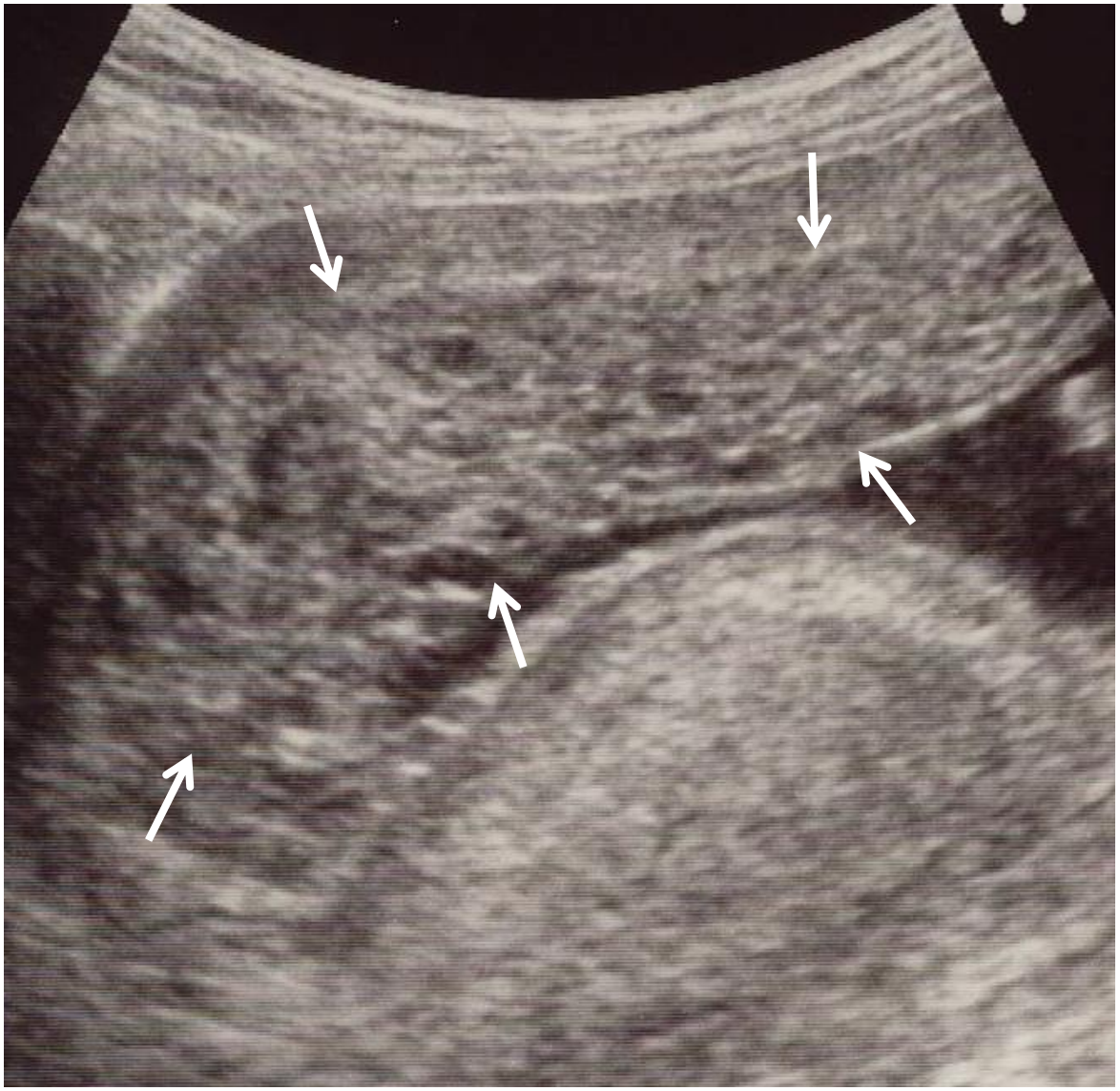
Figure 2. T2-weighted sagittal images of magnetic resonance imaging (MRI). **a**: MRI at 17 weeks of gestation. Whole area of the placenta (surrounded by arrows) was occupied by small cysts 2 – 15 mm in diameter. **b**: MRI at 34 weeks of gestation. Almost normal appearance of the placental parenchyma was observed (arrows).

Figure 3. Serial study of placental ultrasonographic images. **a**: At 22 weeks of gestation **b**: At 26 weeks of gestation **c**: At 29 weeks of gestation. Serial ultrasonic evaluation revealed a gradual reduction in size of placental vesicular lesions. After 29 weeks of gestation, placental multi-cystic pattern was indistinct.

Figure 4. **a**: Ultrasonography at 38 weeks of gestation. Dilated superficial placental vessels were observed on the fetal side (arrow). **b**: Macroscopically, fetal plate of the placenta showed aneurismal and various dilations of chorionic vessels. **c**: Microscopically, stem villi contained some dilated vessels with thrombosis. Some terminal villi contained increased density of fibroblastic cells (arrows).

Figure 5. Presented gestational age of multi-cystic pattern in 44 cases and the current case

Figure 6. Presented gestational age of aneurismal and varicose dilation of chorionic vessels in 48 cases and the current case



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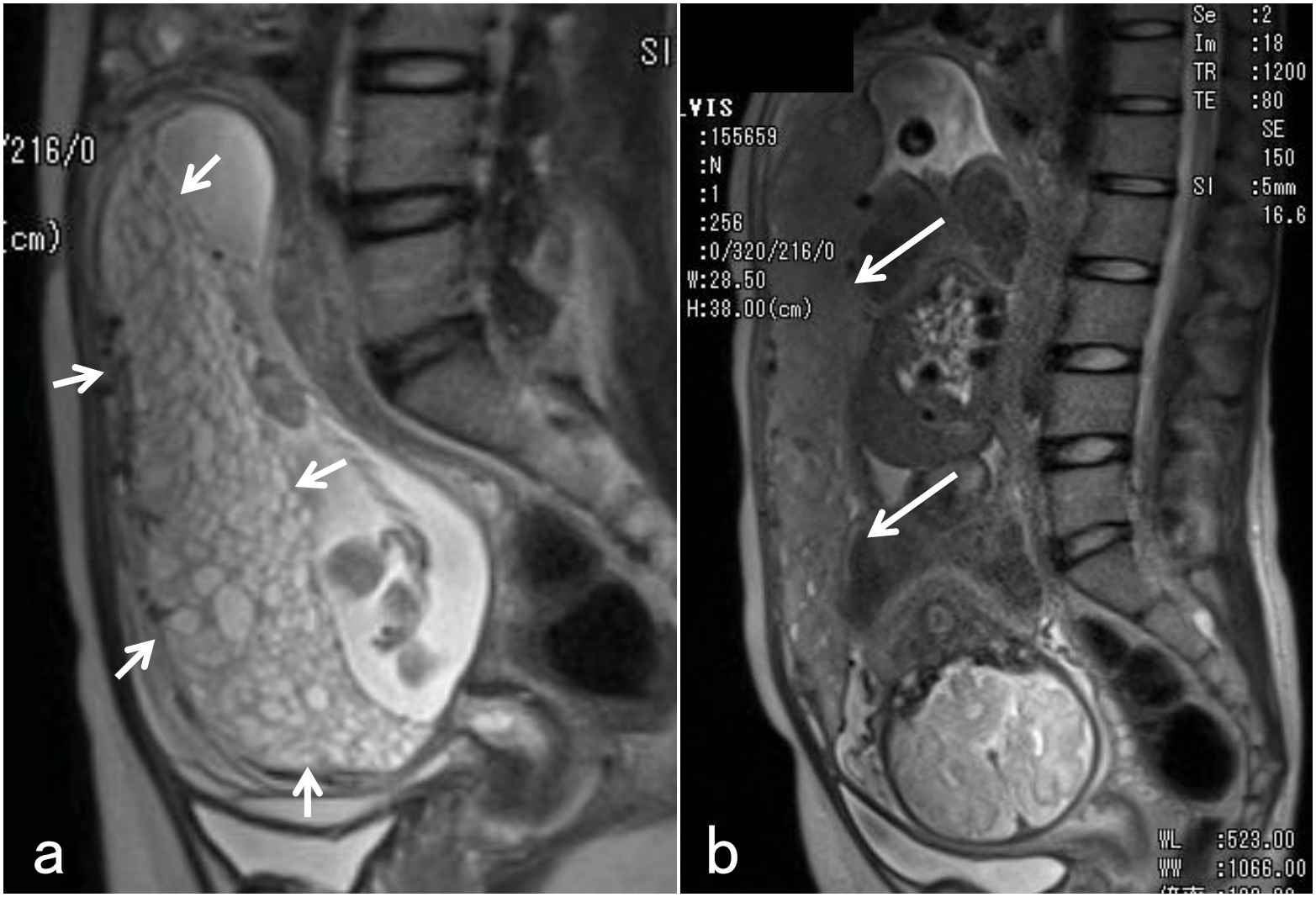
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Figure 2

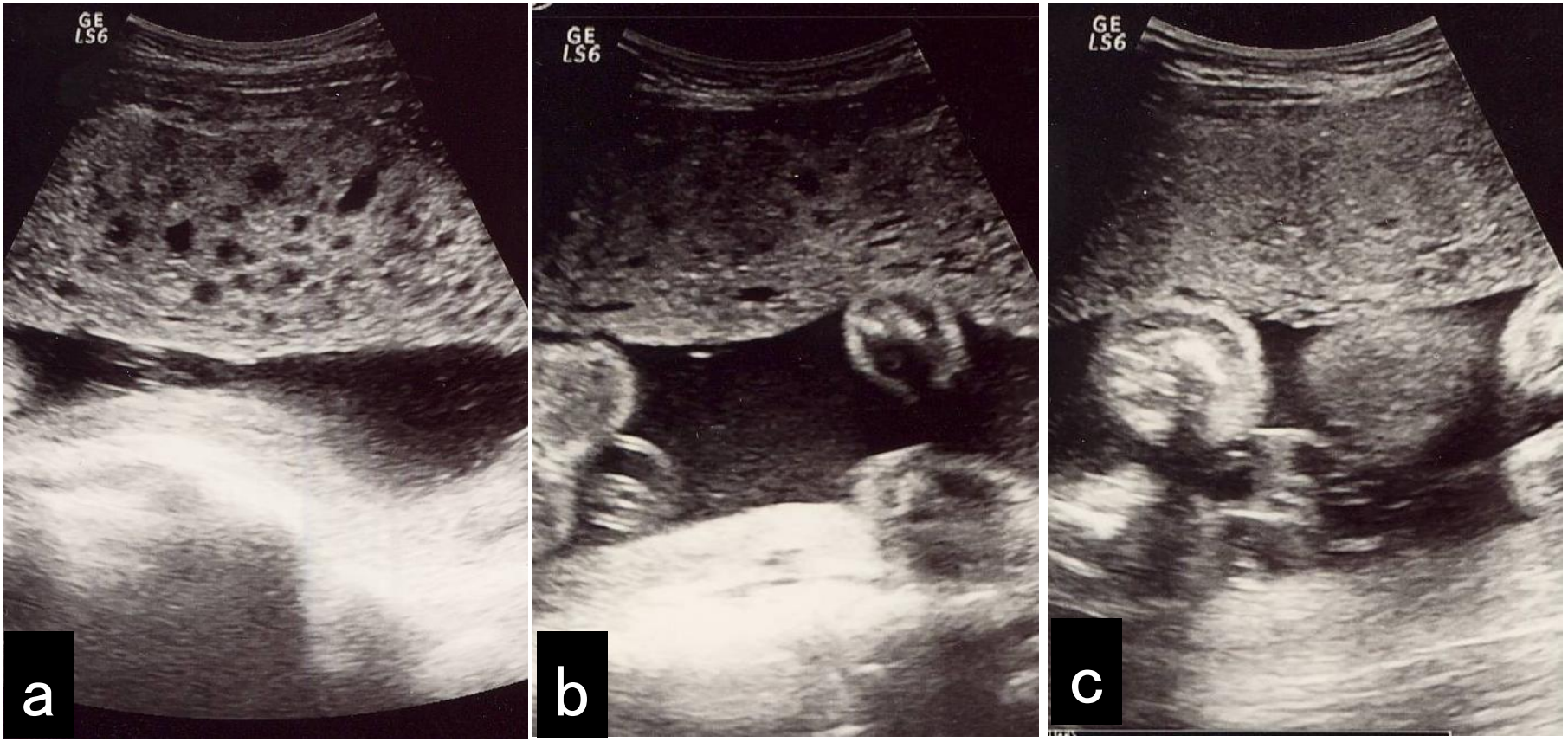
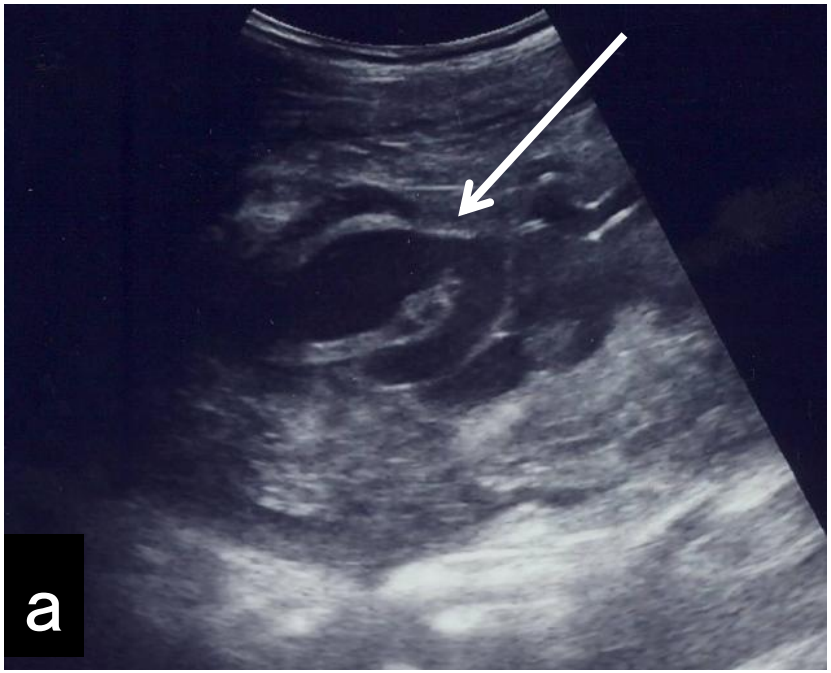
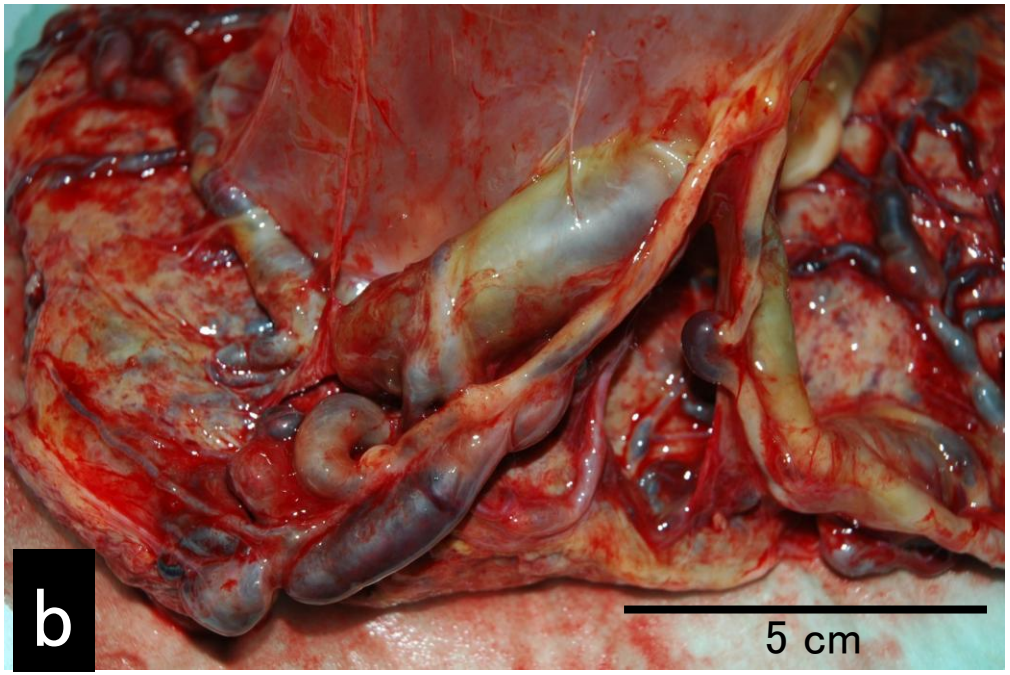


Figure 3





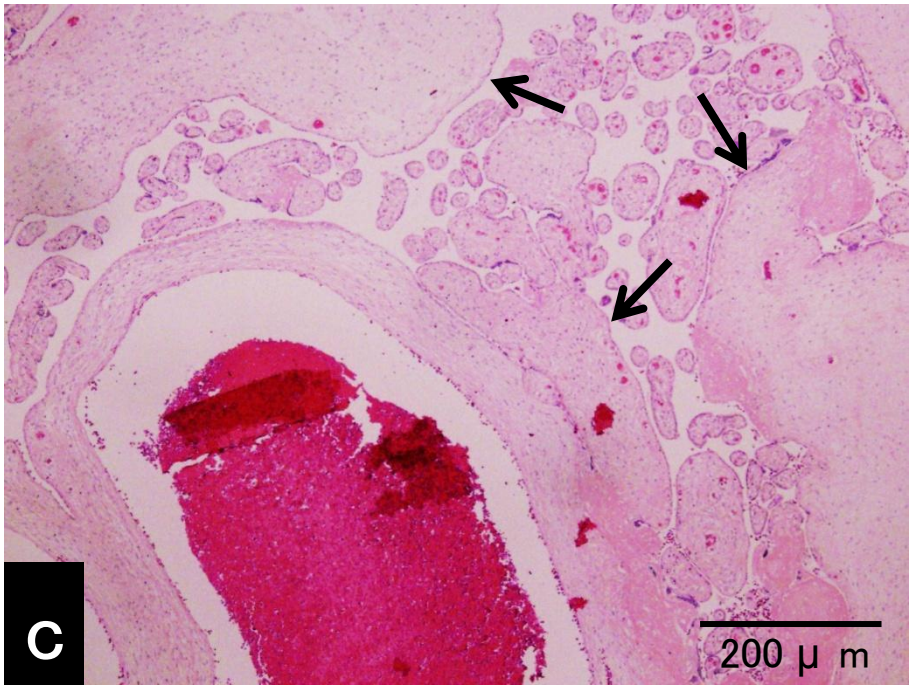
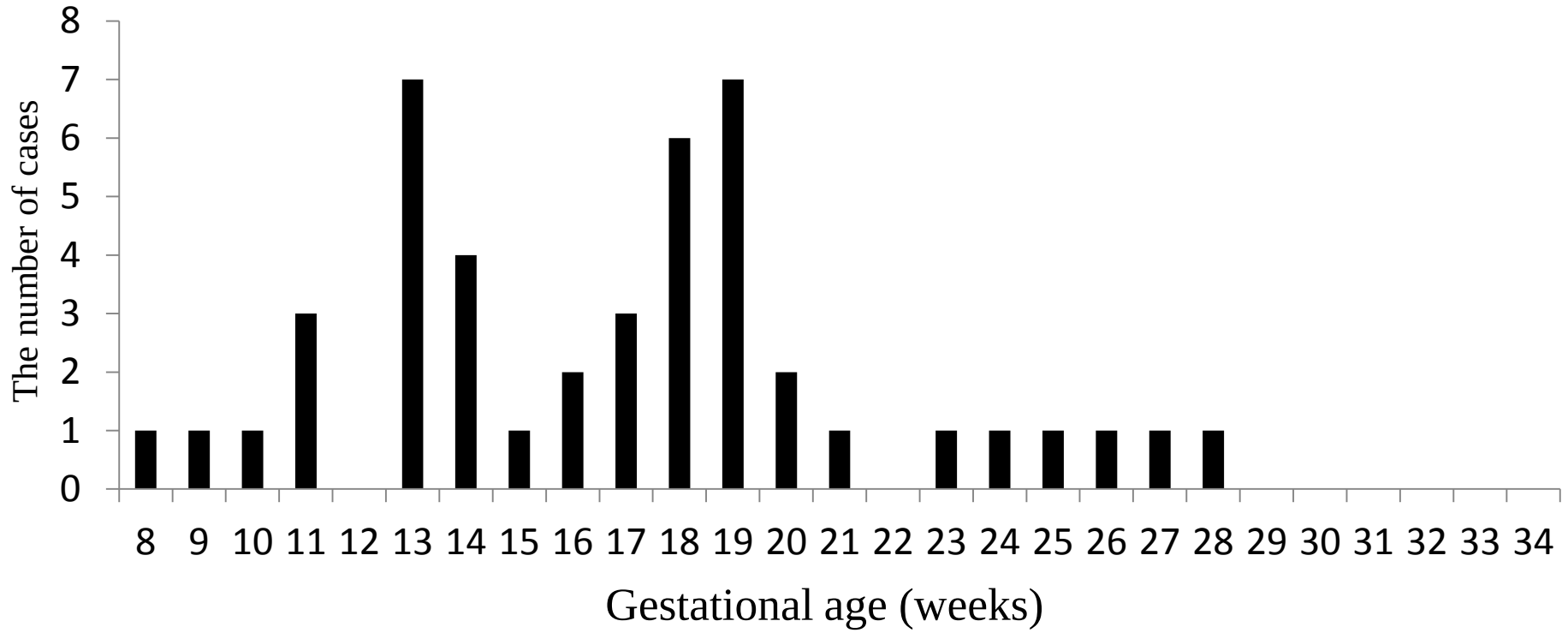


Figure 4


The number of cases
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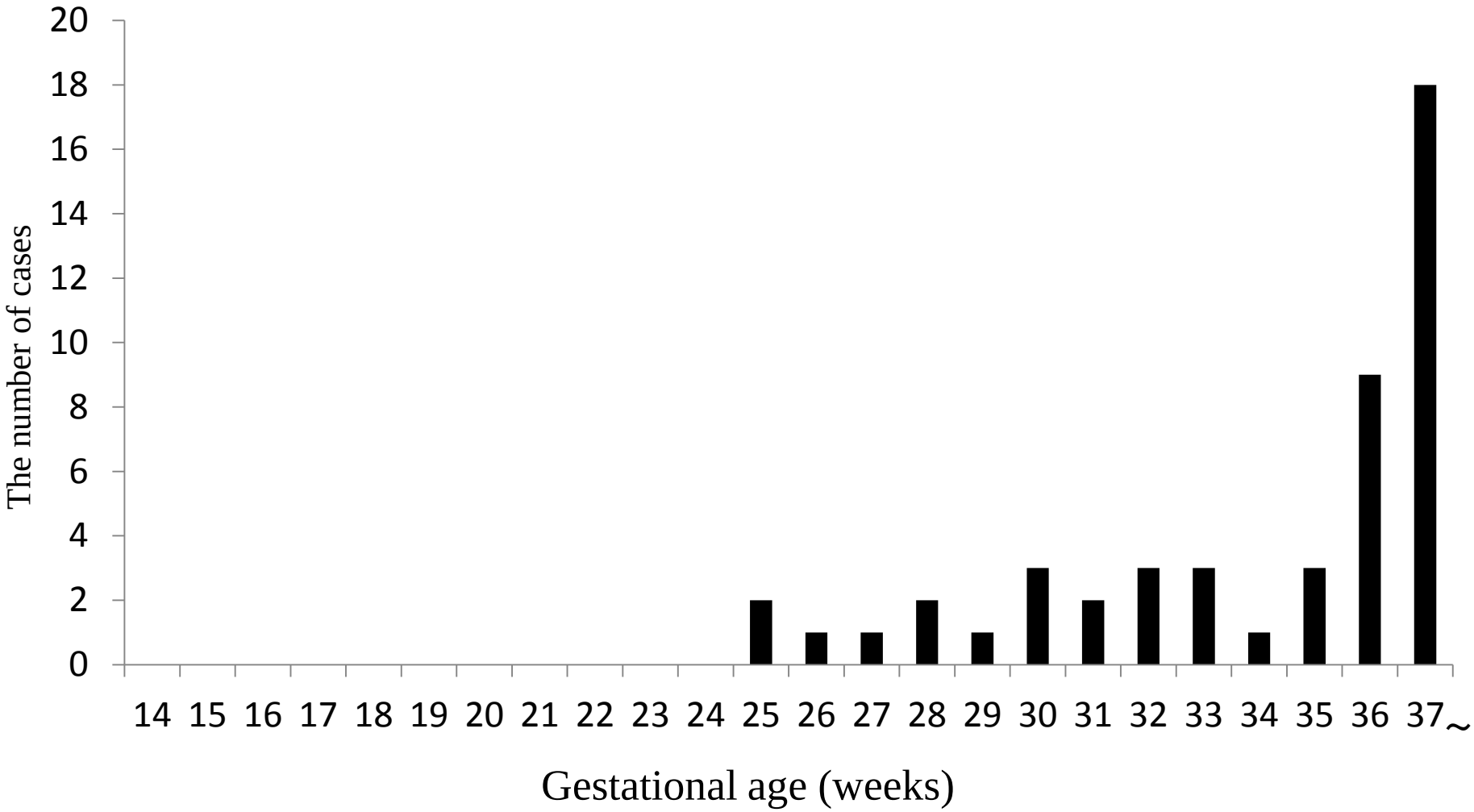
Gestational age (weeks)

Figure 5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Gestational age (weeks)

Figure 6