Child With Suspected Klinefelter Syndrome

Suggestive history and physical findings	Initial laboratory and/or radiologic work-up can include:	When to refer	Items useful for consultation	Additional information
Symptoms/Signs: • Tall stature (0.7 SDS > midparental target height) with decreased upper to lower segment ratio (~ height – arm span > 2 cm) • Small testes for age • Learning disabilities • Delayed speech development • Reduced penile length • Delayed/ stalled out puberty • Gynecomastia • Hypertelorism • High arched palate • Hypotonia • BMI above mean Differential Diagnosis	**Blood tests:** • Karyotype • FSH, LH • Testosterone (may be normal in boys < 10 years old and some older boys) Other tests to consider after consultation with Pediatric Endocrinologist: • Bone Age x-ray • TSH, FT4 • Estradiol, Sex Hormone Binding Globulin • Fasting glucose, lipids, HgbA1c • Hct/hgb • 25-OH Vitamin D	**Routine:** Nearly always Find a Pediatric Endocrinologist	Previous growth data/growth charts Pertinent medical records Recent laboratory and radiologic studies including the bone age film (not just the report)	Additional Information Klinefelter Syndrome: A Guide for Families References

Differential Diagnosis:

Delayed Puberty/ small genitalia for age:

- Constitutional delay of growth and puberty: Usually height is < target height %
- Primary gonadal failure: typically no syndromic features
- Hypogonadotropic hypogonadism
    - Possible associations: sensorineural hearing loss; anosmia/hyposomia; cleft palate; renal abnormalities

Tall Stature:

- Genetic tall stature
- Marfan syndrome: +/- Family history, ectopia lentis (upward subluxation), aortic root dilatation, dural ectasia, long slender limbs and arachnodactyly (thumb sign and wrist sign) pectus carinatum, scoliosis, dolichocephaly, myopia,
- Homocystinuria: Similar skeletal findings to Marfan syndrome, downward subluxation of lens, osteoporosis, mental impairment, thromboembolic episodes
- Sotos syndrome: Developmental delay, advanced bone age, macrocephaly, frontal bossing, high anterior hairline, frontotemporal hair scarcity, prominent mandible and pointed chin
- Beals syndrome: Similar to Marfan but joint contractures, folded ear helixes, micrognathia
- Beckwith-Wiedemann syndrome: Prenatal and postnatal overgrowth with omphalocele, macroglossia, visceromegaly, developmental delay
- Simpson-Golabi-Behmel syndrome: X-linked R, similar to BWS but upturned nasal tip, broad nose, high arched/ cleft palate, hypoplastic or absent index fingernails, relatively normal cognitive development.
- Weaver syndrome: Developmental delay, camptodactyly, advanced bone age, broad face, hypertelorism, flat occiput, depressed nasal bridge, hypertonia
- Fragile X
- Endocrine abnormalities
    - Pituitary gigantism
    - Lipodystrophy
    - Precocious puberty
    - Hyperthyroidism
    - Aromatase deficiency
    - Estrogen resistance
    - Familial Glucocorticoid deficiency

Additional information:

- More common than suspected: 150/100,000 live born males
- Less than 10% diagnosed before puberty
- More than 75% have learning disabilities
- Gynecomastia is present in less than 50% of pubertal boys with Klinefelter syndrome and is usually very mild until adulthood
- Increased risk for breast and mediastinal malignancies
- Multi-disciplinary care is critical: primary care, speech pathologists, psychologists, endocrinologists, urologists and fertility specialists.

Suggested References and Additional Reading:

- Gies, I., et al. (2014). "Management of Klinefelter syndrome during transition." Eur J Endocrinol **171**(2): R67-77.
- De Sanctis, V., et al. (2013). "Klinefelter syndrome and cancer: from childhood to adulthood." Pediatr Endocrinol Rev **11**(1): 44-50.
- Aksglaede, L., et al. (2013). "47,XXY Klinefelter syndrome: clinical characteristics and age-specific recommendations for medical management." Am J Med Genet C Semin Med Genet **163C**(1): 55-63.
- Groth, K. A., et al. (2013). "Clinical review: Klinefelter syndrome--a clinical update." J Clin Endocrinol Metab **98**(1): 20-30.
- Zeger, M. P., A. R. Zinn, et al. (2008). "Effect of ascertainment and genetic features on the phenotype of Klinefelter syndrome." J Pediatr **152**(5): 716-722.

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