Isolated Gonadotropin-Releasing Hormone Deficiency (Kallman syndrome)

Genetics

-More than 25 genes; KAL1 (ANOS1), FGFR1 (AD), CHD7

-X-linked, AD, AR

Clinical findings/Dysmorphic features

-Low serum concentrations of the gonadotropins LH (luteinizing hormone) and FSH (follicle-stimulating hormone) in the presence of low circulating concentrations of sex steroids

-Typical IGD (40%): normal sense of smell vs. Kallman syndrome (60%): impaired sense of smell/anosmia

-Absent or partial puberty at presentation in adolescents

-Low serum testosterone or estradiol on biochemical testing

-Type 1 can also include mirror hand movements, ataxia, GU anomaly, high palate, pes cavus

Etiology

-Incidence of KS of 1:30,000 in males and 1:125,000 in females

-Males predominate with a male-to-female ratio of nearly 4:1

Pathogenesis

-Impaired function of anosmin results in a migratory defect of the olfactory and GnRH neurons from the olfactory placode during development

-Abnormal FGFR1 gene products result in impaired receptor signaling

Genetic testing/diagnosis

-X-linked: Sequencing of ANOS1 (KAL1) is the highest-yield molecular test

-Sequencing ANOS1 (KAL1) (5-10%), FGFR1 (8-16%)

Others

-Treatment: Normalize gonadal steroid levels