Isolated acute funisitis in the absence of acute chorioamnionitis: What does it mean?

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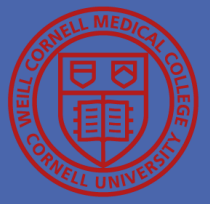

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Background

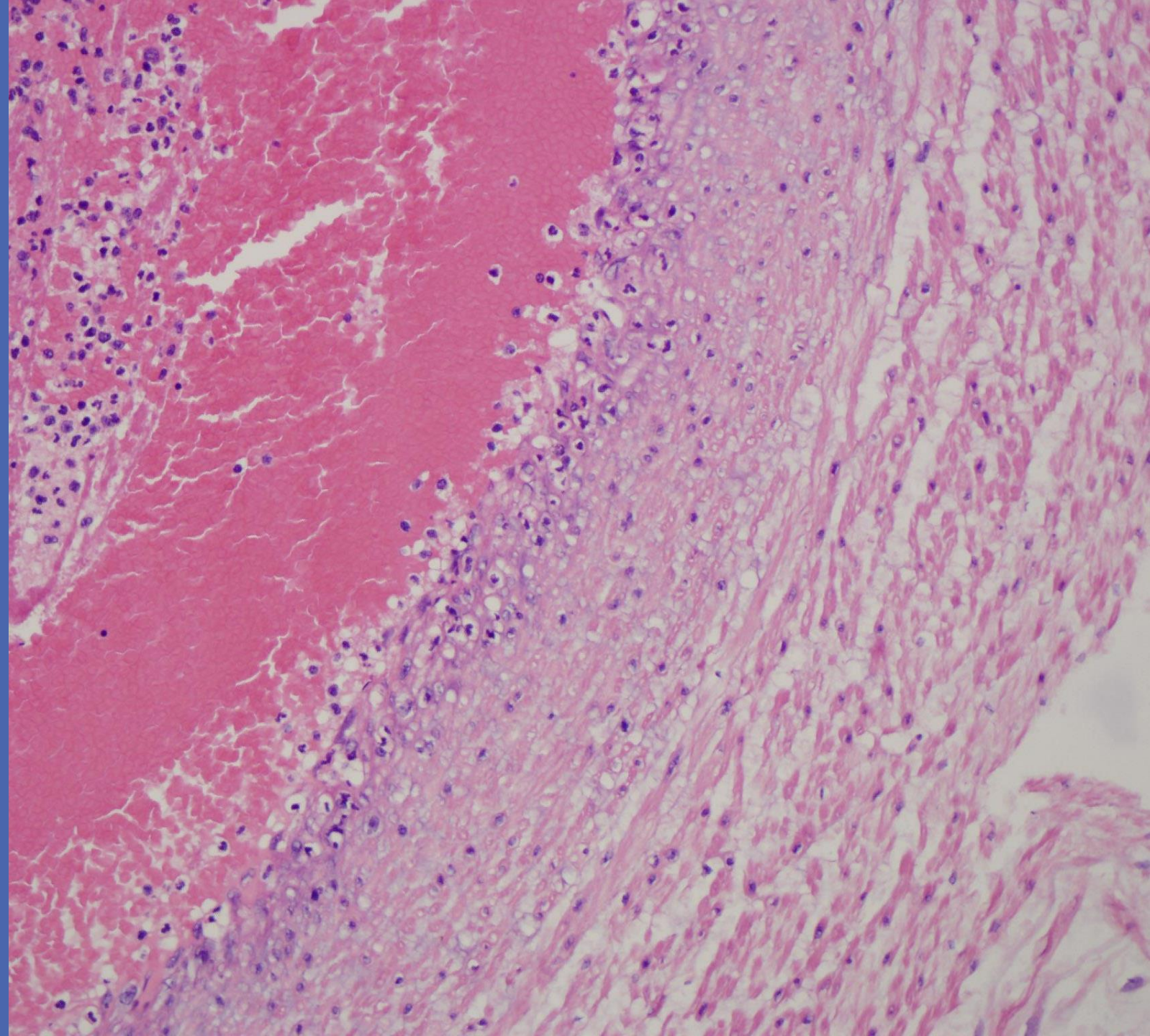
- A uniform sampling criteria, placental growth descriptors, pathology terminologies and diagnostic criteria have been developed to allow us to more consistently and objectively describe placental lesions (1,2).tr
- **Acute chorioamnionitis** (AC) is the most frequent diagnosis in placental pathology reports (3-5)
- AC with **acute funisitis** (AF) are considered part of the inflammatory response to ascending intra-amnionitic infection (3,6)
- Intrauterine infection is associated with:
  - Preterm birth
  - Intrauterine growth restriction
  - Intrauterine fetal demise
  - Preterm rupture of membranes
  - Cervical insufficiency
  - Neonatal sepsis
  - Neonatal ICU admission
  - Long-term neurodevelopmental injury (3,7-10)

Background

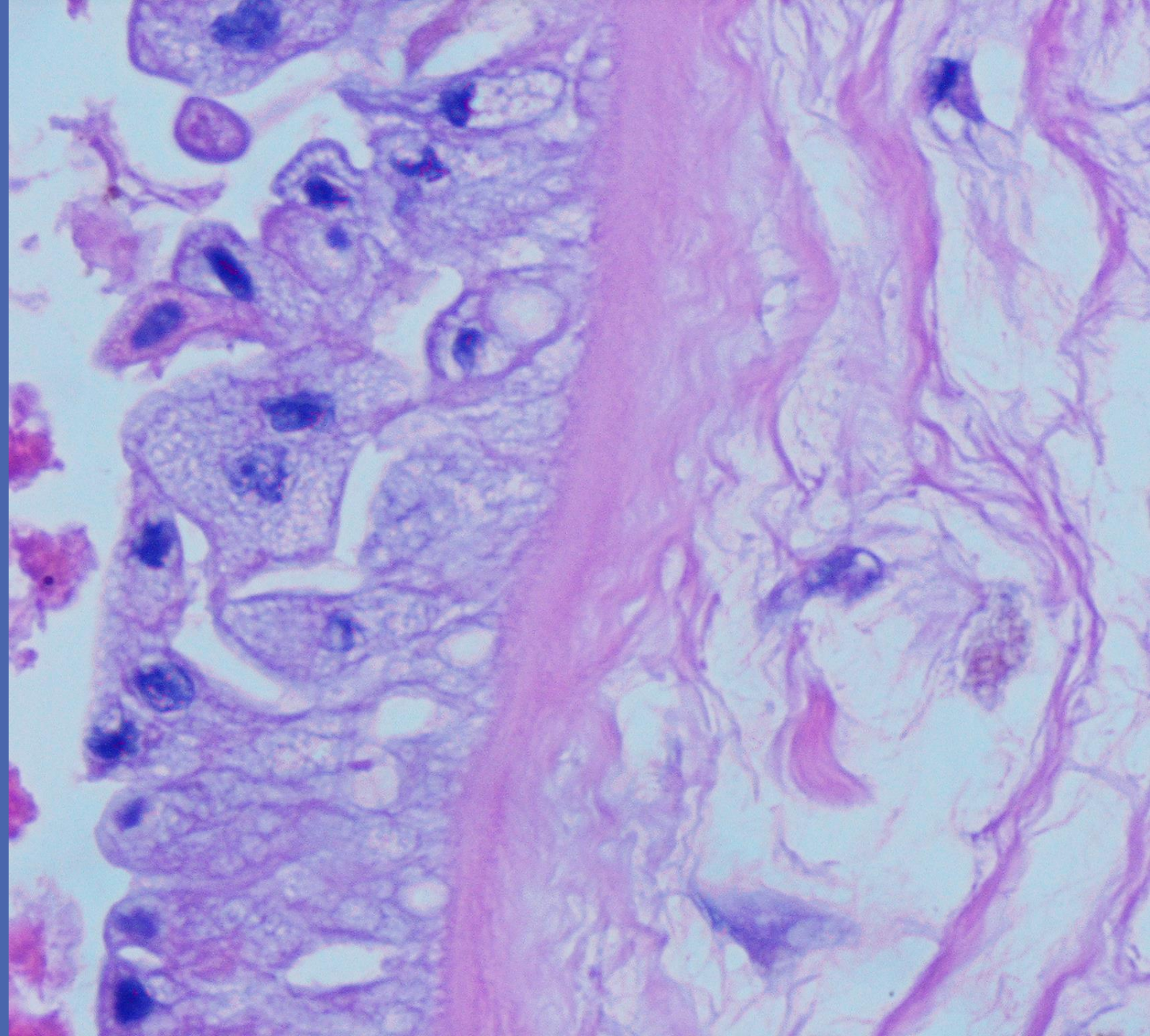
- However, acute and chronic inflammation is found in up to ¼ of placentas in normal pregnancies with normal outcomes (11-14)
- Infection/inflammation does not always result in a poor outcome

- **Meconium** is also associated with increased perinatal morbidity and morality (15,16) and poor long-term neurologic outcome (17)
- When intrauterine **infection** and **meconium** are **both present**, it is unclear whether meconium is a fetal response to infection or if the presence of meconium makes for a more hospitable environment for bacteria → infection

Acute funisitis, medium power



Meconium-stained membranes, high-power



Objective

- When a placenta demonstrates both AC and AF, it can be assumed that a progressive infectious process has occurred
- But, what is not clear: the significance of **AF without AC**.
- The objective of our study: to evaluate clinical and pathologic features of cases of **isolated AF** to determine how it can contribute to our understanding of adverse clinical outcomes.

Methods

- Surgical pathologic database at our hospital – searched for 3rd trimester placentas from 1997 – 2017
- Placental reports reviewed by one of the authors (placental pathologist)
- Cases: placentas with AF without AC
- Controls: without diagnosis of AF or AC
- Collected data: GA at delivery, mode of delivery, diagnosis of IUGR, IUFD, placental weight, birthweight, Apgar scores

Histopathologic findings

- The following histopathologic findings were examined: cord complications, meconium (and location of meconium), lesions associated with fetal vascular malperfusion (FVM), and lesions associated with maternal vascular malperfusion (MVM)

- Categorical variables compared using Chi square analysis
- Continuous variables compared using student t-test

Results

- 181 controls (no AC or AF)
- 156 cases (isolated AF)
- Median maternal age: 33 yrs (30-370
- Median GA delivery: 39wks (38-40)
- Median birthweight: 3270g (2891-3629)
- Median placental weight: 450g (378-518)

Table 1: Demographics

	No funisitis (controls) N = 181	Isolated funisitis N = 156	p-value	CI (95%)
Maternal age (yrs)*	34 [31 – 37]	33 [29 – 36.75]	.090	-.164 – 2.224
Gestational age at delivery (weeks)*	39 [38 – 40]	39 [39 – 40]	.259	-.194 - .718
Neonatal gender			0.126	
Male	89 (51.1%)	82 (59.9%)		
Female	85 (48.9%)	55 (40.1%)		

* Results presented as median [interquartile range]

Table 2: Delivery and fetal outcomes

	No funisitis (controls) N = 181	Isolated funisitis N = 156	p-value	CI (95%)
Mode of delivery			0.638	
Vaginal delivery	74 (41.3%)	57 (38.8%)		
Cesarean delivery	105 (58.7%)	90 (61.2%)		
Fetal outcomes				
IUGR	20 (11.0%)	6 (3.8%)	.014	
IUFD	1 (0.6%)	7 (4.5%)	.027	
Birthweight (grams)*	3205 [2816.5 – 3607.5]	3410 [3070 – 3696]	.054	-273.687 – 2.455
Placental weight – (grams)*	441 [370 – 500]	460 [390 – 550]	.034	-48.819 - 1.907

* Results presented as median [interquartile range]

Table 3: Histopathologic findings

	No funisitis (controls) N = 181	Isolated funisitis N = 156	p-value
Meconium- any location	70 (38.7%)	132 (84.6%)	<.001
Meconium in membranes	69/70 (98.6%)	62/132 (47.0%)	
Meconium in cord	1/70 (1.4%)	36/132 (27.3%)	
Myonecrosis	-	34/132 (25.6%)	
Maternal vascular malperfusion	58 (32.0%)	46 (29.5%)	<.001
Fetal vascular malperfusion	19 (10.5%)	20 (12.8%)	.027
Cord complications	58 (32.0%)	37 (23.7%)	<.001

Discussion

- There was a clear and significant increase in presence of meconium in cases of isolated IF vs controls
- This was especially true with presence of meconium in the cord and associated myonecrosis
- It may be that IF most commonly occurs as a result of damage to the cord and/or the muscle fibers of the cord from meconium, rather than ascending infection

Discussion

- Damage to the cord from inflammation and/or meconium, would explain the increase in GVM lesions in isolated IF group
- This may also explain increased IUFD in insolated IF group

- Why smaller placentas, more IUGR and more cord complications and MVM in controls? Selection bias – placentas only submitted when there is a concerning maternal and/or fetal finding

Study strengths & weaknesses

- Major strength: We separated cases of AF in the absence of AC to examine outcomes related to **funisitis in isolation** (most studies combine these lesions)
- Weaknesses: sample size is relatively small – some differences between groups may not be able to be identified
- Control group may not represent a control population, because not all placentas routinely submitted to pathology

Conclusions

- Isolated funisitis is highly associated with the presence of meconium and meconium-associated myonecrosis of umbmilical vessels.
- The inflammation in isolated funisitis may be the result of damage to the muscle fibers of the cord due to meconium
  - Additional studies are necessary to understand the significance of these findings.

Future studies

- We hope to perform larger studies to enable us to compare cases of isolated AF with cases that exhibit both AF and AC, as well as with controls
- Antepartum and intrpartum clinical indicators that are associated with IF may hopefully be identified and with further study, enable greater understanding of this lesion

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