Smith-Magenis syndrome

Genetics

-Deletion or mutation of RAI1 (Retinoic acid-induced protein 1; 17p11.2)

-Deletions are de novo; SNVs can be de novo or inherited

Clinical findings/Dysmorphic features

-Mild-moderate infantile hypotonia, feeding problems, FTT

-Short stature, brachydactyly, ophthalmologic abnormalities, early speech delay with or without hearing loss, peripheral neuropathy, sleep problems; mild-moderate ID

-Stereotypic maladaptive behaviors (self-injurious behaviors, inattention, hyperactivity, impulsivity, disobedience, “self-hug” and “lick and flip” page motion)

-Facial: brachycephaly; midface retrusion; relative prognathism with age; broad, square‐shaped face; everted, "tent"-shaped vermilion of the upper lip with mild micrognathia; deep‐set, close‐spaced eyes; coarsening face over time

Etiology

-Prevalence ~1:15,000

Pathogenesis

-RAI1 functions in transcriptional regulation --> haploinsufficiency as disease mechanism

Genetic testing/diagnosis

-Visible interstitial deletion of chromosome 17p11.2: routine G-banded analysis with adequate resolution (≥550 band); can be overlooked particularly when the indication is not SMS

-FISH or aCGH required in cases of submicroscopic deletions and/or to resolve equivocal cases

-90% have FISH-detectable deletion and of those ~70% have the common 3.5-Mb deletion