5yo girl with vaginal bleeding

Matthew Wise, MD
Med-Peds Endo

January 26, 2012

HPI

- 5y 10m Caucasian girl
- 2mo prior:
  - labial swelling
- 1mo prior:
  - painless vaginal bleeding x5days,
  - pads q4-6h
  - breast buds noted
- Presents to PCP, parents distressed

Advice to PCP?

- Consider OB/Gyn eval
- Growth Chart
- Bone Age
- Early AM FSH, LH, estradiol
- TSH
- Trans-abdominal US

Further Hx, ROS

- - body odor, hair
- - acne
- - known exposure to estrogen products
- - recurrence of bleeding in past 3-4weeks
- + mood irritable
- + growth spurt over 4-5 month period

Med/Surg History

PMH

- Seasonal allergies
- Reactive airway disease
- Bilateral inguinal hernia repair 3mo
- Salivary gland surgery 2yrs

Birth

- Full term, uncomplicated

Developmental

- Normal timing of milestones

Allergies: NKDA

Meds:

1. Zyrtec
2. Benadryl

Family and Social History

Family

- Mother 44yrs, Graves' disease; RAI; hypothyroid
- Father 45yrs, healthy
- 22yo sister – dx with teratoma at 11, involving ovary, presenting with abdominal mass and urinary sx – surgically removed; recurrent ovarian cysts
- No FH of early puberty

Social

- Mother is pediatric nurse
- Father is paramedic
- 8 siblings, mother pregnant
- Kindergarten

Physical Exam

Age 4.5: Wt (45%) Ht (50%)
Age 5.5: Wt (45%) Ht (50%)

97.6 F, 98, BP 101/73, RR 13, Wt 21.2 (65%), Ht 115.5cm (63%)

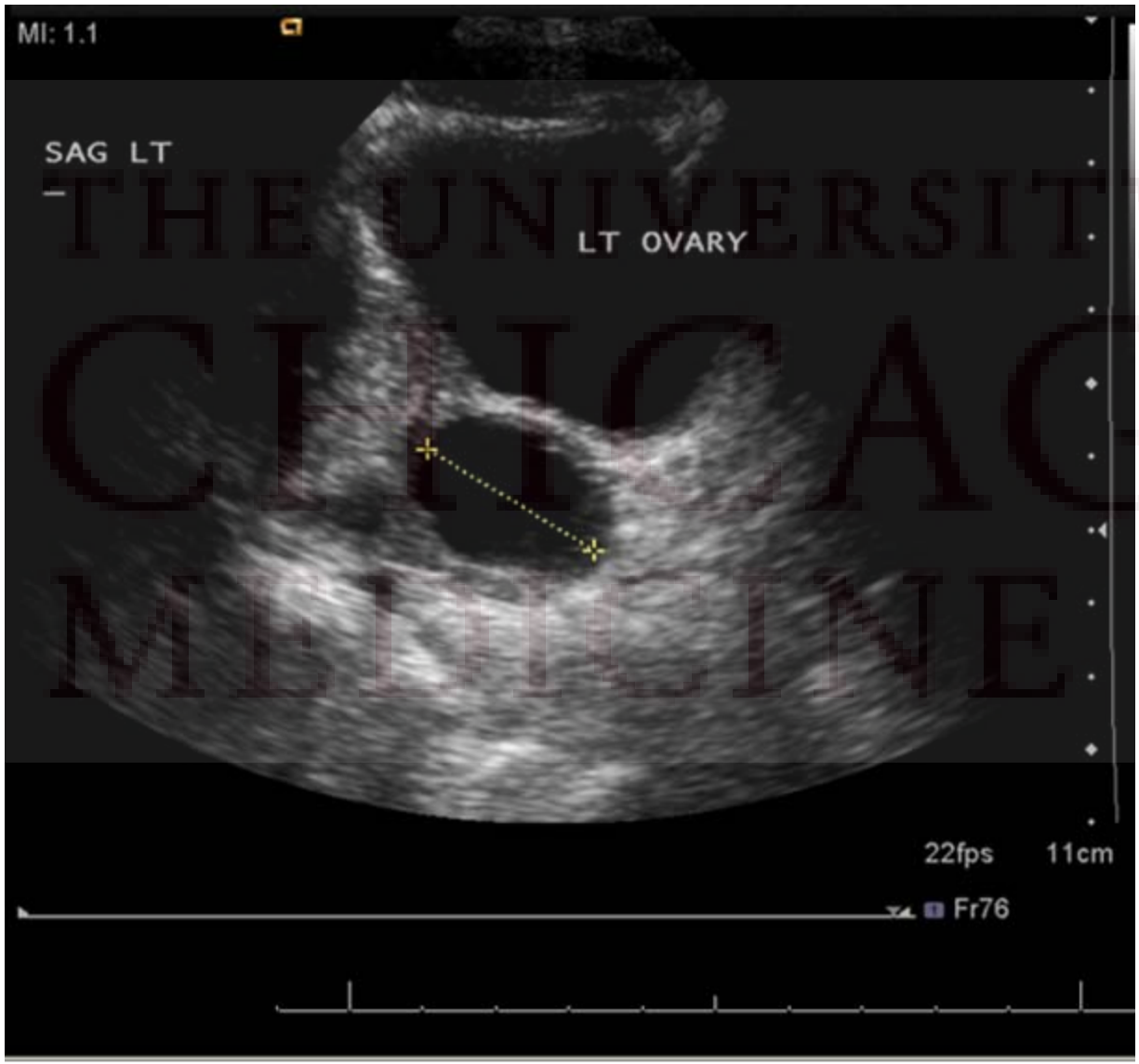
- Gen: Well appearing, non-cushingoid/non-acromegalic
- Head/Face: no dysmorphia, EOM-I, PERRLA, no oral/midline lesions
- Neck: no thyromegaly, no acanthosis
- Resp: CTA B
- CV: RRR no m/r/g
- Abd: Soft, scaphoid, non-tender, no masses
- GU: Breasts tanner II (buds) 1cm R, 0.8cm L; no axillary/pubic hair
  no clitoromegaly; mildly estrogenized vaginal mucosa/labial edema
- Derm: 1cm café-au-lait with irregular border L inguinal; brown nevi scalp, upper back; no acne, no body hair

Laboratory/Radiologic Data

<u>3 weeks prior:</u>

- 17:14 LH 0.1 mIU/mL
  FSH 0.1 mIU/mL
  estradiol 27 pg/mL (<20)
  DHEA-S <15 mcg/dL
  TSH 2.6 mIU/mL
- Bone Age: 6.5 years (+1.0 SD)
- Transabd US: L ovarian cyst 2.6x2.6x1.9cm
  Uterus: 9.4 cm^3, L ovary 15.5cm^3, R ovary 7.4cm^3
  endometrial stripe 2.4mm

Trans-abdominal US



Differential Diagnosis

Gonadotropin-Independent Precocious Puberty

Precocious Pseudopuberty (in girls)

Estrogen overproduction

- ovarian cysts
- ovarian granulosa cell tumors
- Sertoli-Leydig cell tumors +/- Peutz-Jeghers syndrome
- McCune-Albright syndrome
- exogenous steroids
- hypothyroidism

Androgen overproduction

- ovarian arrhenoblastomas
- ovarian hyperthecosis
- non-classic CAH
- androgen-secreting adrenal tumors
- glucocorticoid resistance synd (GRS)
- Cushing's syndrome
- exogenous steroids

Central Precocious Puberty – but missing early AM rise in LH/FSH

Recommendations

*Highest suspicion for functional ovarian cyst

Monitor for:

- Recurrence of vaginal bleeding
- Progression/Regression in breast development
- Growth velocity

Repeat in 2mo (sooner if progression, or menses)

- AM gonadotropins, estradiol, DHEA-S
- Transabdominal US

Follow-Up

1 month later:

- Mother felt that pt was irritable, breast tenderness

- Labs: 8am
  - LH <0.1 (pre-pubertal <0.2)
  - FSH 0.8 mIU/mL (pre-pubertal <2.7)
  - Estradiol 3 pg/mL (pre-pubertal 4-12)
  - DHEA-S <15 ug/dL (<45)

Follow-Up

- Repeat Abdominal US

  (delayed until mid-February)

Clinical Questions

1) How common are functional ovarian cysts in pre-pubertal children?
2) Do the ultrasound characteristics aid in diagnosis?
3) What is the expected clinical course and suggested management?

1. How common are functional cysts?

- 2-53% of all pre-pubertal girls have ovarian cysts
  - decreasing frequency with age
  - majority are small < 9mm (average 2-3mm)

- Autonomous ovarian cysts were present in 5% of the girls with ovarian cysts (Millar 1993)
  - majority are large

2. US Characteristics Aid in Diagnosis?

- Size of cyst predicts autonomous function
  - Rodriguez-Macias (1993): 7 patients:
  - King (1993): 4 peripheral (>9mm)
    23 central (<9mm)

Table 2 Acute ovarian follicular cyst: ultrasound and hormonal data at diagnosis

Case	Ultrasound ovarian cyst (mm)	Plasma E2 (pg/ml)	Plasma FSH* (mIU/m)l	Plasma LH* (mIU/ml)
1	65	43	< 0.2/< 0.2	< 0.2/< 0.2
2	40	40	< 0.2/0.6	< 0.2/< 0.2
3	30	270	0.2/0.4	0.2/0.4
4	25	30	0.2/0.7	0.2/0.2
5	50	5	0.5/0.5	0.3/0.9
6	15	10	0.2/2	0.2/0.7
7	46	125	0.2/0.9	0.2/0.3

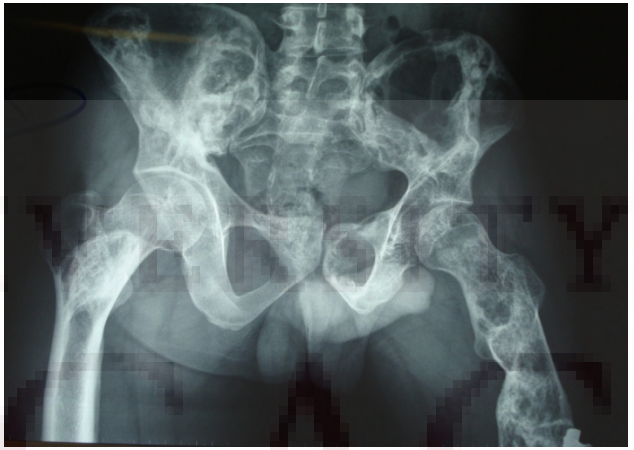
*Basal/LHRH peak response.

- Contralateral ovary enlargement associated with central precocity
  - King (1993): 4 peripheral – unilateral ovarian enlargement
    23 central – bilateral ovarian enlargement

3. Natural History and Management

- Self-limited, no treatment necessary
- Spontaneous regression of cysts and pubertal signs within weeks to few months
- Larger cysts associated with torsion
- Persistence: surgery since can't exclude tumor
- Recurrence: consider McCune-Albright

McCune-Albright



Lumbroso (2004) JCEM

- 39 girls with precocious pseudopuberty, no other signs of McCune-Albright
  - 33% found to have mutation
  - **70% of pts who had cystic fluid analyzed were + for the mutation (9 of 13)**

Take Home

- Distinguishing pseudopuberty (as with ovarian cysts) from central precocious puberty is essential as the management is different
- Autonomously functioning ovarian cysts are generally large, most >1cm and typically >2cm, than cysts seen in central precocious puberty
- Management is conservative with monitoring for spontaneous regression within weeks to few months

References

- de Sousa et al. Precocious pseudopuberty due to autonomous ovarian cysts: a report of ten cases and long-term follow-up. Hormones 2008; 7(2):170-174.
- Rodriguez-Macias et al. Follow up of precocious pseudopuberty associated with isolated ovarian follicular cysts. Arch Dis Chid 1999; 81:53-56
- Scully et al. Case 57-1989. NEJM 1989; 321(21):1463-1471.
- Brandt et al. Ovarian cysts in infants and children. Seminars in Pediatric Surgery 2005; 14:78-85.
- Millar DM et al. Prepubertal ovarian cyst formation:5 years experience. Obstet Gynecol 1993; 81(3):434-438.
- Brauner et al. Clinical, biological, and genetic analysis of prepubertal isolated ovarian cyst in 11 girls. PLoS ONE 2010; 5(6):e11282.
- Strickland J. Ovarian cysts in neonates, children and adolescents. Current Opinion in Obstetrics and Gynecology 2002; 14:459-465.