Clues to Pathology Diagnoses in Abortion

Raymond W. Redline
Case Western Reserve University
Cleveland, OH, USA
Why examine early pregnancy losses?

Rule out Ectopic Pregnancy

- Stat evaluation
  - Gross exam
  - Frozen section

- Final signout
  - completely submit
  - 24 hr turnaround
  - call clinician
Implantation site with trophoblast

Gestational endometrium with Arias-Stella
Why examine spontaneous abortions?

Determine Etiology and Recurrence Risk

Considerations

• Retention of an abnormal gestation
• Pathologic elimination of a normal gestation
• Failure to support a normal gestation
Hydropic Abortion

Failure of chorioallantoic fusion and vasculogenesis

Clinical:
- early missed abortion
- anembryonic pregnancy
  (U/S: absent fetal pole)

Pathology:
- uniformly hydropic villi
- no trophoblast hyperplasia
Non-hydropic Abortion

Failure: deficient trophoblast-endometrial interaction/ inadequate endovascular remodelling

Clinical:
- Threatened abortion
- Incomplete abortion
- Complete abortion
well-vascularized villi + karyorrhexis

decidual necrosis or hemorrhage

Intervillous hemorrhage
Involutional changes after fetal/embryonic death (missed abortion)

- Partially hyalinized and hydropic <10 weeks gestation
- Uniformly hyalinized villi + fusion of chorion and amnion >10 weeks gestation
## Histologic Features by Karyotype

<table>
<thead>
<tr>
<th>Histologic findings</th>
<th>Normal karyotype (N=318)</th>
<th>Abnormal karyotype (N=350)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysmorphic features</td>
<td>2.2%</td>
<td>17.4%*</td>
</tr>
<tr>
<td>Chronic histiocytic intervilloisitis</td>
<td>4.4%*</td>
<td>0.3%</td>
</tr>
<tr>
<td>Massive perivillous fibrin(oid)</td>
<td>5.4%*</td>
<td>0.9%</td>
</tr>
<tr>
<td>Decidual plasma cells</td>
<td>5.4%*</td>
<td>3.7%</td>
</tr>
<tr>
<td>Diffuse chronic deciduitis</td>
<td>9.1%*</td>
<td>4.0%</td>
</tr>
<tr>
<td>Chronic villitis</td>
<td>1.3%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Decidual vasculopathy</td>
<td>0.6%</td>
<td>0</td>
</tr>
</tbody>
</table>

* p<0.050

Redline et al, *Hum Pathol* 30: 93-100, 1999
Dysmorphic villi suggestive of chromosomal abnormality
(Predictive value positive= 90%)

Irregular villous contour

Trophoblast inclusions
Chronic Histiocytic Intervillositis

Massive perivillous fibrin(oid)
### Thrombo-inflammatory lesions in chromosomally normal recurrent abortion

<table>
<thead>
<tr>
<th>Karyotype</th>
<th># of SAB</th>
<th>N=</th>
<th>Thrombo-inflammatory lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1</td>
<td>15</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td>≥ 2</td>
<td>16</td>
<td>31 %*</td>
</tr>
<tr>
<td>Abnormal</td>
<td>1</td>
<td>10</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>≥ 2</td>
<td>9</td>
<td>11%</td>
</tr>
</tbody>
</table>

P< 0.050

Redline et al, Hum Pathol 30: 93-100, 1999
Non-molar abortion: final signout

**Diagnosis number 1: conceptus**
- Developmental stage: early, mid, late 1\(^{st}\) or 2\(^{nd}\) trimester sac
- Constituent parts: fetus, yolk sac, umbilical cord, amnion
- Description of villi: vascularization, malformation, degeneration
- Thromboinflammatory changes: fibrin, leukocytes

**Diagnosis number 2: endometrium**
- General state: well preserved, hemorrhagic, necrotic
- Background: chronic inflammation, plasma cells, excessive fibrinoid
- Vessels: mural hypertrophy, peri/vasculitis

**Example**
-- First trimester chorionic sac with amnion and poorly vascularized dysmorphic villi suggestive of chromosomal abnormality
-- Well preserved gestational endometrium and implantation site
Why examine early pregnancy losses?

Rule out
Gestational Trophoblastic Disease

• Complete mole
• Early complete mole
• Partial mole
• Trophoblastic malignancy
Genomic imprinting: gene expression restricted to one parental haplotype

- Only placental mammals show genomic imprinting
- All known imprinted genes are expressed in placenta
- Maternal haplotype only genes restrict placental development
- Paternal haplotype only genes promote trophoblast proliferation (particularly in the absence of the maternal genome).
Complete Hydatidiform Mole

Uniformly cystic villi
Paternal chromosomes only
Complete Hydatidiform Mole

Diploid (2P: 0M)

- Generalized villous hydrops
- Villous cisterns
- Circumferential trophoblast hyperplasia (cytotrophoblast and synctiotrophoblast)
- Absence of fetally-derived tissue
Complete Hydatidiform Mole

Villous trophoblast hyperplasia
Early Complete Hydatidiform Mole

Histologic criteria: (Keep et al, Hum Pathol 27: 708-13, 1996)

- Block shaped, bulbous villi with perpendicular infoldings
- Focal circumferential trophoblast hyperplasia
- Primitive stellate mesenchymal stroma with karyorrhexis
- Villous stromal canaliculi
- Atypical extravillous trophoblast
Villous Trophoblast Hyperplasia
Atypical implantation site: pleomorphc nuclei in mature extravillous trophoblast
Early Complete Hydatidiform Mole: Ancillary Studies

- P57/KIP2 immunostaining: negative in the nuclei of stromal and cytotrophoblast cells in complete mole. (Only expressed from the female genome)

- PCR-based microsatellite analysis on microdissected maternal and fetal tissue removed from the paraffin blocks
Partial Hydatidiform Mole
Triploid karyotype (2P: 1M)

Scattered cystic villi
Partial Hydatidiform Mole

Triploid karyotype (2P: 1M)

- Hydropic villi (>0.2 mm)
- Circumferential trophoblast hyperplasia
  - Focal or diffuse
  - Syncytiotrophoblast + cytotrophoblast
- Dimorphic villous population (large and small)
- Irregular villous contour

Minor Criteria: abnormal villous vessels, villous stromal karyomegaly, atypical intermediate trophoblast

Redline et al, Hum Pathol 28: 505-11, 1998
Dysmorphic features: irregular villous contour, trophoblast inclusions
Trophoblast hyperplasia
## Villous Trophoblast Hyperplasia

### CWRU Spontaneous Abortion Study

<table>
<thead>
<tr>
<th>Karyotype</th>
<th>Low Grade</th>
<th>High Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete mole</td>
<td>0%</td>
<td>100%</td>
</tr>
<tr>
<td>Triploidy</td>
<td>26%</td>
<td>35%</td>
</tr>
<tr>
<td>Tetraploidy</td>
<td>25%</td>
<td>25%</td>
</tr>
<tr>
<td>Trisomy</td>
<td>16%</td>
<td>5%</td>
</tr>
<tr>
<td>trisomies 7 and 15</td>
<td>43%</td>
<td>14%</td>
</tr>
<tr>
<td>Monosomy X</td>
<td>19%</td>
<td>4%</td>
</tr>
<tr>
<td>Diploid/ normal</td>
<td>5%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Redline et al, Mod Pathol 11: 762-8, 1998
**Nonspecific villous trophoblast hyperplasia**

Recommended signout:

Villi with nonspecific trophoblast hyperplasia, see note.

NOTE: Nonspecific trophoblast hyperplasia is often associated with uncommon karyotypes including Trisomies 2, 7, 15, and 22. A single followup hCG Titer is recommended to ensure return to baseline.
# Choriocarcinoma

<table>
<thead>
<tr>
<th>Condition</th>
<th>Risk</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete mole</td>
<td>2-3%</td>
<td>50%</td>
</tr>
<tr>
<td>Partial mole</td>
<td>0.6%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Miscarriage</td>
<td>0.001%</td>
<td>25%</td>
</tr>
<tr>
<td>Term pregnancy</td>
<td>? very rare</td>
<td>25%</td>
</tr>
</tbody>
</table>
Previllous Trophoblast

Villous Cytotrophoblast
(p63⁺/mib1⁺/inhibin⁻/MelCAM⁻)
Choriocarcinoma, Complete mole

Syctytotrophoblast
(p63⁻/mib1⁻/inhibin⁺/MelCAM⁻)
Increased in Partial mole

Transitional Extravillous Trophoblast
(Transitional EVT)
1) Membranous
2) Intraplacental
3) Basal plate
(p63⁺/mib1⁻+/inhibin⁺⁻/MelCAM⁺⁻)
Epithelioid trophoblastic tumor (ETT)

Trophoblastic column
(p63⁺⁻/mib1⁺/inhibin⁻/MelCAM⁺⁺)

Mature Extravillous Trophoblast (Mature EVT)
1) Membranous
2) Intraplacental
3) Basal plate
(p63⁻/mib1⁻⁻/inhibin⁺⁺/MelCAM⁺⁺)

Extravillous implantation site
Trophoblast (IST)
1) Interstitial
2) Endovascular

Placental site trophoblastic tumor (PSTT)
Choriocarcinoma

Early blastocyst
Previlous Trophoblast

Villous Cytotrophoblast
(p63⁺/mib1⁺/inhibin⁻/MelCAM⁻)
Choriocarcinoma, Complete mole

Synctiotrophoblast
(p63⁻/mib1⁻/inhibin⁻/MelCAM⁻)
Increased in Partial mole

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1) Membranous
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3) Basal plate
(p63⁺⁺/mib1⁺⁺/inhibin⁺⁻/MelCAM⁺⁺)
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(p63⁺⁻/mib1⁻/inhibin⁻/MelCAM⁺⁺)

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Extravillous implantation site
Trophoblast (IST)
1) Interstitial
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Placental site trophoblastic tumor (PSTT)
Previllous Trophoblast

Villous Cytotrophoblast
(p63⁺/mib1⁺/inhibin⁻/MelCAM⁻)
Choriocarcinoma, Complete mole

Synctiotrophoblast
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Trophoblastic column
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1) Membranous
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3) Basal plate
(p63⁻/mib1⁻/inhibin⁺/MelCAM⁺⁺)

Extravillous implantation site
Trophoblast (IST)
1) Interstitial
2) Endovascular

Placental site trophoblastic tumor (PSTT)
Epithelioid trophoblastic tumor (ETT)
Avillous trophoblast: 3 diagnostic categories

(Elston, J Clin Pathol 25: 111-8, 1972)

– Avillous trophoblast NOS (at risk only with prior GTD)

– Trophoblastic neoplasia to be excluded (↑ risk with prior GTD)

– Diagnostic for trophoblastic neoplasia
Avillous trophoblast: Placental site nodule
A villous trophoblast: Exaggerated implantation site
A villous trophoblast, GTD to be excluded (no previous mole)
A villous trophoblast, GTD to be excluded (+ previous mole)
Choriocarcinoma
Placental site
Trophoblastic Tumor

IHC: HPL
Why examine early pregnancy losses

Identify incidental lesions

• Cervical neoplasia
• Uterine perforation
Adipose tissue

Colonic wall