X-linked adrenal hypoplasia congenita

Genetics

-NR0B1 (Xp21.3-Xp21.2)

-XLR

-X-linked AHC vs. Xp21 deletion (includes deletion of NR0B1 (causing X-linked AHC) and GK (causing glycerol kinase deficiency), in some cases deletion of DMD)

-1/3 contiguous gene deletion with GK, DMD; 2/3 isolated AHC (50% de novo)

Clinical findings/Dysmorphic features

-Acute onset of adrenal insufficiency (Nebenniere): hyperkalemia (high K+ in blood), acidosis, hypoglycemia (low blood sugar), shock

-Adrenal insufficiency is infantile onset (~ 3 wks) in ~60%; childhood onset (~1-9 years) in ~40%

-Cryptorchidism, delayed puberty

-Xp21 deletion might cause DD

Etiology

-Current estimates are fewer than 1:70,000 males

Pathogenesis

-OB1 is a neg. regulator of nuclear receptor pathways; defective nuclear localization of protein

Genetic testing/diagnosis

-Diagnosis is established by detection of either a hemizygous pathogenic variant in NR0B1 or a non-recurrent Xp21 deletion that includes NR0B1

-Sequencing: 75%, deletion/duplication analysis: 25%

Others

-Glycerol kinase deficiency: elevated serum concentrations of glycerol (hyperglycerolemia) and triglycerides (pseudohypertriglyceridemia)