Interactive Case Based Learning

Student Endocrinology Exposure and Development

An initiative of PES Education Committee
16-year-old boy presenting with small size of testicles
In light of these concerns, what questions will you ask in the history?
History of Pubertal Progression

- Pubic hair
- Facial hair
- Voice cracking
- Hidden penis, difficulty in urination
- Acne
- Body odor
Growth related questions

• How is the child growing for weight and height

• Height of parents to calculate the mid-parental height
  • [Midparental height calculation]

• Parental history of pubertal delay (“late bloomers”)
Other Relevant History / Review of Systems

- Sense of smell
- Low blood sugar in the neonatal period
- Gynecomastia
- Vision problems
- Loose stools, chronic cough
- Radiation exposure, trauma
- Medication use (i.e. glucocorticoids, chemotherapeutics)
Continued

- Developmental History: social interaction, history of learning disability and problem solving skills
- Psychiatric History: ADHD, anxiety, depression
Clinical examination:

Facial features: look for dysmorphism

Eye: Visual field examinations and pupillary light reflex

CVS: murmur

Spine: Scoliosis and Kyphosis

Musculoskeletal: increased flexibility of joints
Genitourinary Examination: boys

Orchidometer

- The patient's testicular volume is estimated by palpation and comparison with the models on the orchidometer.
- Each of the beads is labeled with its volume, ranging from 1 to 25 ml
Genital development stages for boys

<table>
<thead>
<tr>
<th>Stages</th>
<th>Genital Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Prepubertal</td>
</tr>
<tr>
<td>2</td>
<td>Testicles 4-6mL, early penile, and scrotal skin redness</td>
</tr>
<tr>
<td>3</td>
<td>Enlargement of penis (length at first) and further growth of testes:8-12mL, scrotal growth</td>
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<tr>
<td>4</td>
<td>Increased size of penis with growth in breadth and development of glans, scrotal skin darker, Testicles:12mL</td>
</tr>
<tr>
<td>5</td>
<td>Stage 5 – Adult genitalia, testicular volume of 15mL</td>
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</tbody>
</table>
## Pubic hair development in boys

<table>
<thead>
<tr>
<th>Stages</th>
<th>Pubic hair Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No pubic hair</td>
</tr>
<tr>
<td>2</td>
<td>Pigmented hair at the base of the penis</td>
</tr>
<tr>
<td>3</td>
<td>Hair begins to curl and start to spread laterally</td>
</tr>
<tr>
<td>4</td>
<td>Adult type distribution but does not extend to thighs</td>
</tr>
<tr>
<td>5</td>
<td>Extending up to the thigh</td>
</tr>
</tbody>
</table>
Which auxological measurements are important to take for this patient?
Upper to lower segment ratio

- Lower segment: top of the symphysis pubis to the plantar surface of the foot

- Upper segment calculation: subtract the lower segment from the child's height
  - Higher at birth and then it gradually decreases to 1 at 10 years
  - After 10 years it is <1
Arm span

- Distance between the tips of the middle fingers when the arms are raised to a horizontal position.

- At birth, the arm span is typically less than length (by at least 2.5 cm).

- By approximately 10 years of age in boys and 12 years of age in girls, the arm span exceeds height.
So far, we know about the 16-year-old patient:

- History of pubic hair starting at 11 years of age
- Shy personality
- Mid parental height at 50% but current height 90%ile
- BMI at 30%
- Decreased US/LS and high arm span

Examination:

- Gynecomastia
- Penis size: 6cm
- Tanner 2 testicular volume (6ml bilaterally, firm)
- Tanner IV pubic hair
In light of this clinical vignette, which differential diagnosis are we thinking about?
Differentials

- Pituitary disorder
- Kallman syndrome
- Constitutional delay of puberty
- Klinefelter syndrome
- Systemic causes: celiac and Inflammatory bowel disease
Further Laboratory evaluation showed:

- Luteinizing hormone (LH): 20 IU/L
- Follicle stimulating hormone (FSH): 50 IU/L
- Testosterone value: 100 ng/dl (reference Tanner IV: Tanner 2)
- Chromosomal analysis: 47,XXY
- Blood urea: 15 mg/dl (7-20)
- AST: 20 IU
- ALT: 20 IU
- Tissue transglutaminase: <1U/ml
- TSH: 2.0 uIU/ml, Free T4: 1.2 ng/dl
- Prolactin: 20 ng/ml
Approach to delayed puberty

FSH↓: Issues in the pituitary gland and/or hypothalamus

FSH↑: Issues in the testis
Causes of delayed puberty

Testicular issues
- X chromosome abnormalities
- Anorchia
- Luteinizing hormone receptor gene mutation
- Radiation, chemotherapy
- Trauma / surgery
- Inflammation of the testis

Problems in pituitary and hypothalamus
- Constitutional delay
- Kallman syndrome,
- Chronic illness, malnutrition, exercise
- Tumors (craniopharyngioma)
- Hyperprolactinemia, Cushing Syndrome, panhypopituitarism
- Infectious –meningoencephalitis
Let’s focus on Klinefelter Syndrome
Epidemiology

More common than we think with the prevalence of 1 to 2.5 per 1000 boys.

Only 25 to 50% of patients with Klinefelter syndrome are diagnosed during their lifetimes.
Age wise overview

**Neonate**
- Lack of specific physical features
- Micropenis

**Early childhood Years**
- Problems in learning and social interaction

**Pubertal Years**
- Gynecomastia
- Small Testes
What is the reason for low testosterone levels?
Explanation

Primary testicular failure (hypergonadotrophic hypogonadism).

Testicular failure is due to progressive fibrosis and destruction of both functional (steroidogenic and spermatogenic) compartments of the testes.
What is the reason for gynecomastia?
Some testosterone is converted to estradiol which leads to some breast development, known as gynecomastia.
What is the reason for tall stature in Klinefelter syndrome?
Explaination

Lack of testosterone leads to gradual gain in height without epiphyseal closure

+SHOX Gene Dose Effect
Evaluation / Further Management
Evaluation

- Sex hormones: Testosterone, estradiol, FSH, and LH
- Fasting glucose for glucose intolerance
- Lipids for evaluation of hypertriglyceridemia
- Thyroid function for evaluation of thyroid autoimmunity
- Complete blood counts for evaluation of anaemia
- 25 hydroxy Vitamin D levels for evaluation of osteoporosis
Increased autoimmunity

Relative increase in estrogen in comparison of testosterone.
Radiological Evaluation

- Bone age X Ray for evaluation of bone maturation depending on the age of presentation
- Bone densitometry for evaluation of bone density in certain cases
What is the management?
Testosterone

The goal of testosterone therapy is to cause gradual facial and pubic hair, muscle development without compromising adult height.
Family centered interdisciplinary approach

• Involvement of support groups
• Psychiatrists
• Counsellors
Feedback

Please provide any feedback/suggestions to improve the learning experience.

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