Chorion laeve accreta - another manifestation of morbid adherence

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ABSTRACT

Introduction: Smooth muscle in the decidua of fetal membranes (membrane myofibers, MMF) is not mentioned in standard textbooks.

Methods: The current report presents collected observations on 52 patients with MMF at 2 institutions between 2004 and 2017 - including placentas, postpartum curettages, and hysterectomies.

Results: Clinical presentations include observation of adherent membranes during delivery, disrupted and incomplete membranes in placentas submitted for examination, postpartum bleeding associated with retained fetal membranes, association with membrane hematomas and membrane hemosiderin, morbidly adherent fetal membranes in hysterectomies; and association with grossly adherent pieces of tissue or nodules in fetal membranes.

Discussion: Although MMF can be an incidental microscopic observation in a routine placenta, the suggested diagnostic terminology when there are clinical and/or gross presentations is Chorion Laeve Accreta (ChLA). Further study is needed but MMF appears to be the fetal membrane counterpart of BPMF(basal plate myofibers), possibly due to damage of subjacent myometrium by trophoblastic proteases, so that shear stress during delivery causes myofibers to come out attached to the decidua of fetal membranes. Neither the prevalence of MMF, nor its reliability as a marker for placenta accreta is addressed in this collection. Association of MMF with BPMF, and recurrence of MMF, are documented; but the true frequency of these phenomena remains to be established.

Key words: Placenta accreta; retained fetal membranes; membrane hematoma, chorion laeve accreta, membrane myofibers, basal plate myofibers, morbid adherence

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INTRODUCTION

Standard teaching since before the advent of diagnostic immuno-histochemistry is that morbidly adherent placenta (placenta accreta) is characterised histologically by the direct apposition of placental villi to myometrium. It is traditionally believed to be due to decidual deficiency, often in association with prior Cesarean section (1-4). However, recent studies have suggested that this may actually be a myodestructive disease with disturbance of the protease/antiprotease balance in nonvillous trophoblast (interstitial and/or endovascular) (5-8). This may be best appreciated with the use of immunostains for muscle markers and keratin (5,9).

Clinically, the manifestation of morbid adherence depends on the depth of the involved myometrium. Subclinical accreta may be identified as basal plate myofibers (BPMF), which convey a potential risk of morbid adherence in future pregnancies (10,11). In the mildest recognized form, accreta may present with delayed 3rd stage of labor, while in the severest form - placenta percreta - it may erode abdominal structures and cause extensive hemorrhage. Placenta accreta is a common cause of postpartum hemorrhage, and it was recently suggested that it may also contribute to retroplacental bleeding during delivery, simulating clinical abruption (12).

Smooth muscle in the decidua of fetal membranes (membrane myofibers, MMF) in a delivered placenta was first illustrated in a report on occult placenta accreta in 2007 (3); but no information on gross findings or clinical manifestations has previously been published, and the entity has not found its way into textbooks. This report presents 52 collected cases of MMF, and suggests that it would be worthwhile for future systematic studies to be done on this clinicopathologic entity.

The prototypical clinical presentation occurs in cases of postpartum haemorrhage presumed to be due to retained placenta (13). Infrequently, however,

only amniochorial membranes are seen, even if all material was submitted for histology. In this report we document that smooth muscle in fetal membranes (MMF) may explain the finding of retained fetal membranes, as well as having other clinical manifestations – which we refer to collectively as Chorion Laeve Accreta (ChLA).

METHODS:

This is an observational descriptive study, which was approved by the Human and Ethics committees of all three institutions. It represents a merger of two sets of collections from the personal files of 2 individuals at separate institutions, guided by a coordinating pathologist. Between 2004 and 2017, cases were collected of curettages or evacuations following postpartum haemorrhage for presumed "retained placenta" (13). Placentas with MMF in membrane rolls were also collected, sometimes facilitated by immunostains for muscle markers. Hysterectomies with morbidly adherent fetal membranes were also included (5). All cases were from Women's and Children's Hospital, Adelaide, Australia, or Rochester General Hospital, Rochester, New York, USA.

In 2015 the coordinating pathologist initiated the process of merging the 2 collections. The collections were not the product of a retrospective search, by any set of standardized criteria. Indeed, the two collections had different types of cases, with partial overlap. While one collector had initially focused on curettages with retained fetal membranes, and the other had initially focused on morbidly adherent fetal membranes in hysterectomies; both had observed MMF as incidental findings in "routine" placentas, with no manifestations of morbid adherence. Although the collected placentas had a wide variety of presentations, the unifying feature of what we now term Chorion Laeve Accreta was abnormality noted in the course of placental

delivery and preliminary gross examination, by the obstetrician and/or the pathologist. The dividing line between incidental MMF and ChLA is that incidental MMF was only detected microscopically, with no clinical or gross manifestations. However, even incidental MMF could have a variety of associated pathologic abnormalities, and recurrence in a subsequent pregnancy, including cases requiring subsequent hysterectomy.

RESULTS

This collection from 52 patients included 10 patients with postpartum curettages, 36 placentas, and 6 hysterectomies. All told, only 12 cases of MMF were purely incidental findings on microscopic examination of routine placentas. Maternal ages ranged from 20 to 41 years, with both a mean of 30 years and also a median of 30 years.

Curettages

There were 11 curettages for postpartum bleeding from 10 patients, in which smooth muscle was seen in sections of fetal membranes (MMF). Such cases were seen at both institutions. Membranous tissues were obvious on gross examination in 6 cases. Histologic examination in all cases showed extraplacental membranes with varying degrees of necrosis and acute inflammation, dependent on the time interval between delivery and the post-partum curettage (Figure 1). In 4 curettage cases of MMF, BPMF were reported in the corresponding placentas. The remaining curettage cases had not been scrutinized or immunostained for enhanced detection of BPMF, sometimes because no placenta had been submitted. When curetted membranes were

too necrotic, hemorrhagic, and/or inflamed to detect MMF, re-examination of the original membrane roll was sometimes done, and MMF was thereby demonstrated.

In one woman, MMF was seen in a curettage that followed a spontaneous vaginal delivery associated with a retained placenta with BPMF. A curettage in her subsequent pregnancy was diagnosed as a hydatidiform mole, and had MMF detected with an immunostain for smooth muscle actin, documenting recurrence of ChLA. Another woman with MMF in a curettage for retained fetal membranes required a hysterectomy in a subsequent pregnancy for placenta increta, also associated with MMF; constituting another case of recurrent ChLA.

Placentas

There were 36 placentas with MMF detected in sections of fetal membranes (Figure 2a). The smooth muscle varied from tiny slender aggregates of MMF inside the decidua of fetal membranes, sometimes needing immunostains for confirmation or detection; to confluent plaques or nodules of MMF on the basal surface of decidua parietalis, easily seen on scanning magnification using only hematoxylin and eosin staining. MMF in fetal membranes was sometimes associated with decidual fibrinoid in fetal membranes, which is not a feature of normal fetal membranes.

Immunostains for both actin and desmin had been used to confirm the smooth muscle (Figures 2b,c). Immunostains for keratin (Figure 2d) showed that membrane rolls from placentas with MMF shared the dilated endometrial gland remnants and infiltrative chorion formerly demonstrated in morbidly adherent fetal membranes from hysterectomies for increta (5). Muscle was more conspicuous on actin stains than on desmin stains. Actin stains showed endometrial gland remnants enveloped by muscle, not as clearly apparent on desmin stains; so the MMF were not merely

"adherent". Keratin-positive infiltrative chorion was seen inside the region of MMF, a finding not previously demonstrated (5). No double immunostains had been done, since this is not routine practice at either institution.

Basal plate myometrial fibers were reported in 20 of the placentas. One woman had a preceding placenta with BPMF, while another woman had a subsequent hysterectomy for placenta increta, with MMF, providing an example of recurrent MMF, which had progressed to ChLA. The other placentas had not been scrutinized for BPMF.

In 4 placentas with ChLA, grossly detectable nodules were seen in the membranes by the obstetrician and/or the pathologist: one 0.6 cm nodule composed of confluent dilated endometrial gland remnants, one 3.7 cm endometrial stromal nodule; one 2.5 cm piece of myometrial tissue; and one 4.5 cm portion of decidua parietalis with prominent endometrial gland remnants and microscopic MMF inside the decidua, best seen with immunostains. In 4 other placentas with MMF, there were microscopic subchorionic fibrous nodules (Figure 3), a lesion first identified at the placenta margin in a hysterectomy for placenta percreta (12). Grossly detected membrane hematoma was seen in 2 cases at the site of MMF, and membrane hemosiderin was seen at the site of MMF in 2 cases. Five placentas had retroplacental haemorrhage seen on the H&E slides, and/or separate blood clots in the specimen containers, with both MMF and BPMF on microscopic examination.

Hysterectomies

Six hysterectomies had morbidly adherent fetal membranes. Myometrium attached to the decidua of fetal membranes allowed the uterus to be lifted off the dissecting table via a clamp on the fetal membranes (5). Five had placenta increta. In

one case, the obstetrician observed fetal membranes adherent to the uterus and did a curettage for retained fetal membranes, before proceeding to hysterectomy. Another case had recurrent MMF, since a placenta from 15 years previously had both BPMF and MMF, documenting progression from incidental MMF to ChLA. The sixth hysterectomy was performed soon after delivery (with no placenta submitted), at the patient's request, for postpartum recurrence of chronic pelvic pain; and adherent fetal membranes were grossly obvious, consistent with ChLA (Figure 4).

DISCUSSION

Membrane myofibers (MMF) in a delivered placenta were first illustrated in 2007 (3). In 2016, association of MMF with physical adherence was demonstrated by lifting the hysterectomy specimen off the dissecting table with a clamp on the fetal membranes (5). In hindsight, MMF in hysterectomies resembles MMF in placentas. Actin stains previously demonstrated myometrial degeneration in morbidly adherent fetal membranes (5). As noted in basal plate myofibers (BPMF)(5,12); MMF could either be on the basal surface of decidua parietalis (appearing to be merely adherent); or higher up in the decidua (near dilated endometrial gland remnants).

Keratin stains previously showed association of dilated endometrial gland remnants with infiltrative chorion in morbidly adherent fetal membranes (5). Infiltrative trophoblast is a marker for protease activity (6). Dilated endometrial gland remnants reflect the maternal-fetal dialogue during implantation; when the glands secreted glycogen before endovascular trophoblast was seen in the myometrium (7,8,12,14,15).

Although standard teaching emphasizes association of accreta with decidual deficiency, it was observed in 1987 that MMF in a hysterectomy for increta manifested no decidual deficiency (1). This was also illustrated in delivered placentas with MMF in 2007 (3), and in morbidly adherent fetal membranes in 2016. (5). In addition, the latter paper showed greater dilation of endometrial gland remnants and more infiltrative chorion, when a hysterectomy (after surgically corrected uterine inversion and placental delivery) had retained fetal membranes (5). Also in contrast to placenta accreta, the average age of 30 in these 52 patients would not be considered advanced maternal age.

Association of decidual fibrinoid with infiltrative chorion was also described in morbidly adherent fetal membranes (5). More infiltrative chorion was associated with more prominent fibrinoid (5). The present study confirmed this in delivered placentas with MMF. Normal placentas do not have fibrinoid in decidua parietalis.

Although obstetricians know that retained fetal membranes can lead to infection with hemorrhage, the pathology of retained fetal membranes was not previously illustrated. When retained membranes are necrotic, inflamed and hemorrhagic (Figure 1), re-examination of the membrane roll in the delivered placenta can demonstrate MMF. ChLA can explain retained membranes after postpartum haemorrhage, with no infection.

This report demonstrates that incidental MMF, like BPMF (10,11), can recur. In addition, MMF can progress to clinically manifest Chorion Laeve Accreta. The rate of MMF recurrence and progression may be underestimated in this report.

Clinical morbid adherence may be associated with membrane hematomas (4). The current report suggests that membrane hematomas and membrane hemosiderin may be at the site of MMF. It also documents association of MMF with diverse membrane nodules – including an endometrial stromal nodule (16), a nodule composed of confluent dilated endometrial gland remnants, and subchorionic fibrous nodules (Figure 3).

Morbid adherence can prolong placental delivery and result in retained placenta, so it has been suggested that retroplacental blood may collect behind part of the placenta while another part remains morbidly adherent (12). This report documents association of MMF with prolonged 3rd stage of labor.

Other clinical presentations of MMF include observation of adherent membranes during delivery, disrupted and incomplete membranes in submitted placentas, and association with grossly adherent pieces of myometrium or decidua parietalis.

MMF appears to be the amniochorial membrane equivalent of BPMF. Although MMF in this collection was less common than BPMF in routine practice, this collection does not address the prevalence of MMF. Although many cases of MMF had associated BPMF, the rate of association may be underestimated. "Routine" placentas with both incidental MMF and BPMF sometimes lacked any clinical or gross evidence of morbid adherence. It remains to be evaluated how often MMF is a marker for clinical accreta.

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Figure legends:

Figure 1 – Whole mount image of retained partly necrotic, hemorrhagic extraplacental membranes in a curettage for postpartum bleeding. 1x.

Figure 2 – The amniotic cavity is at the top of each image.

Fig2A- Smooth muscle subjacent to chorion laeve in extraplacental membranes in a placenta. 4x. Hematoxylin and eosin shows smooth muscle (arrow) that can be missed on routine scanning examination. a = amnion, c = chorion, d = decidua.

Fig2B - Desmin immunostain makes the muscle obvious, but is less prominent or informative than actin stain. 4x. A dilated endometrial gland remnant appears as negative image above the muscle (arrow). a = amnion, c = chorion, d = decidua

Fig2C - Smooth muscle actin immunostain shows that the endometrial gland remnant (arrow) is actually inside the muscle. 4x. a = amnion, c = chorion, d = decidua

Fig 2D - Keratin immunostain shows the same undulating chorion seen in morbidly adherent fetal membranes in hysterectomies for increta (5). 4x. Note that the keratin-positive infiltrative chorion near the endometrial gland remnant in the decidua (arrow) is in the zone of muscle shown in Figure 2C .. a= amnion, c = chorion, d = decidua

Figure 3 – Subchorionic fibrous nodule is in the decidua of fetal membranes, beneath the chorion. 10x. It includes an endometrial gland remnant (arrow). Trichrome stain. All such nodules seen to date have associated MMF. a= amnion, c = chorion, d = decidua. The amniotic cavity is to the left in the image.

Figure 4 – Gross photograph of retained fetal membranes (arrow) in a delayed postpartum hysterectomy for recurrent chronic pelvic pain. The placenta was not sent. All prior reported hysterectomies with MMF have increta, some classified as early increta (5).

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