Sotos Syndrome

Genetics

-Gene: NSD1 (Histone-lysine N-methyltransferase, H3 lysine-36 and H4 lysine-20 specific; 5q35) -AD (95% de novo); microdeletion of 5q35 or pathogenic variants in NSD1

Clinical findings/Dysmorphic features

1) Distinctive facial: broad and prominent forehead, sparse frontotemporal hair, downslanting palpebral fissures, malar flushing (reddish cheeks), long and narrow face, long chin

2) Learning disability: early developmental delay, mild to severe intellectual impairment

3) Overgrowth (height and/or head circumference ≥2 SD above mean)

4) Others: behavioral problems, advanced bone age, cardiac anomalies, cranial MRI/CT abnormalities, joint hyperlaxity/pes planus, maternal preeclampsia, neonatal jaundice, neonatal hypotonia, renal anomalies, scoliosis, seizures

Etiology

- 1:14,000 live births

Pathogenesis

-Haploinsufficiency of NSD1 (may be related to genes affecting growth)

Genetic testing/diagnosis

-MLPA or FISH for 5q35 microdeletion including NSD1 (1.9Mb): ~15% (50% in Japanese)

-NSD1 sequencing: 27-93% (12% in Japanese)

-Caused by NAHR! (see 22q11.2 deletion syndrome!)