Placental investigation: patterns and clinical outcomes

Raymond W. Redline
Case Western Reserve University
Cleveland OH, USA
Maternal supply line: the “extended” placenta
Failure of Arterial Remodeling

Brosens, Robertson, Dixon, Pijnenborg, Khong

Persistent muscularization of basal plate arteries
Maternal vascular malperfusion
BIPHASIC VILLOUS ARCHITECTURE IN MATERNAL MALPERFUSION
Global/ partial obstruction: accelerated villous maturation

- Paucity
- Increased syncytial knots
- Agglutination
- Increased intervillous fibrin
Area of paucity >40% = Distal villous hypoplasia
correlates with absent end-diastolic flow by doppler
Segmental/ complete obstruction: villous infarction
Decidual Arteriopathy

Mural Hypertrophy

Chronic perivasculitis

Atherosis
Maternal vascular: loss of integrity
(retroplacental hemorrhage)

Spiral arteries:
Abruptio placenta

Decidual veins:
Marginal abruption

Spiral arteries:
Abruptio placenta
Findings consistent with Abruptio Placenta

Predisposing factors:
- Preeclampsia, vasoactive drugs, trauma

Presentation:
- vaginal bleeding, uterine rigidity,
- abdominal pain, hypotension

Pathogenesis:
- Ruptured spiral artery:
  - sheer stress or ischemia-reperfusion

Adverse outcomes:
- Preterm delivery
- Neurodisability
- IUFD
Acute peripheral separation/ Marginal abruption

Distended marginal vein

Predisposing factors:
- Low implantation, PROM,
- chorioamnionitis

Presentation:
- Vaginal bleeding,
- Precipitous delivery

Pathogenesis:
- Abnormal marginal anatomy
- Inflammation of marginal decidua

Adverse Outcomes:
- Preterm delivery

Marginal retroplacental hemorrhage
Chronic abruption/ peripheral separation

Predisposing factors:
- multiparity, abnormal implantation

Presentation:
- chronic vaginal bleeding,
- oligohydramnios

Pathogenesis:
- abnormal marginal anatomy

Outcomes:
- Preterm delivery
- FGR

Circumvallation and green staining

Chorioamnionic hemosiderosis
Clinical consequences of maternal vascular/ trophoblastic lesions

Symptoms:
- preeclampsia
- impaired fetal growth
- abnormal doppler studies
- oligohydramnios
- pregestational diabetes
- obesity
- thrombophilia

Outcomes:
- Fetal growth restriction (FGR)
- Preterm delivery (PTD)
- Abruptio placenta
- IUFD
- CNS injury
- Long term cardiovascular risk

Recurrence risk:
5-10%
Fetal stromal vascular placenta: umbilical cord, chorionic plate, villous stroma
Fetal stromal vascular placenta: proximal and distal villi
Normal vasculo-syncytial membranes
Normal term villi

Delayed villous maturation
Delayed villous maturation

(AKA distal villous immaturity/ maturation defect)

Pathology:
- Increased villous stroma with central capillaries
- Thick trophoblast layer lacking vasculo-syncytial membranes
- Placentomegaly with decreased fetoplacental weight ratio

Associations:
- Diabetes (increased fetal insulin)
- Maternal obesity
- UC obstruction
- IUFD
- Subset of FGR

Physiology:
- Increased demand (increased fetoplacental mass)
- Decreased placental function (increased diffusion distance)
Fetal stromal-vascular maldevelopment: fetal villous capillary lesions

• Chorangioma (single/multiple) (1-2% of all placentas)
• Chorangiosis (5-10% of term placentas)
• Multifocal chorangiomatosis (<1% of all placentas)
Villous chorangiosis

**Definition:** 10 capillaries/villus in > 10 villi several different areas (some with 15-20 capillaries)

**Pathophysiology:** Angiogenic GF response to excessive glucose or hypoxemia

**Clinical:** High altitude, smoking, excessive air pollution, maternal anemia, diabetes
Chorangioma
(placental hemangioma)

• GA: 32-36 weeks

• Increased in:
  – Multiple pregnancies
  – Preeclampsia

• Possible genetic predisposition

• Complications (rare):
  • Sequestration of platelets
  • A-V shunt with hydrops
  • Fetal growth restriction
**Multifocal chorangiomatosis**

**Pathology:** Multiple foci of excessive capillary growth affecting immature intermediate and stem villi

**Pathogenesis:** Adaptive response to oxygen deprivation and reduced fetal blood flow
FETAL VASCULAR MALPERFUSION BY SITE

Global/ partial:
Chronic partial intermittent UC obstruction

Segmental/ complete:
Fetal thrombosis
Stem vessel obliteration
Avascular villi/ Villous stromal Vascular karyorhhexis

Fetal blood flow

UMBILICAL CORD
CHORIONIC PLATE
PROXIMAL VILLI
DISTAL VILLI

Courtesy of Theonia Boyd, Boston Children's Hospital
Fetal vascular malperfusion

• **Global/ partial-intermittent: fetal-umbilical vessels**
  • Venous dilation, chorionic/ stem villi
  • Intramural fibrin deposition, recent or remote
  • Scattered small foci, avascular villi and/or stromal vascular karyorhexis

• **Segmental/ complete: chorionic-proximal villous vessels**
  • Chorionic/ stem villous thrombi
  • Stem vessel obliteration (fibromuscular sclerosis/ loss of lumina)
  • Large foci, avascular villi and/or stromal vascular karyorhexis
Global/ partial-intermittent: obstructive UC lesions

Dilated veins, chorionic plate (diameter > 4x artery)
Intramural fibrin deposition ("intimal fibrin cushions")
chorionic plate or large stem villi

Recent

1. Increased fetal venous pressure - ? UC occlusion
2. ? Old thrombi incorporated into vessel wall
3. ? Fibrin or myofibroblast-derived matrix

Remote
Scattered small foci of avascular villi
Fetal vascular malperfusion

• Global/ partial-intermittent: fetal-umbilical vessels
  • Venous dilation, chorionic/ stem villi
  • Intramural fibrin deposition, recent or remote
  • Scattered small foci, avascular villi and/or stromal vascular karyorhexis

• Segmental/ complete: chorionic-proximal villous vessels
  • Chorionic/ stem villous thrombi
  • Stem vessel obliteration (fibromuscular sclerosis/ loss of lumina)
  • Large foci, avascular villi and/or stromal vascular karyorhexis
Segmental/ Complete: Large Vessel Thrombi
Secondary lesions: stem vessel obliteration, (fibromuscular sclerosis and loss of lumina)
Secondary lesions: distal villi (avg >15/ slide = FTV)

Large foci of hyalinized avascular villi

Sander 1980

Villous stromal vascular karyorrhexis

Redline 1994

Large foci of hyalinized avascular villi
Clinical consequences of fetal stromal-vascular/lesions

Presentation:
- UC entanglement, ↓ fetal movement, abnormal BPP/NRFHR, gestational diabetes, obesity

Outcomes:
- IUFD, CNS injury, less commonly FGR

Recurrence risk:
- Low, with rare exceptions
Acute Chorioamnionitis

Pathogenesis: Infection: *ascending*, hematogenous, contiguous

Predisposing factors: ROM, Abnormal cervix, Pathogenic flora

Presentation: PTL, PROM, Fever, ↑ WBC
Histologic Chorioamnionitis
Maternal Inflammatory Response

Stage = Duration
1. Subchorionitis/ chorionitis
2. Chorioamnionitis (amnion + chorion)
3. Necrotizing chorioamnionitis (>25% amniocytes)

Grade = Intensity
1. Mild-moderate (subchorionic PMN)
2. Severe (subchorionic PMN abscesses)

Redline et al, Pediatr Devel Pathol 2003
Early acute subchorionitis (Maternal Stage 1/3)

*Diffuse infiltration of neutrophils from intervillous space into subchorionic fibrin

*chorionic plate and amnion-negative
Acute chorioamnionitis (stage 2)
Necrotizing acute chorioamnionitis (Maternal Stage 3/3)

*Neutrophil karyorrhexis
*amniocyte necrosis
*amnion BM thickening/eosinophilia
Severe acute chorioamnionitis (subchorionic microabscesses, Maternal Grade 2/2)

Membranes

Chorionic plate

Confluent Neutrophils (> 20 cells in max extent) below chorion
Histologic Chorioamnionitis

Fetal Inflammatory Response

Stage = f (Duration x Fetal Maturity)
  1. Chorionic Vasculitis/ Umbilical Phlebitis
  2. Umbilical Arteritis
  3. Concentric Umbilical Perivasculitis

Grade = Intensity (chorionic vessels)
  1. Mild-Moderate (PMN)
  2. Intense (confluent PMN)
Umbilical phlebitis (Fetal Stage 1/3)

Umbilical arteritis (Fetal Stage 2/3)
Concentric umbilical perivasculitis
(Fetal Stage 3/3)

Neutrophils (+ associated debris) in concentric bands-halos around one or more umbilical vessels
Severe chorionic vasculitis (Fetal Grade 2/2)

Confluent-near confluent intramural neutrophils in chorionic vessels with degenerative changes in VSMC
Chronic Villitis

Definition: Lymphocytes and increased macrophages in placental villi

Subtypes:

- Chronic villitis, infectious
- Chronic villitis, idiopathic

(AKA “villitis of unknown etiology” = VUE)
Chronic villitis (idiopathic) = graft versus host reaction

Fetoplacental Antigens

Maternal Immune Response

Maternal T cells
(Blue with two X-chromosome signals)
Chronic villitis: idiopathic/ (“VUE”)
Classification scheme

Location: Basal/ Parenchymal/ Both

Extent: Low Grade (<10 villi/ focus) focal: > 1 focus, 1 slide
        multifocal: >1 slide
        High Grade (>10 villi/ focus) patchy: >1 focus
diffuse: >5% of all villi

Associated lesions: decidual plasma cells
extensive perivillous fibrin
fetal vascular involvement

Kraus et al, 2004
Low grade VUE

High grade VUE

≤10 villi/ focus

> 10 villi/ focus
High Grade VUE involving fetal vessels

Obliterative fetal vasculopathy
Avascular distal villi
## Cerebral Palsy at Term vs. Placentas Routinely Submitted to Pathology Department

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>N=</td>
<td>205</td>
<td>250</td>
<td>100</td>
</tr>
<tr>
<td>Fetal malperfusion: global/partial</td>
<td>32(16)</td>
<td>11(4)</td>
<td>5(5)</td>
</tr>
<tr>
<td>Meconium associated vascular necrosis</td>
<td>28(14)</td>
<td>8(3)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Fetal malperfusion: segmental/complete</td>
<td>24(12)</td>
<td>6(2)</td>
<td>0(0)</td>
</tr>
<tr>
<td>VUE, high grade</td>
<td>23(11)</td>
<td>7(3)</td>
<td>3(3)</td>
</tr>
<tr>
<td>Histologic ACA, severe fetal response</td>
<td>10(6)</td>
<td>8(3)</td>
<td>1(1)</td>
</tr>
<tr>
<td>Meconium, without vascular necrosis</td>
<td>73(36)</td>
<td>--</td>
<td>29(29)</td>
</tr>
<tr>
<td>Histologic ACA, mild-mod fetal response</td>
<td>26(13)</td>
<td>15(6)</td>
<td>16(16)</td>
</tr>
<tr>
<td>Maternal malperfusion</td>
<td>23(11)</td>
<td>34(14)</td>
<td>6(6)</td>
</tr>
<tr>
<td>VUE, low grade</td>
<td>13(6)</td>
<td>10(4)</td>
<td>8(8)</td>
</tr>
<tr>
<td>Chronic abruption</td>
<td>8(4)</td>
<td>7(3)</td>
<td>1(1)</td>
</tr>
</tbody>
</table>

Redline, 2008