PLACENTAL EVALUATION IN CLINICAL PRACTICE

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CONTENT

1. Placental evaluation: IUGR
2. Placental evaluation in stillbirth: pre-mortem changes
3. Placental evaluation in stillbirth: post-mortem changes
4. Placenta quiz
1. PLACENTAL EVALUATION: IUGR

ADEQUATE FETAL GROWTH DEPENDS ON ADEQUATE SUPPLY OF OXYGEN AND NUTRIENTS TO FETUS
IUGR

- **Maternal factors**
- **Fetal factors**
- **Placental factors**

*Fetal growth is dependent upon adequate maternal-placental blood flow,*

*placental-fetal blood flow,*

*and villous permeability*

- maternal vascular malperfusion
- fetal vascular malperfusion
- high-grade chronic villitis
- massive perivillous fibrin
- chronic histiocytic intervillitis
- chronic abruption
FETAL AND PLACENTAL WEIGHT

- Low fetal body weight percentile
- Low placental weight percentile
- Fetal:placental weight ratio: Increases with ↑ GA = ~ 7:1 at term

ratio > 9-10:1 suggests placental insufficiency
CASE 1

GI, 26w
IUGR (male 504 g)
sectio because of abnormal CTG

MACROSCOPY:
Placental weight: P3-P10
No other abnormalities
Conclusion:

Placenta, 26 weeks of gestation:
- Low placental weight (P3 en P10) in correlation with gestational age
- Other placental findings: features of maternal vascular malperfusion and fetal vascular malperfusion.
- Increased presence of nucleated red blood cells and erythroblasts in fetal vessels probably due to fetal stress/hypoxia which can occur in conditions of severe maternal vascular malperfusion

GI, AD 26w
IUGR (male 504 g)
sectio because of abnormal CTG
CASE 2

Partus per sectio at 33w.
Severe IUGR
Abnormal dopplers.

MACROSCOPY:
333 gr (P10 - P25)
No visible lesions
CASE 2

Partus per sectio at 33w.
Severe IUGR
Abnormal dopplers.

Conclusion:

- high grade chronic villitis of unknown etiology with signs of a chronic histiocytic intervillitis and chronic deciduitis
2. PLACENTAL EVALUATION: STILLBIRTH

PREMORTEM CHANGES
1ST TRIMESTER PREGNANCY LOSS
(UP TO 13 WEEKS OF GESTATION)
10-20% RESULT IN PREGNANCY LOSS

40-70% CHROMOSOMAL ABNORMALITIES

MATERNAL:  - AUTOIMMUNE DISORDERS
            - ENDOCRINOPATHY (I.E., DIABETES, OBESITY, LUTEAL-PHASE DEFECTS, POLycystic Ovary syndrome)
            - THROMBOPHILIA
            - SEVERE ACUTE ILLNESS (E.G., PNEUMONIA, APPENDICITIS)
            - INFECTION (RARE): LISTERIA, TOXOPLASMA, HERPES SIMPLEX VIRUS, COXSACKIEVIRUS, CYTOMEGALOVIRUS
            - UTERINE ANOMALIES (INTRAUTERINE ADHESIONS, UTERINE SEPTUM, AND LEIOMYOMATA)
            - TERATOGEN EXPOSURE AND SMOKING/DRUG USE
1ST TRIMESTER PREGNANCY LOST:
PLACENTAL EVALUATION

1. Confirming Intrauterine Pregnancy
2. Implantation site decidua and maternal vessels
Normal invasive trophoblast
1ST TRIMESTER PREGNANCY LOST: PLACENTAL EVALUATION

1. Confirming Intrauterine Pregnancy
2. Implantation site decidua and maternal vessels
3. Distinguishing Hydropic Degeneration From Hydatidiform Mole
4. Villous Changes in Pregnancy Loss With abnormal Karyotype
Hydropic degeneration

Intermediate trophoblasts in the villous stroma
Dysmorphic villi with trophoblast inclusions
multinucleated invasive trophoblasts at the implantation site
1ST TRIMESTER PREGNANCY LOST:
PLACENTAL EVALUATION

1. Confirming Intrauterine Pregnancy
2. Implantation site decidua and maternal vessels
3. Distinguishing Hydropic Degeneration From Hydatidiform Mole
4. Villous Changes in Pregnancy Loss With abnormal Karyotype
5. Chronic histiocytic intervillositis
6. Embryo
2ND TRIMESTER PREGNANCY LOSS

(13 WEEKS - 27 WEEKS OF GESTATION)
IUFD IS RELATIVELY UNCOMMON IN 2ND TRIMESTER (1-5%)

1. 24% CHROMOSOMAL ABNORMALITIES

2. INFECTIONS:
   
   ASCENDING INFECTION: 40-60% OF 2ND-TRIMESTER FETAL DEATHS
   
   (GROUP B STREPTOCOCCUS, NEISSERIA GONORRHOEAE, GARDNERELLA SPP., MYCOPLASMA/UREAPLASMA, FUSOBACTERIUM SPP.)

   HEMATOGENOUS (TORCH)

3. PLACENTAL INSUFFICIENCY: MVM/ FMH/FVM/CHRONIC ABRUPTION

4. MATERNAL
2ND TRIMESTER PREGNANCY LOSS:

PLACENTAL EVALUATION

- Look for evidence of **amniotic fluid infection**
- Look for fetal thrombi and organizing changes of **fetal vascular malperfusion**
- Look for changes of **uteroplacental malperfusion**
- Look for **villous parenchymal processes**
- Look for evidence of **hematogenous infection**
Fig. 3 Pathological changes in maternal vascular malperfusion (MVM). PIH Pregnancy induced hypertension; PET Pre eclamptic toxemia
Box 3.1 List of Recognisable Placental Conditions that May Cause Recurrent Pregnancy Loss
Massive perivillous fibrin deposition.
Chronic histiocytic intervilllositis.
Villitis of unknown aetiology (VUE).
Maternal vascular malperfusion.
3RD TRIMESTER PREGNANCY LOSS

- Look for evidence of amniotic fluid infection
- Look for fetal thrombi and organizing changes of fetal vascular malperfusion
- Look for changes of uteroplacental malperfusion
- Look for villous parenchymal processes
- Look for evidence of hematogenous infection
- Look for evidence of *fetal-maternal hemorrhage*
- **Delayed villous maturation**
fetal-maternal hemorrhage:

- hydropic pale placenta
- NRBC in fetal circulation and intervillous thrombi

DD. Fetal anemia due to hemolytic anemia, Parvo or CMV

Clinical diagnosis: Kleihauer-Betke or flowcytometry
3RD TRIMESTER PREGNANCY LOSS

- Look for evidence of amniotic fluid infection
- Look for fetal thrombi and organizing changes of fetal vascular malperfusion
- Look for changes of uteroplacental malperfusion
- Look for villous parenchymal processes
- Look for evidence of hematogenous infection
- Look for evidence of fetal-maternal hemorrhage
- Delayed villous maturation
Delayed villous maturation

Areas of immature-appearing villi comprised of at least 10 abnormal villi demonstrating poor vasculosyncytial membrane formation, centrally placed capillaries, continuous cytotrophoblast (later third trimester)

**At least 30% of parenchyma of at least 1 full-thickness slide should be involved**

- associated with maternal diabetes, obesity, excessive weight gain in pregnancy
- Less commonly associated with chronic variable umbilical cord obstruction, fetal chromosomal abnormalities

**May be clinically silent with lack of prenatal and US markers**

Increased risk of **fetal death at > 37 weeks**
Up to 5% risk of recurrent stillbirth
Delayed villous maturation

Normal a term  Pattern 1  Pattern 2

Stallmach et al. Obstet Gynecol 2001; 97: 505-9
Delayed villous maturation:
Pattern 3
3. PLACENTAL EVALUATION: STILLBIRTH

POSTMORTEM CHANGES
POSTMORTEM CHANGES

Consequences of....

Regardless of etiology

- 1. Cessation of fetal blood flow
- 2. Altered maternal perfusion
- 3. Maternal inflammation to non-viable products of conception
- 4. Labor associated changes related to placental separation.
POSTMORTEM CHANGES

Consequences of....

- 1. Cessation of fetal blood flow
- 2. Altered maternal perfusion
- 3. Maternal inflammation to non-viable products of conception
- 4. Labor associated changes related to placental separation.
1. CESSATION OF FETAL BLOOD FLOW

**Villous capillary changes**

- Intravascular karyorrhexis
- Villous stromal-vascular karyorrhexis
- Extravasation of erythrocyte fragments into the villous stroma
- Villous capillaries involution → avascular villi

**Muscular (stem, chorionic) vessel changes**

- Intravascular karyorrhexis → extravasation of erythrocytes into the peri-luminal mural wall
- Fibroblast ingrowth into the vessel lumen, resulting in luminal septation.
- Stem villous obliteration
→ karyorrhectic debris

extravasation of erythrocytes

avascular villi

FETAL CAPILLARY CHANGES
MUSCULAR (STEM, CHORIONIC) VESSEL CHANGES
1. Cessation of fetal blood flow

2. Altered maternal perfusion

3. Maternal inflammation to non-viable products of conception

4. Labor associated changes related to placental separation.
2. ALTERED MATERNAL PERFUSION

- Excessive syncytial knots **diffusely**
- Clustering of villi and obliteration of intervillous spaces
- Intervillous fibrin deposition (fine fibrine network)

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---> excessive placental fibrosis (6 to 8 weeks)--->interpretation difficult

---> look at **PATTERN** of distribution of lesions
Mors in utero: 17 w AD
POSTMORTEM CHANGES

Consequences of....

- 1. Cessation of fetal blood flow
- 2. Altered maternal perfusion
- 3. Maternal inflammation to non-viable products of conception
- 4. Labor associated changes related to placental separation.
3. MATERNAL INFLAMMATION TO NON-VIABLE PRODUCTS OF CONCEPTION

- maternal neutrophil migration into the extraplacental membranes

  → postmortem chorioamnionitis
Subacute necrotizing chorioamnionitis
POSTMORTEM CHANGES

Consequences of...

- 1. Cessation of fetal blood flow
- 2. Altered maternal perfusion
- 3. Maternal inflammation to non-viable products of conception
- 4. Labor associated changes related to placental separation.
4. LABOR ASSOCIATED CHANGES RELATED TO PLACENTAL SEPARATION.

- features of placental abruption, with adherent retroplacental blood and microscopic recent placental infarction

Key: compare the temporal evolution of placental changes to the time fetal death
DIFFERENTIAL DIAGNOSES

- Temporal and spatial heterogeneity to the patterns
- Demise to delivery interval

Fetal vascular malperfusion
Postmortem changes are diffuse and primary vasculary insufficiency is focal

Comparison of demise-to-delivery interval
ASSOCIATED FINDINGS

Meconium

- Meconium is rarely released in response to fetal stress prior to the third trimester.
- Third trimester: fetuses may release meconium in response to stimuli, including hypoxia and infection.
- meconium vascular necrosis
ASSOCIATED FINDINGS

Villous edema

- **nonspecific finding**, can be present in stillbirth placentas.
- more commonly in *preterm* placentas and in placentas with chorioamnionitis, acute and complete umbilical cord occlusion....
ASSOCIATED FINDINGS

- intact fetal red blood cell extravasation into the villous stroma
- acute cord prolapse
- placental–uterine separation
- DD. villous stromal-vascular karyorrhexis

Intravillous hemorrhage
<table>
<thead>
<tr>
<th>Features</th>
<th>Postdemise Interval</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
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</thead>
<tbody>
<tr>
<td><strong>Placental Histology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intravascular karyorrhexis in small villous vessels of several different regions</td>
<td>≥ 6 hours</td>
<td>94%</td>
<td>100%</td>
<td>1.000</td>
</tr>
<tr>
<td>Multifocal (10-25%) stem vessel luminal abnormalities</td>
<td>≥ 48 hours</td>
<td>94%</td>
<td>100%</td>
<td>1.000</td>
</tr>
<tr>
<td>Extensive (&gt; 25%) stem vessel luminal abnormalities</td>
<td>≥ 2 weeks</td>
<td>78%</td>
<td>98%</td>
<td>0.875</td>
</tr>
<tr>
<td>Extensive (&gt; 25% of terminal villi) avascular villi</td>
<td>≥ 2 weeks</td>
<td>100%</td>
<td>93%</td>
<td>0.750</td>
</tr>
</tbody>
</table>
4. PLACENTA QUIZ
Q1: How many coils are there?
Q 1: HOW MANY COILS?

- A. 5
- B. 6
- C. 7
- D. 8
Q 1: HOW MANY COILS?

- A. 5
- B. 6
- C. 7
- D. 8
Q2 Clinical data

- Mother 35 yrs G1 P0.
- child 3000 gr
- placenta 710 gram (38 AD: > P90)

Macroscopy:
- RIP diameter 9 cm.
Q.2

- A. Foetus Papyraceus
- B. Chorangioma
- C. Teratoma
Q.2

- A. Foetus Papyraceus
- B. Chorangioma
- C. Teratoma
Q3 Clinical data

• G4P0
• AD 41+4
• Weight child 5060
• APGAR 4/6/8
Q3: REASON LOW APGAR?

- A. Chorioamnionitis
- B. Meconium aspiration
- C. Chorioamnionitis and funiculitis
Q3 Reason low apgar’s?

A. Chorioamnionitis
B. Meconium aspiration
C. Choriamnionitis with funiculitis
D. Don’t know
Q 4

- GA 23+2 induction
- Multiple congenital anomalies at ultrasound
  - Hydrops fetalis, cerebral anomalies
- Placenta 460 g (>>p90)
- No lesions macroscopically
H&E 1x
Diagnosis?

A. Acute villitis
B. Chronic villitis of unknown origin (VUE)
C. Chronic inflammation with plasmacells
D. Viral induced villitis
Answer: D

- Chronic villitis, CMV induced

- Histology:
  - Lymphocytic villitis
  - Plasmacells
  - Iron deposition and calcifications
  - Viral changes
  - CMV +
Q5

- GA 38+4, rupture of membranes >24h
- Intra-uterine growth restriction

- Placenta 334 g (<p10)
H&E 0.5x
H&E 10x
Diagnosis?

A. Infarction

B. Acute villitis

C. Intervillous abcesses
Answer: C

• Intervillous abcesses

• Associated with acute villitis and villous necrosis

• Micro-organisms:
  • Listeria monocytogenes, Staphylococcus, Escherichia coli, Campylobacter and Chlamydia

• This case showed some Gram positive cocci; possible listeriosis
Q6
Diagnosis?

A. Reactive changes due to meconium

B. Amnion nodosum

C. Vacuolation due to gastroschisis

D. Vacuolation due to glycogen storage disease
Answer: C

- Vacuolation due to gastroschisis
- Fine, uniform, extensive vacuolation
- Vacuoles contain lipid; origin is unknown
- Not found in combination with omphalocele
Meconium exposure: vacuolation is more coarse with greater variability. Meconium pigment can be seen in some vacuoles.
• Meconium:
  • Meconium-filled macrophages
  • Vacuolization, heaping up of cells, dissociation, necrosis

• Glycogen storage disease:
  • Vacuoles filled with glycogen-like material,
    PAS positive
H&E 60x
Diagnosis?

A. Eosinophilic vasculitis

B. Chronic vasculitis

C. Acute chorioamnionitis with fetal response

D. Subacute vasculitis
Answer: A

- Eosinophilic / T-cell vasculitis
- Fetal-derived chronic inflammatory infiltrate
- Eosinophils & small lymphocytes
- No neutrophils
- Incidence: 0.2%
- Associated with chronic villitis
- No specific clinical associations / consequences
CD3 20x
Q9 a term
Q9 a term
H&E 5x

Diagnosis?
A. Maternal vascular malperfusion
B. Fetal vascular malperfusion
C. Chronic villitis
Answer: B

- Fetal vascular malperfusion
- Obstruction in fetal blood flow
- Histology:
  - Thrombosis, segmental avascular villi, villous stromal-vascular karyorrhexis