16-year-old female with amenorrhea

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Pediatric Endocrinology Fellow
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Chief Complaint

- 16 6/12 yo F presents for evaluation of primary amenorrhea
HPI

- 2 months earlier: mentioned this lack of menstruation to the anesthesiologist during wisdom teeth extraction
- Evaluation was recommended
- Labs done by her PCP showed “normal level of hormones”
- She was then referred to endocrine
HPI

- Normal breast development which began in 5th or 6th grade
- No pelvic cramps, back pain, or lower abdominal pain
- Normal linear growth, weight gain, and development
ROS

- Constitutional: Negative for appetite change, fever, or unexpected weight change
- Endo: Negative for temp intolerance or polyuria
  + Amenorrhea
- HEENT: + Myopic, wears glasses. **Negative for vision changes**
- CVS: Negative for palpitations or chest pain
- GI: Negative for n/v/c/d or abdominal pain
- GU: Negative for urgency, frequency and enuresis
- Skin: Mild acne. **Negative for other skin lesions**
- Neuro: **Negative for headaches or weakness**
- Psych: Negative for mood changes or sleep problems
Further History

- PMH: Primary amenorrhea
- PSH: Right knee arthroscopy at 15 yrs
- FH: Mother, sister, maternal aunt, maternal grandmother had menarche at ~13 yrs
- SH: Lives with parents and younger brother. Older sister is in college. She is in the 11th grade and enjoys playing volleyball.
Physical Exam

- Vitals: T 35.6 °C, HR 81, BP 122/82, RR 16, Wt 67.7 kg (86th%ile), Ht 164.2 cm (59th%ile), BMI 25.1 (86th%ile)
- General: Well-developed, no distress
- HEENT: clear oropharynx, PERRL, EOMI
- Neck: No thyromegaly
- CV/ Pulm/ Chest: RRR, CTAB, Tanner 5 breasts, +axillary hair
- GI: S/ ND/ NT. No masses in inguinal region
- GU: nL external F genitalia with nL vaginal introitus, no clitoromegaly, Tanner 5 pubic hair
- Neuro: alert, no focal deficits, 2+DTRs
- Skin: Warm. No hirsutism, acanthosis nigricans, or acne
Differential Diagnosis?
DDx

- Pregnancy
- Imperforate hymen
- Uterine agenesis (Mayer-Rokitansky-Kuster-Hauser syndrome)
- Complete androgen insensitivity syndrome
- PCOS
- Non-classic CAH
- Primary ovarian insufficiency
- Hyperprolactinemia
Labs/Imaging

- FSH 7.2
- LH 4.2
- Estradiol 20 (30-400 pg/ mL)
- Free testost. 6 (3-9 pg/ mL)
- Total testost. 24 (15-60 ng/ dL)
- AMH 4.0 (0.9-9.5 ng/ mL)
- Karyotype 46, XX
- Urine preg. Negative
- Bone age: c/ w age
- Pelvic U/ S: Uterus not identified. Both ovaries visualized.
Clinical Questions

- How often is Mayer-Rokitansky-Kuster-Hauser syndrome (MRKH) associated with ovarian dysgenesis?
- What is the relationship between anti-Mullerian hormone (AMH) levels and fertility?
MRKH

- AKA Congenital Absence of the Uterus and Vagina (CAUV)
- Incidence = 1:4500 females
- Majority of cases appears to be sporadic
  - Autosomal dominant inheritance has been reported
- Congenital aplasia of the uterus and upper part of the vagina due to incomplete development of the Mullerian duct
MRKH

- Normal development of secondary sexual characteristics
- 46, XX karyotype
- 1st clinical sign is usually primary amenorrhea
- Subdivided:
  - Type I (isolated) or Rokitansky sequence
  - Type II
  - MURCS (Mullerian duct aplasia, Renal dysplasia and Cervico-thoracic Somite anomalies)
## MRKH & Ovarian Dysgenesis

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients (n)</th>
<th>Malformation of the ovary</th>
<th>Malformation of the Fallopian tube</th>
<th>Changes in the renal system</th>
<th>Changes in the skeletal system</th>
<th>Changes in the nervous system</th>
<th>Inguinal hernia</th>
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Values in parentheses are percentages.

ND = not described.
AMH & Folliculogenesis

- AMH is secreted by growing follicles
- Acts in the ovary by 2 major mechanisms:
  - 1: Inhibits initial recruitment of primary follicles
  - 2: Inhibits the sensitivity of antral follicles to FSH
Assessment of ovarian reserve with anti-Müllerian hormone: a comparison of the predictive value of anti-Müllerian hormone, follicle-stimulating hormone, inhibin B, and age

Ryan M. Riggs, MD; E. Hakan Duran, MD; Margaret W. Baker, JD; Thomas D. Kimble, MD; Elie Hobefa, MD; Larry Yin, MD; Lira Matos-Boddin, BS; Ben Leider, MD, PhD; Laurel Stadtmauer, MD, PhD
“poor responders”
< 4 oocytes retrieved
(n = 11)

“excessive responders”
> 15 oocytes retrieved
(n = 38)
AMH Levels & Fertility

Follow-up

- Patient seen by ob/gyn 1 month later
- Repeat labs:
  - FSH 6.7
  - LH 3.4
  - Estradiol 28 (30-400 pg/mL)
- DEXA- spine BMD appropriate for age
- No immediate concerns noted. Low concern for hypoestrogenism at this time.

Plan:
- Repeat labs and pelvic U/S in 4 months
Summary

- MRKH presents as 1° amenorrhea in a phenotypically nL female with 46, XX karyotype and nL 2° sexual characteristics
- MRKH may be associated with ovarian and/ or Fallopian tube malformations in up to 10% of patients
- Research has shown a stronger correlation between AMH levels and # of retrieved oocytes than age, FSH, inhibin B, LH, or estradiol
- Therefore, AMH may potentially be used as an accurate assessment of ovarian reserve and prediction of oocyte retrieval rates
  - sensitivity (83-84%) and specificity (67-79%)
References


