3 Year-Old Girl with Vaginal Bleeding

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History of Present Illness

- 3 y 11 mo girl presents with breast development x 1 week and vaginal bleeding x 2 days
- Evaluation in the ED was negative for trauma
- Denies exposure to estrogen-containing products, steroids, tea tree oil
- Has always been tall, no noticeable growth spurt
- No acne, no mood changes
## Past History

### Past Medical History
- Eczema

### Birth History
- Full term, NSVD

### Past Surgical History
- None

### Allergies
- None

### Medications
- Hydrocortisone 2.5% cream
- Ketoconazole 2% shampoo twice weekly
Family History
• Mother: 68 inches tall
• Father 68 inches tall
• No early or late puberty
• No ovarian, uterine cancers

Social History
• Lives with her mother, father, 2 older brothers and a younger sister. Attends pre-school.
Review of Systems

- Constitutional: Negative for weight gain or appetite change
- HENT: Negative for congestion and rhinorrhea
- Respiratory: Negative
- Cardiovascular: Negative
- Gastrointestinal: Negative for abdominal pain
- Genitourinary: + vaginal bleeding and vaginal discharge
- Musculoskeletal: Negative for myalgia
- Skin: + Breast development x 1 week. Brown "birthmarks” increased number since age 1 year
- Neurological: Negative for headaches
- Psychiatric/Behavioral: Negative for behavioral problems and agitation
Physical Exam

- BP 100/56 HR 120 Ht: 106.2 cm (91%ile) **Ht age: nearly 5 years** Wt: 17.5 kg (80%ile) BMI 15.6 kg/m2 (57%ile)
- Constitutional: Well-developed and well-nourished. Playful.
- Neck: No goiter. No adenopathy.
- Cardiovascular: RRR no murmurs
- Pulmonary/Chest: CTAB. **Bilateral breast buds**
- Genitourinary: Many Tanner II hairs on the mons pubis. Hyperpigmented labia minora, dried blood intralabially, no clitoromegaly, no lesions or bruising. Diaper was partially covered in brownish-red blood with few clots
- Musculoskeletal: Normal range of motion.
- Neurological: Normal DTRs. CN intact bilaterally.
- Skin: **3 cm brown macule with jagged borders on left posterior thigh, 1 cm brown macule with smooth borders on lateral right brow, 2 x 0.5 cm macules on back and left hand.** No axillary hair, acne or hirsutism.
Differential Diagnosis: Precocious Puberty

• Gonadotropin-Dependent  •  Gonadotropin-Independent

– Idiopathic
– Hypothalamic hamartomas
– CNS tumors
– Suprasellar defects (ex: Rathke cleft cysts)
– Trauma
– Neurofibromatosis type 1
– Primary hypothyroidism-Van Wyk-Grambauch

– Estrogen overproduction:
  • Ovarian cysts
  • Ovarian granulosa cell tumors
  • McCune-Albright syndrome
  • Sertoli-Leydig cell tumors (+/- Peutz-Jeghers syndrome)

– Androgen overproduction
  • Non-classic CAH
  • Androgen-secreting adrenal tumors
  • Ovarian hyperthecosis
Evaluation

7:52 am
• LH <0.1 mIU/mL
• FSH <0.1 mIU/mL
• Estradiol 48 pg/mL (4-12)
• DHEA-SO4 <15 ug/dL

• Bone age: 4 years 3 months at chronological age 3 years 11 months (SD +/- 7-8 months)
Transabdominal Pelvic Ultrasound

- Enlarged uterus with pubertal configuration: 4.3 x 1.7 x 2.7 cm
- Cystic lesion of right ovary with slight irregularity of its wall measuring 4.6 x 3.3 x 2.5 cm

Normal left ovary: 2.1 x 1.3 x 1.6 cm.
Diagnosis

• Gonadotropin-independent precocious puberty due to autonomous estrogen production from a large solitary ovarian cyst

• Plan:
  – Recheck U/S in 2-3 weeks due to size
  – Counseled on risk of ovarian torsion
  – Consider McCune-Albright if recurs
Follow-Up: 8 weeks

1 week later
- Cessation of menses, regression of breast tissue
- Growth of 1.8 cm in 1.5 months

8:20 am
- LH <0.1
- FSH 1.4
- Estradiol 4 pg/mL

Pelvic Ultrasound
- Uterus: Decreased from 4.3 x 1.7 x 2.7 cm to 2.0 x 0.9 x 1.4 cm
- Right ovary: Decreased from 4.6 x 3.3 x 2.5 cm to 2.6 x 1.1 x 1.3 cm
  - Cyst max diameter 4.6 cm → 2.4 cm
- Left ovary: stable
McCune-Albright

- Somatic mutation of $G_s\alpha$ protein-constitutive activation of cAMP
  - Endo: activation of TSH, GH, ACTH
  - Non-Endo: tachycardia, liver disease, hypophos
- Classic triad:
  - Sexual precocity with recurrent ovarian cysts absent gonadotropins
  - Café-au-lait macules
    - Irregular borders, segmental
  - Polyostotic fibrous dysplasia
McCune-Albright

- May present diagnostic challenge in young girls
  - Frequency and characteristics of recurrent ovarian cysts are not predictive\(^1\)
  - 1-5 Café-au-lait macules are found in up to 10% of healthy individuals
  - Sexual precocity may pre-date bone changes by many years\(^2\)
    - Early detection enhanced by technetium-99m methylene diphosphonate
  - Molecular analysis is limited by large variation in distribution and degree of \(G_\alpha\) mutation within indiv
References

