Mullerian Anomalies

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Objectives

Participants should be able to:

- Describe the prevalence and presentation of mullerian anomalies
- Review the embryologic origins of the mullerian system and mechanisms of defects
- Determine the appropriate process of evaluation
- Discuss treatment modalities and the success attributed to each
Case #1

30 yo G0 told she had a “split uterus”
- Moderate dysmenorrhea, mild dyspareunia
- Regular menses, +PMM, No STDs, No abnormal paps.
- History of Lupron & OCPs – both with improvement of symptoms
- Desires pregnancy

PMH: JRA – resolved

PSH: Molar extraction
HSG

Ultrasound/Sonohysterogram

Laparoscopy
DIAGNOSIS??

- Single unified fundus with septum to Os
- Markedly divergent uterine horns
- Thin connection between uterine horns, not consistent with septum
- Extensive endometriosis
Mullerian Anomaly
Prevalence and Presentation
Prevalence

- **0.4-3% non-infertile**
- **4-6% infertility**
- **5-10% RPL**
- **25% late SAB, early PTD**

Raga 1997

Acien 1997

- **Arcuate**
- **Septate**
- **Bicornuate**
- **Unicornuate**
- **Didelphic**

Raga et al (1997)  
Byrne et al (2000)
Presentation

- Infancy
  - Mucocolpos

- Adolescence
  - Primary amenorrhea, mass (hematocolpos), difficulty with tampon insertion

- Reproductive years
  - RPL, stillbirth, infertility, Breech

- Undetected
Add’l Associations

- Infertility
- IUGR
- Malposition
- PTL
- Retained placenta
- Renal anomalies
Renal Anomalies

- 20-40% w/ Müllerian anomalies have concomitant renal anomaly
- >35% w/ Renal anomaly have müllerian anomaly
RPL

- RPL (5-10% - excluding arcuate)
  - #1 association: septate
    - Increased muscular/Reduced connective tissue on pathology
    - Reduced vascularity
    - Abnormal endometrial development
      - Reduced sensitivity to pre-ovulatory hormones
    - Narrowing of cavity
Case #2

26 year old female  G0
– 18 mo history of infertility
– Long-standing dysmenorrhea, no dyspareunia
– Regular menses, + PMM
– GYN history otherwise negative
HSG

Ultrasound/Sonohysterogram

Laparoscopy
Embryologic origins of Mullerian anomalies
Embryology

- Intermediate Mesoderm
  - Metanephros
    - Renal system
  - Mesonephros
    - Epididymis, Vas, Seminal Vesicle
  - Paramesonephros
    - Fallopian tubes, uterus, cervix, upper 2/3 of vagina
  - Gonadal Ridge

5-6 weeks
Müllerian System

- Fusion near urogenital sinus

- Larsen (1998) *Human Embryology*
Müllerian System

- Fusion to contralateral duct
  - Caudomedial
- Lateral fusion defects
  - Bicornuate, Didelphys

- Mesenchymal:Epithelial cross-talk

Müllerian System

- Fusion of ducts to posterior UGS (sinovaginal bulbs) & canalization
- Endometrium developed by 20wks
  - Vertical fusion defects
    - Transverse vaginal septum
  - Resorption defects
    - Complete by 22nd wk

• Larsen (1998) *Human Embryology*
Complete differentiation relies on:

- Organogenesis
  - Formation of 2 intact müllerian ducts
  - Müllerian agenesis, Unicornuate uterus
- Lateral Fusion
- Vertical fusion
- Recanalization
Canalization follows fusion
- Can begin at any location along the line of fusion
- Can proceed in any direction
Muller et al 1967

- At 13-20 wks resorption
  - 1st isthmic
  - Proceeds cranially and caudally
- Supported by:
  - Vaginal & Cervical septum with normal uterine cavity
  - Septum in lower uterine segment with normal fundal cavitation – not seen
<table>
<thead>
<tr>
<th></th>
<th>Hypoplasia/agenesis</th>
<th>Unicornuate</th>
<th>Didelphus</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Vaginal</td>
<td>Communicating</td>
<td>Didelphus</td>
</tr>
<tr>
<td></td>
<td>Cervical</td>
<td>Non-Communicating</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fundal</td>
<td>No cavity</td>
<td>Complete</td>
</tr>
<tr>
<td></td>
<td>Tubal</td>
<td>No horn</td>
<td>Partial</td>
</tr>
<tr>
<td></td>
<td>Combined</td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>V</th>
<th>Septate</th>
<th>Arcuate</th>
<th>DES drug related</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Complete</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Partial</td>
<td></td>
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**Classification - American Fertility Society 1988**
Class I - Hypoplasia/Agenesis

Mayer-Rokitansky-Kuster-Hauser
- Agenesis of the uterus, cervix, and upper portion of the vagina.
- Requires gestational carrier
Class II - Unicornuate

Arrested development of 1 müllerian duct
- Incomplete (2/3)
  - rudimentary horn with or without functioning endometrium
    - Cavitated (1/2)
      » Communicating (1/3)
    - Attached by band or full connection to unicornuate
Unicornuate + Renal Anomalies

- Incidence
  - 31-100% *(66%)

- Most common
  - Renal agenesis – ipsilateral to rudimentary or absent horn

- 2nd most common
  - Ipsilateral pelvic kidney

*Buttram & Gibbons, Silber
Figure 3: Hysterosalpingogram of case 2. A unique unicornuate uterus that a fallopian tube without left uterine horn and cavity branches from right cervical canal.
Class III - Didelphys

B. Uterus Didelphys
Fig. 1 A
Lateral fusion failure + Vertical fusion failure (hemivaginal septum) + ipsilateral renal agenesis

Fig. 1 B
Variations in presentation
Class IV - Bicornuate

Partial

Complete

C. Bicornuate Uterus
Class V - Septate

- Complete
- Partial
Septate Uterus
Septate
Class VI - Arcuate
Class VII – DES

Suppresses Wnt7a, alters expression of Hoxa9 & 10 through Erα in the murine model
Table II. Reproductive performance of different types of uterine malformation\(^a\). Figures in parentheses are percentages

<table>
<thead>
<tr>
<th>Type of malformation</th>
<th>II Unicorneate ((n = 8))</th>
<th>III Didelphys ((n = 8))</th>
<th>IV Bicornuate ((n = 26))</th>
<th>V Septate ((n = 43))</th>
<th>VI Arcuate ((n = 42))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total pregnancies</td>
<td>16</td>
<td>15</td>
<td>56</td>
<td>145</td>
<td>110</td>
</tr>
<tr>
<td>Early abortion</td>
<td>6 (37.5)(^c)</td>
<td>3 (20.0)</td>
<td>14 (25.0)</td>
<td>37 (25.5)</td>
<td>14 (12.7)(^b)</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>0</td>
<td>1 (6.6)</td>
<td>0</td>
<td>3 (2.1)</td>
<td>3 (2.7)</td>
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<tr>
<td>Late abortion</td>
<td>1 (6.2)</td>
<td>1 (6.6)</td>
<td>2 (3.6)</td>
<td>9 (6.2)</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>Preterm delivery</td>
<td>4 (25.0)(^c)</td>
<td>8 (53.3)(^c,d)</td>
<td>14 (25.0)(^c)</td>
<td>21 (14.5)(^c,g)</td>
<td>5 (4.5)(^b)</td>
</tr>
<tr>
<td>22–28 weeks</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>28–37 weeks</td>
<td>3</td>
<td>5</td>
<td>11</td>
<td>17</td>
<td>5</td>
</tr>
<tr>
<td>Term delivery</td>
<td>5 (31.3)(^g)</td>
<td>3 (20.0)(^g,b)</td>
<td>26 (46.4)(^g)</td>
<td>75 (51.7)(^g,c)</td>
<td>86 (78.3)(^f)</td>
</tr>
<tr>
<td>Living children</td>
<td>7 (43.7)(^g)</td>
<td>6 (40.0)(^g)</td>
<td>35 (62.5)(^f)</td>
<td>90 (62.0)(^g)</td>
<td>91 (82.7)(^f)</td>
</tr>
</tbody>
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Optimal Evaluation & Treatment of Mullerian Anomalies
Evaluation

“Gold Standard”
- Laparoscopy/Hysteroscopy

Historically HSG/Laparotomy

Current Standard Evaluation
- Saline Infusion Sonohysterogram (SIS) w/ 3D US or MRI
Hysterosalpingogram

- Beneficial for evaluation of tubal patency
- Poorly differentiates septum from bicornuate
  - 55% accuracy
  - Acute vs Obtuse angle is suggestive, but large amount of cross-over
- Low dose radiation
  - Oligomenorrhea & Pregnancy
- Renal Evaluation
  - None
Ultrasound, SIS

- **Accuracy**
  - 93-100% Sensitivity
  - 80-100% Specificity

- **Renal evaluation**
  - Incomplete
MRI

- High sensitivity (92-100%)
- Specificity (100%)
- Characterize muscular/fibrous nature
  - ? Clinical correlation
  - ? Clinical significance

Renal Evaluation
  - Best

Reduced accuracy
  - Remnant/small uteri, cervical dysgenesis and rare anomalies, overestimation of cervical mucosal folds, fibroids may alter, vaginal abnormalities
Telinde’s
Conclusion

- Uterine anomalies do not always fit into the classic categories
- Evidence level is limited to observational studies with selection bias often
- Some strong associations have been developed
  - Higher Risk PTD and SAB
  - Unicornuate
    - Renal anomalies
    - Risk of uterine horn rupture/Ectopic pregnancy
  - Septal metroplasty → Decreased recurrent fetal loss


Buttram VC and Gibbons WE. Fertil Steril 1979; 32:40-46

Silber CG, Magnes RL, Farber M. Mt Sinai J Med 1990; 57: 374-377

Nezhat CR, Smith KS. Hum Reprod 199; 14 (8): 1965-8