Radiological Evaluation of Central Precocious Puberty

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Radiology Core Clerkship
I. Brief review of pubertal physiology
II. Features of precocious puberty
III. Introduction to our patient
IV. Bone age determination methods and roles in diagnosing precocious puberty
V. Role of neuroimaging in evaluating central precocious puberty
VI. Treatment of central precocious puberty
Puberty is a predictable sequence of physiological and physical changes that is initiated after the activation of the hypothalamic-pituitary-gonadal axis.
Sex hormones (i.e. testosterone and estrogen) cause the development of secondary sexual characteristics.

http://www.unsystem.org/SCN/archives/adolescents/p08.gif
With thyroid hormone and growth hormone, sex hormones promote bone growth by stimulating chondroblasts to proliferate at the growth plate. In both girls and boys, estrogen closes the plate in late adolescence.
If pubertal changes occur too early, too late, or out of sequence, the clinician should be suspicious of underlying pathology.

http://www.merck.com/media/mmhe2/figures/MMHE_23_270_01_eps.gif
**PRECOCIOUS PUBERTY**

**DEFINITION**

- Puberty before 8 in girls; before 9 in boys

**Implications**

- Accelerated bone growth in childhood and decreased adult height.
- Psychological distress.
PRECOCIOUS PUBERTY

CLINICAL FEATURES

- **Two Forms**
  - (1) **Central Precocious Puberty**:
    - Pubertal changes in normal predictable sequence.
    - Early activation of hypothalamic-pituitary-gonadal axis (HPG-axis).
    - ↑ gonadotropins and ↑ sexual steroids.
  - (2) **Peripheral Precocious Puberty**:
    - 1 or 2 pubertal changes; out of sequence
    - HPG-axis independent source of sex steroids from other sources (ie adrenal disease; tumors)
    - ↓ Gonadotropins via negative feedback of ↑ sexual steroids
4½ year old girl who presents with:
- Tanner 3 breasts
- Uterine bleeding
- Height in 95th percentile
- No neurological deficits
- High clinical suspicion for precocious puberty
Advanced bone age in a patient with new development of secondary sexual characteristics suggests the onset of puberty.
STUDY #1
Plain film of hand/wrist

- Left Hand/Wrist Radiograph
  - Simple
  - Minimal Radiation Exposure
- Use radiograph to determine bone age
  - Assess degree of bone maturation.
    - Is Bone age <, =, or > Chronologic age?
    - If Bone age 2 years > Chronologic age → Advanced.
Bone Age Determination by Greulich and Pyle Method

Greulich and Pyle Method

- “Radiographic Atlas of Skeletal Development of Hand and Wrist”
- Radiograph is compared to standard radiographs by age and gender in atlas.
Bone Age Determination by Tanner-Whitehouse

- **Tanner-Whitehouse**
  - 20 Regions of Interest
  - Each region is graded at stages of development (A-I)
  - A numerical score is given to each stage and the sum corresponds to a particular age group.
  - More reproducible and accurate but time consuming. (Bull et al. *Arch Dis Child* 1999)

http://homepages.inf.ed.ac.uk/rbf/CVonline/
OUR PATIENT:
Advanced bone age on hand radiograph

Our Patient:
Chronologic Age: 4 Bone Age: 7

Control Patient:
Chronologic Age: 7 Bone Age: 7
Clinical and radiographic evidence confirms diagnosis of precocious puberty.

Central or Peripheral?

Our Patient’s Hormonal profile:
- Elevated Gonadotropins
- Elevated sex steroids
CNS Lesions Associated with Central Precocious Puberty (CPP)

- 85% Idiopathic-no identifiable CNS lesion
- Other 15% may have significant morbidity:
  - Hypothalamic Hamartoma
  - Craniopharyngioma
  - Ependymoma
  - Optic Fibromas
  - Optic Gliomas
  - Subarachnoid Cysts
  - Hydrocephalus
  - Cerebral Vascular Accidents
  - Encephalitis

Arcuate Nucleus regulates sexual development-localized

Found in area between the Mamillary bodies and pituitaty infundibulum-TUBER CINERUM

brainmind.com/BrainMaps4.html

Courtesy of Boston Children’s Hospital
Magnetic Resonance Imaging

- No radiation
- Allows exact localization and assessment of size of masses
- Shows effect on structures adjacent to lesion
- Superior to CT in detection for precise delineation and character of intracranial pathology

Out of 9 CPP patients who had both MRI and CT, 4 patients had lesions found on MRI that were not found on CT (Kornreich et al. Ped Rad 1995)

CT can be employed if contraindications to MRI w/ GAD contrast
T1 weighted w/o GAD
Sagittal

Courtesy of Boston Children’s Hospital
Non-enhancing ovoid mass continuous with hypothalamus in tuber cinereum. Signal similar to gray matter.
OUR PATIENT

T2 weighted Coronal

Enhancing on T2
**Hypothalamic Hamartoma**

- Heterotopic, nonmalignant, hypothalamic mass
- Thought to act independently of normal cortical inhibitory signals, thereby causing CPP.
9 y/o boy with Neurofibromatosis 1 and CPP

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<th>T1 weighted post GAD and FAT SAT</th>
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- Slight peripheral enhancement and thickening of optic chiasm
- Optic Glioma

Courtesy of Boston Children’s Hospital
4 y/o Boy with CPP

T1 weighted w/ GAD
Sagittal

Enhancing spherical mass continuous inferiorly w/ optic chiasm w/o orbital extension

Optic Glioma

(Kornreich et al. Ped Rad 1995)
Ng, et al. Arch Dis Child 2003

Arachnoid Cyst with Obstructive Hydrocephalus

Hypothalamic Pilocytic Astrocytoma
TREATMENT

- If associated neurological symptoms or risk of malignancy, surgery may be indicated
- If idiopathic, no associated neurological symptoms, and no risk of malignancy → medical management:
  - GnRH activates HPG axis if administered in a pulsatile manner.
  - If given continuous, GnRH shuts down axis.
  - Continuous Lupron (GnRH agonist) can slow accelerated puberty and improves final height by shutting down the HPG axis.
- Follow-up radiographs and pelvic ultrasounds in girls can assess efficacy of treatment.

(Carel et al. J Clin Endo Metab 2003)
SUMMARY

- Radiological tests are important for both the diagnosis and management of Precocious Puberty.
- Advanced bone age in the setting of the onset of secondary sexual characteristics confirms early onset puberty.
- Hormonal Profile differentiates Central and Peripheral Precocious Puberty.
Although most cases are idiopathic, neuroimaging, preferably MRI, is indicated in all children with CPP, given morbidity associated with some of the intracranial lesions.

Medical versus Surgical management depends on the etiology, presence of associated neurological symptoms, and risk of malignancy.

Treatment of CPP is critical given the risk of psychological distress and decreased adult height.
REFERENCES

4. Ng, et al. “Cranial MRI scans are indicated in all girls with central precocious puberty.” *Arch Dis Child*, 2003; 88:414-418.

Images
4. brainmind.com/BrainMaps4.html
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