11 year old boy with microphallus

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HPI

- 11 and 11/12 year old boy born with microphallus
- Microphallus and unilateral cryptorchidism noted shortly after birth
- Labs at 2 weeks of life:
  - Testosterone <20 ng/dL
  - LH <0.15 mIU/L
  - FSH none detected
- Cryptorchid testis spontaneously descended
- Received testosterone injections 25 mg x 3 in infancy with resulting increase in phallus
- Seen at age 5 6/12 years
  - Stretched phallic length 4.3 cm (3.8-8.2 cm)
  - Instructed to follow up around time of puberty
HPI

- Upon return to Pediatric Endocrinology clinic at age 11 and 11/12 years, phallus seems to have increased in length since last visit.
- Linear growth has been appropriate.
- Pubic hair x several months but no other pubertal changes yet.
- Currently not concerned that he is behind other boys in his class in terms of development and maturity.
- Poor ability to smell revealed only upon specific questioning.
PMH

- Born FT with BW 8 lbs
- Microphallus as noted previously
- Strabismus s/p eye surgery at age 3
Family History

- Father 47 years old, 210 lbs, 68 inches, normal pubertal history
- Mother 41 years old, 145 lbs, 66 inches, menarche at 11 years
- MPH 69.5 inches
- No pubertal disorders in family
- Mother has RA and fibromyalgia
- MGM and MGGM with DM2
Social History

- LAHW with father and 8 year old sister
- Parents divorced with joint custody
- Father is farmer
- 6th grade, gets As and Bs, likes to read a lot
- Has close group of friends
Physical Exam

- Wt 62.2 kg (97%), Ht 147 cm (40%)
- T 96.1, HR 78, BP 114/64
- Eyes: PEERL, EOMI
- OP: braces, otherwise unremarkable
- Neck: Normal thyroid, no LAD
- CV: RRR, nl S1 and S2, no edema
- Resp: CTAB
- GI: Soft, ND, NT, no HSM
- Skin: Mild acanthosis lateral neck
- MSK: NI gait, station, strength, and tone
- Neuro: 2+ DTRs
- GU: Testes 1.5 cm bilaterally, SPL 5.0 cm (3.7-9.0), slight glanular hypospadias, T2 pubic hair
- Smell test: Identified 2/3 smells incorrectly
Differential Diagnosis of microphallus

- Hypogonadotropic hypogonadism
  - Isolated
    - KAL1
    - KAL2
    - FGFR1
    - GNRHR
    - GPR54
    - SNRPN
    - LEP
    - LEPR
    - DAX1

- Multiple pituitary deficiency
  - PROP1
  - HESX1
  - LHX3
  - PHF6

- LH receptor defects
- Hypergonadotropin hypogonadism
- Testosterone synthesis defects
- PAIS
- Structural anomalies
Initial Work-up

- Bone age 12.5 years -> final predicted height 69 inches
Return visit

- Returned at 12 and 6/12 years
- More attuned to poor sense of smell
- Still feels growing fine
- No change in pubic hair or other new pubertal changes noted
  - Not concerned
- Physical Exam
  - Wt 65.9 kg (96.7%), Ht 150.8 cm (41%)
  - Testes 1.2 cm R, 1.3 cm L
  - SPL 5.5 cm
  - T2 pubic hair
Labs

- LH <0.1 mIU/mL
- FSH 0.4 mIU/mL
- Testosterone
  - Total 8 ng/dL
  - Free 4 pg/mL
Prediction of spontaneous puberty

- Retrospective comparison of males with complete HH vs. partial HH vs. constitutional delay
- All had baseline FSH and LH as well as GnRH testing
Mini-puberty of early infancy

- Transient surge in the hypothalamic GnRH pulse generator-pituitary gonadotropin-gonadal apparatus
- FSH, LH, and testosterone
- Increase in testicular volume, Sertoli cells
- Inhibin B
- Function?
Function of Mini-Puberty

- Future fertility
  - Sertoli cells central to spermatogenic function
  - Study of adult men with HH receiving GnRH treatment
    - Increased testicular volume and sperm count response predicted by baseline inhibin B and history of at least partial pubertal development

- Masculinization of the brain?
  - 8 subjects with microphallus reported male gender identity and psychosocial behavior regardless of whether treated before or after age 2 years
Our Patient

- History of microphallus and cryptorchidism as well as labs in infancy and current FSH consistent with hypogonadotropic hypogonadism
- Hyposmia suggests Kallmann syndrome
- Enrolling in reproductive disorder genetics study
- Will be treated with testosterone replacement
References