Placental Pathology in Adverse Perinatal Outcome

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Outline

- Goals of a placental pathologic examination
  - What the placenta can and can’t tell you

- Indications for placental examination
  - Maternal
  - Fetal/neonatal
  - Placental

- Placental storage prior to examination

- Overview of placental examination
  - Gross
  - Microscopic

- Examples of placental pathology in obstetric complications and adverse perinatal outcome
Goals of a placental examination

- Placenta: diary of intrauterine life
- Diagnostic of abnormalities:
  - Pregnancy
  - Labor
  - Infant
- Prognostic
- Medicolegal
Indications for placental examination

- Maternal disease
  - Systemic disorders
    - Hypertensive disorders (chronic, gestational, preeclampsia)
    - Diabetes (pregestational, gestational)
    - Collagen vascular disease
    - Severe anemia
  - Premature delivery <34 weeks
  - Peripartum fever/infection
  - Unexplained bleeding
  - Clinical concern for infection during pregnancy (HIV, CMV)
  - Unexplained pregnancy complication
    - IUHR
    - Stillbirth
  - Abruption
  - Severe oligohydramnios

- [**C-section: not an indication for placental examination**]

Langston et al., Arch Pathol Lab Med 1997; 121:449-76.
Indications for placental examination

- Fetal/neonatal conditions
  - Admission to NICU
  - Stillbirth/perinatal death
  - IUGR
  - Hydrops fetalis
  - Major congenital abnormalities/dysmorphic features/abnormal karyotype
  - Twins
    - Discordant twin growth (>20%)
    - Fused twin placenta with same sex twins (?monochorionicity?)
  - Compromised clinical condition:
    - Apgar score <6 at 5 minutes
    - Cord blood pH<7.0
    - Ventilatory assistance >10 minutes
    - Severe anemia (Hct<35%)

Langston et al., Arch Pathol Lab Med 1997; 121:449-76.
Indications for placental examination

- Placental abnormalities (any gross abnormality or unusual appearance)
- Umbilical cord
  - Too short (<35 cm) or too long (>100 cm)
  - True knot
  - Thrombosis
  - Marginal/velamentous insertion
- Membranes
  - Discoloration
- Disc
  - Too small or too big
  - Mass
  - Infarct

Langston et al., Arch Pathol Lab Med 1997; 121:449-76.
Placental storage prior to examination

- Store for at least 3 days (recommended: 7 days) after birth, refrigerated
  - **Do not freeze: introduces artifact**
  - Cultures: sterile swab of fetal surface (under amnion)
  - Karyotype: tissue from fetal surface
    - **superior to fetal tissue in the setting of stillbirth**

- Pathology requisition sheet
  - Gestational age, route of delivery
  - Infant weight, sex, Apgars at 1 & 5 minutes
  - Indication for placental examination
    - Any specific question for pathologist
Placental exam: general

- Umbilical cord
  - length
  - insertion
  - # vessels
  - twist

- Membranes
  - insertion
  - color

- Disc
  - weight & dimensions
  - lesions (maternal and fetal surface)
Umbilical cord

1. Photograph
2. Note cord insertion
3. Measure length
4. Note twist
5. Note # vessels
6. Cut representative sections to fix
Umbilical cord
Membranes

1. Insertion
2. Color
3. Jelly roll
Membranes
Placental disc

1. Cut disc at 1.0 inch intervals
2. Evaluate for lesions
3. Fix and sample
Placental disc
EXAMPLES OF PLACENTAL PATHOLOGY IN OBSTETRIC COMPLICATIONS AND ADVERSE PERINATAL OUTCOME
Amniotic fluid infection

- **Clinical presentation:**
  - Maternal fever during labor (clinical chorioamnionitis)
  - Neonatal distress
    - Respiratory distress
    - Sepsis

- **Pathologic correlate:**
  - Histologic chorioamnionitis
  - Staging: I/II/III (**does not correlate with clinical severity**)
  - Are fetal vessels affected?
Chorioamnionitis
Chorioamnionitis

- **Stage I (subchorionitis):** just under the chorion
  - Seen in many cases with GBS
- **Stage II (chorionitis):** inflammatory cells in the chorion
- **Stage III (chorioamnionitis):** inflammatory cells above the chorion/under the amnion
- “Necrotizing” chorioamnionitis
Fetal vasculitis: funisitis
Funisitis: Candida
Chorioamnionitis: fetal vasculitis

- **Fetal vasculitis**
  - Chorionic plate
  - Stem vessel
  - Umbilical cord

- **Funisitis**
  - Inflammatory cells in the Wharton’s jelly
  - **Do PAS-fungus stain on all preterm cases to rule out Candida**
Examples of placental reports

- **Term placenta:**
  - Mature placenta
  - Chorioamnionitis
  - Umbilical cord and chorionic plate vasculitis

- **Preterm placenta:**
  - Immature placenta
  - Chorioamnionitis
  - Funisitis (PAS stain is negative for fungal microorganisms)
Hypertensive diseases of pregnancy

- Gestational hypertension
- Pre-eclampsia
  - Mild (late-onset)
  - Severe (early-onset)
- HELLP
- Associated complications
  - Abruption
  - IUGR
- Placenta: usually small (disc weight <10th percentile for gestational age)
Trophoblastic remodeling of maternal vessels

Before…

…After
Abnormal remodeling of maternal vessels

- **Decidual vasculopathy**
  - Thickening of maternal vessel wall
  - Fibrinoid necrosis
  - Chronic inflammation

- **Atherosis**
  - Macrophage infiltration of vascular wall
“Hypermature” placenta

- Increased syncytial knots
Infarct
Intervillous fibrin
Abruption
(retroplacental hemorrhage)
Abruption (retroplacental hemorrhage) with attenuation of underlying parenchyma
Abruption
(retroplacental hemorrhage)

(with associated infarct)
Abruption
(retroplacental hemorrhage)

(intravillous hemorrhage)
Example of placental report

- Small hypermature placenta (250 g, <10\textsuperscript{th} percentile for gestational age, with increased syncytial knots)
- Decidual vasculopathy
- Multiple central infarcts
Example of placental report

- Small mature placenta (320 g, <10\textsuperscript{th} percentile for gestational age)
- Decidual vasculopathy
- Retroplacental hematoma (see COMMENT)

COMMENT: The findings are consistent with the clinical diagnosis of placental abruption.
Intrauterine growth restriction

- Multifactorial
- Placental causes
  - Preeclampsia (severe, early-onset)
  - Chronic villitis (of unknown etiology)
    - Sometimes associated with perivillous fibrin deposition
  - Fetal thrombotic vasculopathy
Placental disc: microscopic lesions: chronic villitis

- Chronic villitis
  - TORCH (minority)
    - CMV (inclusions)
    - Syphilis (perivascular onion skinning)
    - Toxoplasmosis (cysts in Wharton’s jelly)
  - **Unknown etiology** (majority)
    - Immune-mediated
Example of placental report

• **Small mature placenta** (250 g, <10\(^{th}\) percentile for gestational age)

• **Chronic villitis**, extensive (see COMMENT)

• **COMMENT**: There is extensive inflammation in the chorionic villi; special stains (Gram, Giemsa, PAS-fungus) are negative. These findings are consistent with villitis of unknown etiology (VUE), which is the likely cause of IUGR in this case. VUE can recur in up to 50% of subsequent pregnancies.
Placental disc: microscopic lesions: fetal thrombotic vasculopathy
Fetal surface: Thrombosis of chorionic plate vessels
Fetal surface:
Thrombosis of chorionic plate vessels
Fetal thrombotic vasculopathy

- Massive, associated with thrombosis of large fetal vessels
  - Maternal/fetal coagulopathy
- Multifocal/regional
  - Preeclampsia
  - Diabetes
  - Secondary to inflammation
  - In the absence of the above three conditions:
    Abnormal umbilical cord, predisposing to obstruction ("cord accident")
    - Ex. long UC, hypertwisted, abnormal insertion, true knot, nuchal/body cord
Abnormal cord insertion
Abnormal umbilical cords
Cord lesions: tight true knot
Placental pathology in setting of abnormal umbilical cord

- **The presence of fetal thrombotic vasculopathy can identify the cord abnormality as the cause of IUGR or stillbirth (secondary to “cord accident”)**
- **Important, as cord abnormalities are common in live births**
  - Up to 20% have nuchal cord
Example of placental report

- Small mature placenta (295 g, <10\textsuperscript{th} percentile for gestational age)
- Fetal vascular changes consistent with demise-to-delivery period of 12-24 hours
- Hypertwisted umbilical cord (7 twists/10 cm)
- Fetal thrombotic vasculopathy, multifocal, with upstream thrombosis in two chorionic plate vessels (see COMMENT)

COMMENT: There are multiple foci of avascular villi, consistent with the diagnosis of fetal thrombotic vasculopathy, associated with thrombi in two chorionic plate vessels. These findings are likely secondary to compromised umbilical blood flow secondary to the hypertwisted umbilical cord (consistent with “cord accident”).
Placenta Creta

- **Definition:** implantation *without* intervening decidua
  - Accreta: to superficial myometrium
  - Increta: into the myometrium
  - Percreta: up to or through serosa

- **Incidence:** 1 in 2500 deliveries
  - 10-fold increase over the past 10 years, primarily due to rise in c-section rates
  - 10-25% of placenta previa
Placenta Creta

- **Risk factors**
  - Maternal age greater than 35 years
  - **Previous uterine instrumentation**
    - Curettage
    - C-section
  - Uterine structural defects
    - Leiomyoma

- **Pathophysiology**
  - Placental implantation over an area of uterine scar (reduced/absent decidua)
    - Scar dehiscence at or near delivery leading to increta/percreta
  - **Controversial: increased invasion of extravillous trophoblast?**
Placenta Creta

- **Gross pathologic findings:**
  - Focal accreta (manual delivery of placenta):
    - Disruption/fragmentation of maternal surface
  - Gravid hysterectomy:
    - retained/attached placenta
    - Perforation/rupture

- **Microscopic findings:**
  - Absence of decidua
Normal maternal surface
Fragmented maternal surface
Fragmented maternal surface: focal/partial accreta
Placenta accreta
Placenta increta
Placenta percreta
Placenta percreta (with perforation)
Understanding placental disorders

- Clinical Presentation (mother)
  - Detailed medical/Prenatal history
  - Maternal Blood Banking

- Placental Pathology
  - Tissue Banking

- Molecular Biology
  - RNA expression profiling
  - Genotyping

- Neonatal Outcome
  - Cord Blood Banking
  - Detailed NICU Follow-up
Questions?

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