Problems in Obstetric Pathology

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Cystic Lesions: late pregnancy
A. Placental Mesenchymal Dysplasia (microscopic)
Mesenchymal dysplasia

Clinical: Subchorionic cysts after 8 wks with progression

Pathogenesis: Hypoxia, excessive growth factors, androgenic/biparental mosaicism, Subgroup with Beckwith Wiedemann syndrome (20%, ch11 UPD only)

Pathology: placental enlargement, abnormal stem villi with marked cystic dilatation, stromal overgrowth, and abnormalities affecting fetal vessels of all sizes

Recurrence Risk: rare, genetic forms of BWS

Adverse outcomes: IUGR, IUFD, neonatal death, extraplacental tumors
Polyphenotypic pregnancy: normal villi, mesenchymal dysplasia, and complete mole
Biparental stroma and trophoblast (normal pattern)

P57/KIP2 immunostain

Stromal diandry/ biparental trophoblast (mesenchymal dysplasia pattern)

Stromal and trophoblastic diandry (complete mole pattern)
Mild variant of mesenchymal dysplasia vs. other mosaicism, developmental abn
B. Twin pregnancy, one with complete hydatidiform mole
C. Increased intraplacental trophoblast: islands and cysts

Stanek 2012
Dysmorphic villi
Fetal stromal-vascular maldevelopment: dysmorphic villi

1. **Mesenchymal dysplasia**: stem villous cysts, overgrowth
2. **Aneuploidy**: Irregular villous contour, abnormal vascular patterning, trophoblast inclusions
3. **Beckwith-Wiedemann Syndrome**: placentomegaly, abnormal vascular proliferations, increased fibrinoid
4. **Other**: (? confined placental mosaicism): some elements of 1-3; also stem villous /distal villous size discordance
Irregular villous contour and trophoblast inclusions
Abnormal vascular pattern
Stem villous edema and proximal/distal villous discordance
Trophoblast proliferation/ atypia
Intraplacental choriocarcinoma
HCG Immunostain

Choriocarcinoma

Metastatic Colorectal Carcinoma
Early (Intraepithelial) Intraplacental Choriocarcinoma
Non-neoplastic lesions

Intervillous fibrin with bizarre X-cells (seen with ICE1-type BWS)

Chorangioma with trophoblast hyperplasia (? “so-called chorangiocarcinoma”)
Other trophoblast abnormalities
Metabolic storage diseases with marked vacuolation of syncytiotrophoblast

- GM1-gangiosidosis, type 1 infantile type (beta galactosidase-1 deficiency)
- I-cell disease (mucolipidosis, type 2)
- Salla disease (infantile sialic acid storage disease)
- Galactosialidosis (carboxypeptidase A “protective” protein deficiency)
Trophoblast Basement Membrane Mineralization

• Hydrops fetalis

• Chromosomal abnormalities

• Antenatal Bartter Syndrome

• Occasional severe cases of maternal and fetal malperfusion

• Remote IUFD
Villous stroma: edema
Diffuse Villous Edema/ Hydrops Fetalis

Chronic anemia

Blood group incompatibility
Fetomaternal hemorrhage
Parvovirus B19
Intrinsic RBC abnormalities

Fetal circulatory impairment

Heart: (right sided lesions, arrhythmias, myocarditis)
Obstructed venous return
(Abdominal/Thoracic mass)
AV shunting (Chorangioma)

Other (hepatic, renal, lymph-vascular)

Aneuploidy
(45,X0, Down syndrome)
Genetic diseases
(Metabolic storage disease)
TORCH infection
(CMV, Syphilis, Toxoplasmosis)
Pathogenesis: Impaired fetal circulatory function, lack of villous structural integrity

<table>
<thead>
<tr>
<th>Placental Lesions</th>
<th>CP Cases</th>
<th>Controls</th>
<th>OR (95% CI)</th>
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<tbody>
<tr>
<td>Severe villous edema</td>
<td>N=60</td>
<td>N=59</td>
<td>5.7(1.5-21.0)</td>
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<td></td>
<td>14(23)</td>
<td>3(5)</td>
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Outcomes: Neonatal death, Neurodisability

Focal villous edema, distal villi (nonspecific/multiple causes)

(associated with umbilical arterial pH <7.0 at >37 wks, Early Hum Devel, 2015)
Neovillogenesis: seen in slightly immature placentas, delayed villous maturation

(Immature mesenchymal villi, CD15 positive population; Seidmann, Placenta 2014; 35: 925-31)
Villous stroma: increased cellularity
Idiopathic chronic villitis ("villitis of unknown etiology")
VUE- differential diagnosis ("Hemorrhagic endovasculitis")

Villous stromal-vascular karyorrhexis
VUE- differential diagnosis: “increased Hofbauer cells”

Acute chorioamnionitis

Delayed villous maturation
VUE - differential diagnosis: Fetal Leukemia
Intervillous space: chronic inflammation
Chronic Histiocytic Intervillositis

- Diffuse infiltration of intervillous space by CD68+ histiocytes, some T cells
- Associated perivillous fibrin common (villitis not allowed)
- Recurrent miscarriage, FGR, IUFD, maternal autoimmunity
- Biomarker: ↑ maternal serum PLAP
- Rx: aspirin, corticosteroids, LMWH, hydroxychloroquine
Placental Malaria

- Histiocytic intervillitis
- Trophoblast necrosis
- Malarial parasites and pigment
- Primiparous patients without previous exposure
Villitis, active chronic, with intervillositis

• Uncommon

• Etiology
  – Nonsyphilitic spirochetes
  – gram negative bacilli
  – Rickettsia, tularemia, measles
  – Coccidiomycosis
  – HSV, VZV, measles virus

(but fulminant VUE accounts for > 95% of such cases)
Intervillous space: Fibrin/ Fibrinoid
Pathogenesis: placental fibrin(oid)

Malperfusion of intervillous space/ stasis:
Increased intervillous fibrin with X-cells
(accelerated villous maturation)

Trophoblast injury with coagulation/ metaplasia:
Nonspecific perivillous fibrin deposition
Perivillous fibrin plaque

Massive perivillous fibrin(oid) deposition
“maternal floor infarction”, Gitterinfarkt” (MFI)
Massive perivillous fibrin(oid) deposition: “Maternal floor infarction (MFI)”

Fibrinoid with intermediate trophoblast (“X-cells”)

Villous degeneration with “bright red fibrin”

Alternative gross patterns

Alternative histologic patterns
Clinical associations: autoimmunity, thrombophilia, some infections, fetal LCHAD heterozygosity

Adverse outcomes:
SAB, PTD, FGR, IUFD
Recurrent pregnancy loss (up to 60% recurrence rate)

Pathogenesis:
- ? Trophoblast injury with metaplasia (villous to extravillous)
- Fibrinoid matrix secretion by trophoblast (fibronectin, laminin, COL4, entactin)
- ? Activation of coagulation cascade
**Increased intervillous fibrin:**
(c/w maternal malperfusion)
- subchorionic
- stem villi
- basal plate

**Perivillous fibrin plaque:**
- term placentas
- no known clinical correlates or adverse outcomes
- differential dx: villous infarct
MFI Differential diagnosis:

Villous infarction  
VUE with diffuse fibrin
Fetal vessels: intraluminal cells
**Increased NRBC**

- Fetal bone marrow response
- Profound/ sustained hypoxia
- 6-12 hours or more to develop

**Hypoxic-ischemic process (hrs-days):**
> 1 normoblast/ high power field, 10 fields counted (Redline 2008)

**Fetal anemia/ hydrops (wks-months):**
pre-normoblast RBC precursors and/or EMH

**Differential Dx: Lymphocytes:**
- Also transiently increased in hypoxia
- Irregular nuclear membrane
- Clumped heterochromatin
- Lack glassy eosinophilic cytoplasm
Parvovirus B19 inclusions
TRANSIENT MYELOPROLIFERATIVE DISORDER (TRISOMY 21)
FETAL LEUKEMOID REACTION
ACUTE CHORIOAMNIONITIS