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

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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).

- **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

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

* Results presented as median [interquartile range]
Table 2: Delivery and fetal outcomes

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Mode of delivery</td>
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<tr>
<td>Vaginal delivery</td>
<td>74 (41.3%)</td>
<td>57 (38.8%)</td>
<td>0.638</td>
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<tr>
<td>Cesarean delivery</td>
<td>105 (58.7%)</td>
<td>90 (61.2%)</td>
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<td></td>
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<tr>
<td>Fetal outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IUGR</td>
<td>20 (11.0%)</td>
<td>6 (3.8%)</td>
<td>.014</td>
<td>-273.687 – 2.455</td>
</tr>
<tr>
<td>IUFD</td>
<td>1 (0.6%)</td>
<td>7 (4.5%)</td>
<td>.027</td>
<td></td>
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</tbody>
</table>

* Results presented as median [interquartile range]
Table 3: Histopathologic findings

<table>
<thead>
<tr>
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<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meconium- any location</td>
<td>70 (38.7%)</td>
<td>132 (84.6%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Meconium in membranes</td>
<td>69/70 (98.6%)</td>
<td>62/132 (47.0%)</td>
<td></td>
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<tr>
<td>Meconium in cord</td>
<td>1/70 (1.4%)</td>
<td>36/132 (27.3%)</td>
<td></td>
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<tr>
<td>Myonecrosis</td>
<td>-</td>
<td>34/132 (25.6%)</td>
<td></td>
</tr>
<tr>
<td>Maternal vascular</td>
<td>58 (32.0%)</td>
<td>46 (29.5%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>malperfusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fetal vascular</td>
<td>19 (10.5%)</td>
<td>20 (12.8%)</td>
<td>.027</td>
</tr>
<tr>
<td>malperfusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cord complications</td>
<td>58 (32.0%)</td>
<td>37 (23.7%)</td>
<td>&lt;.001</td>
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</tbody>
</table>
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 umbilical 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 intrapartum clinical indicators that are associated with IF may hopefully be identified and with further study, enable greater understanding of this lesion
References


