Rounded intraplacental hematoma - A high risk placental lesion as illustrated by a prospective study of 26 consecutive cases

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**ARTICLE INFO**

**Keywords:**
- Placenta
- Hematoma
- Stillbirth
- Rounded intraplacental hematoma
- Infarction hematoma
- Echogenic cystic lesion

**ABSTRACT**

**Background:** A rounded intraplacental hematoma (RIH) is a recently delineated placental lesion. Following the observation of two cases of RIH in placentas associated with stillbirth in 2012, we postulated that RIHs were associated with a higher risk obstetric phenotype when compared to other lesions characteristic of maternal vascular malperfusion (MVM). We aimed to investigate this further by reviewing the associated maternal and fetal characteristics in a series of prospectively identified cases.

**Methods:** Pregnancies where a RIH was identified on placental examination were prospectively collected from February 2014–July 2016. Comparison was made with pregnancies with placental evidence of MVM but without RIH.

**Results:** 26 placentas with a RIH were identified and 26 placentas with MVM were selected for comparison. There was a statistically significant increased incidence of stillbirth in the RIH group as compared with the MVM-only group (\(p = 0.022\)). Also, pregnancies with RIHs had a lower maternal age (\(p = 0.041\)), decreased incidence of antenatally diagnosed growth restriction (\(p = 0.023\)), a trend to increased incidence of clinical abruption (\(p = 0.051\)) and heavier mean infant birthweight (\(p = 0.034\)). Both groups had a high incidence of pre-eclampsia, Caesarean section and preterm delivery when compared with the general population.

**Discussion:** This is the first study to prospectively identify and collect RIHs using standardised pathological criteria and more than doubles the number of reported cases to date. We present 2 comparable, high-risk cohorts but with a significantly increased incidence of stillbirth in those in which RIHs were seen. Further study of these lesions is justified with an emphasis on the potential for antenatal detection using ultrasound evaluation of placental texture.

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1. **Introduction**

Rounded intraplacental hematoma (RIH) was a term first used by Fitzgerald et al., in 2011 to delineate a distinctive type of hemorrhagic placental lesion. This was facilitated by characteristic morphological features that separated them from other parabasally located placental thrombohematomas such as intervillous thrombi [1]. In that study RIHs were described as parabasally located, tending to have a round shape or a number of rounded areas and were often associated with marked surrounding placental compression and infarction when they were located in the intervillous space.

The study noted that the 13 cases of rounded RIH had a statistically significantly higher risk of decidual vasculopathy and infarction than the other parabasally located thrombohematomas. As a group, pre-eclampsia (PET), pregnancy-induced hypertension (PIH) and Haemolysis, Elevated Liver enzymes, Low Platelet count (HELLP) syndrome was also more common [1]. Two of the RIH cases had undergone termination of pregnancy (TOP) for severe fetal growth restriction (FGR). PIH, PET or HELLP syndrome affected 5 of the 13 RIH cases, FGR affected 7 of the cases and the mean age of the placentas examined with RIHs detected was 30 weeks (median 29 weeks) suggesting a high incidence of preterm delivery. Based on their morphological appearance the authors postulated that these lesions form as a result of disruption of vasculopathic decidual arterioles in a setting of maternal vascular underperfusion.

Bendon subsequently described 6 cases of a lesion the author termed “Infarction Hematoma” characterised by “central spherical blood clot with sometimes a few non compacted lines of fibrin, which was...
surrounded by a variable thickness of infarction” [2]. In association with these findings he reported a high incidence of stillbirth (5 of 6 cases) with the remaining case showing poor neonatal Apgar scores at delivery (2/5 at 1 and 5 min). PET, PIH or HELLP affected 2 of the 6 cases, a further 1 was delivered due to abruption, 1 had a history of PET in a previous pregnancy and 2 had a history of previous fetal losses.

In 2014 Aurioles-Garibay et al. described a case report of “hematoma surrounded by a rim of infarcted tissue” on pathological examination of the placenta of a multiparous woman who developed severe, acute onset PET with growth restriction and fetal death at 21 weeks 4 days gestation. A rounded cystic area measuring 13 × 14 mm had been identified in the placental mass antenatally [3].

We postulated that the lesions described by Fitzgerald et al., Bendon and Aurioles-Garibay et al. were the same pathological entity and that this entity, that we refer to as a RIH, may be associated with particularly poor obstetric outcomes, based on the above three papers and the discovery of these lesions in 2 placentas examined at our institution after stillbirths in 2012. However, the number of cases reported was small at 19 and in these 19 cases selection was vulnerable to significant recall bias given that all cases were retrospectively described.

We hypothesized that RIHs were markers of a particularly severe clinical phenotype within the group of pathological lesions characteristic of maternal vascular malperfusion (MVM). We aimed to investigate this further by establishing the maternal and fetal characteristics in a series of prospectively identified RIH cases and by comparing these to a group of MVM cases (without RIHs) from the same time period.

2. Methods

This was a case-control study for which ethical approval was granted by the Clinical Research Ethics Committee of the Cork Teaching Hospitals.

A RIH was defined as a hematoma, occurring within the placental parenchyma, having a round shape or a number of rounded areas, generally abutting the basal plate and which was often, but not always, surrounded by a rim-like area of placental infarction. They were distinguished from intervillous thrombi using the criteria of Fitzgerald et al. [1] where intervillous thrombi were described as having a rhomboid (rather than rounded) shape, occasional pointed corners at their periphery, only mild compression of surrounding parenchyma and frequent parallel laminations.

Cases of RIH were prospectively collected from February 2014–July 2016 in Cork University Hospital’s Department of Histopathology. Cork University Maternity Hospital is a tertiary unit that has in the region of 7500–8000 deliveries per year. Only placentas with suspected pathological abnormalities are referred for full pathological examination and all referred placentas during the study period were reviewed by a single perinatal pathologist (BF). Medical scientists who macroscopically assess and process placentas during pathological examination in our institution were trained on the recognition of these lesions. Maternal and fetal outcomes from all cases were retrospectively reviewed in 2016 by means of maternal chart review. In addition, cases’ slides and gross placental images were reassessed at this time with the objective of further defining RIH’s pathological characteristics.

2 RIH cases from outside the study period (2012) were also reviewed for assessment of the gross and histological findings in RIH’s but these cases, which were outside of our prospective study period, were excluded from statistical analyses.

Comparison MVM cases were also chosen from within the same prospective study period. These were identified from a search of the pathology department’s laboratory information management system (LIMS) for placetas coded as having pathological evidence of MVM. MVM cases were defined by the presence of pathological lesions characteristic of MVM including atherosclerosis, persistently muscularised basal plate decidual vessels, distal villous hypoplasia, increased perivillous fibrinoid, villous agglutination, accelerated villous maturation and infarcts (that did not meet the definition of RIH). Placentas had only been coded as showing MVM if these lesions were seen in combination, or with sufficient extent or severity to warrant, in the pathologist’s opinion, an overall diagnosis of MVM.

Birth centile of the infants was calculated using GROW charts customised for an Irish patient cohort [4]. Placental weight centiles were calculated [5]. Data were inputted to and analyzed by the statistical software packages SPSS for Windows version 20.0 (SPSS, Chicago, IL, USA). Tests were considered statistically significant if p < 0.05.

3. Results

1758 sequential placentas (from 19471 deliveries) were subjected to full pathological examination during the study period. 26 of these were identified as having RIHs giving an incidence of 1.48% within this cohort of placentas with suspected underlying pathology.

3.1. Baseline maternal characteristics (Table 1)

Those with RIH placentas were statistically younger than those with MVM only. With a mean age of 31.52 years they were also slightly younger than the current national mean average of delivery of 31.9 years [6]. There were two dichorionic, diamniotic twin pregnancies with RIH. In the first case, a RIH was seen in the placental share of the baby who was stillborn at term. The liveborn baby’s placental share was normal. In the second case delivery was undertaken at 26 + 6 weeks gestation in the maternal interest due to evolving pre-eclampsia. Severe growth restriction of one infant had been noted from 22 weeks gestation. Again the RIH was seen in the affected twin’s placental share although maternal vasculature malperfusion was seen in both shares.

The mean BMI of both the RIH and MVM only groups was in the overweight category which appears largely in line with other Irish studies which suggest both a high incidence of raised BMI in the general pregnant population and a high representation of this cohort in pregnancies with adverse outcomes [7,8].

15.38% (n = 4) of the RIH cases were documented assisted conceptions. Other significant background medical conditions in the RIH group included Type 1 diabetes (n = 1), previous pulmonary embolus (n = 1), rheumatoid arthritis (n = 2), Graves’ Disease (n = 2) and ulcerative colitis (n = 1).

15.38% (n = 4) of the MVM-only cases were documented assisted conceptions. Other significant background medical issues in the MVM-only group included Type 2 diabetes (n = 1), essential hypertension (n = 2), hyperprolactinaemia (n = 1), ulcerative colitis (n = 1), coiled cerebral aneurysm (n = 1), previous thyroid carcinoma (n = 1) and asthma (n = 1).

3.2. Previous pregnancy complications

There was no history of stillbirth in either those who had RIHs or MVM only. There was 1 previous history of neonatal death in the MVM-only group due to complications of extreme prematurity following delivery for severe PET at 24 weeks gestation.

Of those who were multiparous, 26.67% (n = 4) of 15 women with RIHs had a previous history of PET. 1 had an intra-uterine death (IUD) in this (the index) pregnancy. 33% (n = 3) of 9 multiparous cases with MVM-only had a previous history of PET. All had PET recurrences requiring preterm delivery.

13.33% (n = 2) of the 15 multiparous women with RIHs had a prior history of gestational diabetes (GDM) and both were diagnosed with GDM again in this pregnancy. None of the MVM-only cases had a previous history of gestational diabetes.

3.3. Index pregnancy (Table 2)

There was a statistically significant increased incidence of
antenatally diagnosed fetal growth restriction in the MVM-only cohort as compared with the RIH cohort (p = 0.023). However, with an incidence of estimated fetal weights of less than the 10th centile of 25% and 60% respectively, both groups had a significantly increased incidence of FGR as compared with the general population.

The incidence of delivery by Caesarean section was 88.5% in the MVM group and 73.1% in the RIH group. However, when stillbirths were excluded; the incidence of Caesarean section in the RIH group rose to 85% i.e. 17 of 20 livebirths. The incidence of Caesarean section was not statistically significant between groups but appears markedly increased in comparison to the general population which in Ireland have an incidence of caesarean delivery of 28% and 67% for singleton and multiple deliveries respectively [6].

Mean gestational age at delivery was preterm in both the RIH cases and MVM-only cases although the RIH cases trended towards being more mature. There was a trend towards PET/PIH being more common in those with MVM-only (53.8% and 76.9% for RIH and MVM-only cases respectively). However, in both groups there was a markedly increased incidence as compared with the overall pregnancy population, where the incidence of PET is quoted in the region of 2–3% of pregnancies [9].

3.4. Delivery outcomes (Table 3)

6 of 28 babies born to the 26 mothers with RIHs were stillborn. All had post mortem examinations. No fetal malformations, genetic abnormalities or non-placental causes of death were detected in any of those infants. Placental MVM was the attributed cause of death in all cases; with confirmed complicating retroplacental haemorrhage in 3 cases. All mothers of these stillborn infants were multiparous with no previous history of stillbirth.

33.3% (n = 2) RIH cases where a stillbirth occurred presented with clinical abruption at term. One had a previous history of PET and had commenced antihypertensive medication for PIH in the week prior to presentation. The other had no history of PET but developed severe HELLP syndrome requiring ICU admission and renal dialysis post-natally. Both had previous Caesarean sections and underwent emergency Caesarean section for delivery due to stabilization difficulties peripartum. Both had massive peripartum haemorrhage.

5 women in total presented with clinically suspected abruption and had RIH's on placental histology in contrast to none in the MVM only group (p = 0.051).

Of the 31 babies born to 26 mothers in the MVM only group; all were liveborn. There was 1 neonatal death in this cohort in a baby with Patau’s syndrome.

Babies from the RIH cases were statistically significantly larger than the MVM-only cases (p = 0.0342). The infants of MVM-only cases had a mean birth weight centile below the 10th centile (9.5th).

3.5. Placental pathology

Gross pathological findings in placentas containing RIHs were variable with lesions showing heterogeneous appearances both within and between cases (Figs. 1–4). Usually the fetal surface of the placenta was unremarkable but in one very large example the chorionic plate could be seen to bulge towards the amniotic cavity with associated discolouration (Fig. 3A). The maternal surface could sometimes be seen to contain small, irregular pits that on sectioning corresponded to the point of contact between the RIH and the basal plate (Fig. 2C). On the cut surface of the placenta a spectrum of changes were identified that reflected differing size and age of lesion. Lesions varied from 0.5 cm (Fig. 1B) to several centimetres (Fig. 3B) and were identified most often in the central 4/5ths of the disc but could be seen peripherally (Fig. 2B). In 11 cases RIHs were multiple, including in 4 of the 6 stillbirths. Fresh RIHs were rounded with central areas of haemorrhage with some evidence of surrounding parenchymal compression but with little gross evidence of infarction (Fig. 1C). Most commonly however there was some evidence of evolving infarction. Sometimes these changes of evolving infarction tended to be thicker and more extensive on the chorionic plate aspect of the RIH and did not evenly surround the haematoma (Fig. 2D). In most instances this rim of infarction was less than 1–2 cm (Fig. 2A) but in the largest example seen (Fig. 3), 40% of the total placental volume was involved. In parallel with increasing age the central area of haemorrhage appeared to decrease in size and showed
degenerative change in the hematoma so that it sometimes appeared centrally necrotic or to consist of a small fluid-containing cavity (Fig. 2A and B, D).

In one case clear gross continuity between a large RIH and a retroplacental hematoma was demonstrated (Fig. 4).

On microscopic examination, the appearances of the RIH also reflected the lesions age. Fresh examples showed mostly compression of the surrounding parenchyma but older examples showed progressive changes of placental infarction (Fig. 5). In two cases, dilated "feeder" vessels could be seen entering the base of the RIH within the placental basal plate (Fig. 6).

Although no statistically significant differences were noted between the groups the incidence of retroplacental hemorrhage was threefold more common in the RIH group (Table 4).

92% (n = 24) of the RIH group showed other lesions of MVM. This included 6 of the 6 stillbirths. In the two RIH cases without other degenerative change in the hematoma so that it sometimes appeared centrally necrotic or to consist of a small fluid-containing cavity (Fig. 2A and B, D).

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evidence of MVM one had no other significant pathology while the second case had a velamentous cord insertion, old extramembranous haemorrhage and an intervillous thrombus. The two cases with the greatest extent of parenchymal involvement by RIH(s), 30% and 40% respectively, were in the stillbirth group.

4. Discussion

This is the first study to prospectively identify and collect RIHs using standardised pathological criteria and more than doubles the number of reported cases to date. We present 2 comparable, high-risk cohorts but with a significantly increased incidence of stillbirth in those in which a RIH was seen on placental pathological examination. The trend towards larger infant birthweight and occurrence in young, multiparous women highlights a high-risk maternity population that may not be identified based on current risk stratification tools. Emphasis needs to be placed therefore, on further increasing the number of reported cases to further define the features of this patient cohort so that the risk of stillbirth and other adverse outcomes can be minimised.

The strengths of this study are its prospective nature, placental review by a perinatal pathologist and the use of a consistent lesion definition. Weaknesses are the small number of cases ultimately identified. We also cannot identify the frequency of RIHs in the general placental population as only placentas from abnormal pregnancies are sent to our laboratory for examination. Due to the uncommon nature of this lesion (1.48% of an at risk placental population) collaborative studies may be required to obtain high numbers of cases.

Table 1

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<th>RIH Cases (n = 26)</th>
<th>MVM only cases (n = 26)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Mean Maternal Age</td>
<td>31.52 (± 4.8) years</td>
<td>34.67 (± 5.9) years</td>
<td>p = 0.041</td>
</tr>
<tr>
<td>% Twin Pregnancy</td>
<td>7.69% (n = 2)</td>
<td>19.23% (n = 5)</td>
<td>p = 0.4164</td>
</tr>
<tr>
<td>Multiparous</td>
<td>57.69% (n = 15)</td>
<td>34.62% (n = 9)</td>
<td>p = 0.2641</td>
</tr>
<tr>
<td>Mean BMI</td>
<td>29.17 (n = 24)</td>
<td>28.19 (n = 25)</td>
<td>p = 0.576</td>
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Fig. 5. Microscopic appearance. In A, in this low power microscopic image, a thin rim of placental compression and infarction is evident between the arrows. A second old RIH (arrowhead) has been displaced and distorted by the larger newer lesion. In B the RIH (arrowhead) is small relative to a larger area of surrounding area of infarction. In C the RIH at the arrow has a surrounding rim of compression and infarction (arrowhead) which contrasts with the RIH seen in D which has no associated infarction.

Fig. 6. Feeder Vessels. In some RIH examples abnormal, dilated vessels (arrows) are seen entering the base of the RIH (star) from the basal plate.
From a pathology perspective these lesions may have been previously identified as infarcts, hemorrhagic infarcts or intervillous thrombi. We believe that the definition used here helps to separate RIHs from their mimics and provides consistency in terminology. Further studies by other groups are however necessary to test this definition in diagnostic practice. The criteria used by Fitzgerald et al. to distinguish primarily hemorrhagic lesions from intervillous thrombi (IVT), and illustrated in that paper, are important as IVT are far more common and do not carry the same clinical associations [1]. To again emphasise these differences, RIHs are primarily round in appearance whereas IVT are rhomboid or triangular and often have a point (Fig. 7). RIHs often have a surrounding rim of placental compression and infarction whereas IVT displace rather than compress surrounding parenchyma; any associated or coincidental infarction is often only focal and does not form a consistent rim surrounding the lesion. IVT also typically have distinct parallel laminations whereas laminations are not generally a prominent feature of RIHs.

The frequent association of RIHs with other pathological lesions of MVM (92% of cases) and the frequent association with PET/PIH (53.8% of cases) support the characterisation of RIHs as lesions of MVM. There is however clear pathological overlap with lesions representing loss of maternal vascular integrity as the lesion is favoured to be primarily hemorrhagic (see below); from a pragmatic standpoint however categorisation with lesions of MVM seems more appropriate.

Our 26 cases show a spectrum both histologically and clinically of age of lesions at presentation. The apparent chronicity of many RIHs at presentation suggests a potential for antenatal recognition of these high-risk lesions.

The role of ultrasound in allowing real-time correlation with postnatally confirmed placental lesions is widely acknowledged but potentially underutilised in current practice. Echogenic cystic lesions

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<th>Table 2</th>
<th>Illustrates some of the index pregnancy complications encountered in these cohorts.</th>
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<tr>
<td></td>
<td>RIH Cases (n = 26)</td>
</tr>
<tr>
<td>Mean Gestation at Delivery (Weeks)</td>
<td>237.23 ± 33.98 days</td>
</tr>
<tr>
<td>Antenatal Diagnosis of PET/PIH</td>
<td>53.8% (n = 14)</td>
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<tr>
<td>Antenatal Diagnosis of Fetal Growth Restriction</td>
<td>23.1% (n = 6)</td>
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<tr>
<td>Gestational Diabetes</td>
<td>11.5% (n = 3)</td>
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<tr>
<td>Caesarean Section as Mode of Delivery</td>
<td>73.1% (n = 19)*</td>
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<tr>
<td>*85% (n = 17) of livebirths</td>
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<th>Table 3</th>
<th>Illustrates some of the key pregnancy outcomes.</th>
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<tr>
<td></td>
<td>RIH Cases</td>
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<tr>
<td>Mean Birth weight Centile (n = 27)</td>
<td>28.89th (SD 32.59)</td>
</tr>
<tr>
<td>Stillbirth (n = 6)</td>
<td>23.08%</td>
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<tr>
<td>Clinical Abruption (n = 5)</td>
<td>19.23%</td>
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<tr>
<td>Massive Post Partum Hemorrhage (n = 3)</td>
<td>11.5%</td>
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\[\text{Fig. 7.} \text{ Gross appearance of intervillous thrombi (IVT). In A fresh IVT is evident. It has a typically rhomboid shape with a tendency to form at least one pointed corner (arrowhead). There is no apparent compression of surrounding parenchyma. In B an old IVT has a triangular shape with a typical point (arrow). There is no central cavitation.}\]
(ECLs) have previously been described on antenatal ultrasound and are associated with adverse pregnancy outcomes [10]. Intraplacental haemorrhages have been identified as the pathological correlates of these lesions [10] but that study predated descriptions of RIHs [1]. One case report documents antenatal identification of an intraplacental lesion that was later pathologically confirmed as an infarction hematoma, a lesion we believe is the same as a RIH [3]. A second, recent case report documents the antenatal detection of multiple RIHs where there was ultimately a stillbirth occurring in association with ultrasound detected ECLs and RIHs. This would provide an opportunity to intervene to prevent stillbirth. Using clearly defined histological criteria for the diagnosis of RIHs, methods such as wire needle localisation of ECLs, as used by Proctor et al. [10] would help to investigate this link further. Similarly, close pathological correlation of ultrasound-detected abnormalities may help refine ultrasound criteria for ECL diagnosis or perhaps subdivide ECLs, maximising identification of at-risk patients.

Infarction hematomas, described by Bendon, and more recently defined in the Amsterdam Placental Workshop Group Consensus Statement [12] as a hemorrhage encased in infarction, were postulated to form as a result of reperfusion of an infarcted area of the placenta [2]. We support a different mechanism of formation that is primarily a hemorrhagic process. As previously stated, we believe that RIHs and infarction hematomas are the same lesion with ‘infarction hematomas’ essentially forming a subset of RIHs where infarction is present. RIH is therefore a more inclusive term and includes hemorrhagic lesions where infarction hasn’t yet developed. We believe that RIHs are likely to represent the intraplacental equivalent of a category of retroplacental haemorrhage that are due to decidual vasculopathy. We have also seen examples of RIHs where the process was very acute and the lesion was purely hemorrhagic without infarction. For this reason we would argue that the term RIH should be used as infarction is not obligatory and to maintain the conceptual link between intraplacental haematomata and retroplacental hematoma.

When blood already freely flows within the intervillous space it may be difficult to visualise how a RIH might form. The pressure in the intervillous space is however only about 10 mmHg whereas it is 70 mmHg in the spiral arterioles [13]. If a focal area in the intervillous space was suddenly exposed to near full spiral arteriolar pressure e.g. through “rupture” of a vasculopathic decidual vessel, then there could be a sudden local expansion of the intervillous space in that area giving a RIH. As the area expands the surrounding villi would be pushed together and compressed, effectively walking off the lesion and limiting its spread. This compressed tissue then undergoes infarction having been compressed and cut-off from its oxygen supply. The same basic process in a different direction gives a retroplacental hematoma and clinical abruption. This is supported by the trend toward increased incidence of confirmed retroplacental haemorrhage at placental examination.

Given the high rate of stillbirth seen in RIH cases, even when compared to other high-risk groups, further study of these lesions is justified with an emphasis on the potential to identify them antenatally using ultrasound evaluation of placental texture.

**Author’s contributions**

GN conducted the study, acquired and summarised clinical and pathology data conducted pathology reviews and drafted the manuscript. BF conceived and led study, identified cases and conducted pathology reviews. KO’D collected cases and obtained patient charts. All authors were involved in data analysis, case discussions, project discussions and reviewing the manuscript.

**Author’s declarations of interest**

None.

**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.placenta.2019.02.011.

**References**


