Congenital hearing loss - Connexin 26 and 30

Genetics

-GJB2/DFNB1 (Connexin 26), GJB6/DFNA3 (Connexin 30); 13q11-12

-AR

Clinical findings/Dysmorphic features

-Congenital mild to profound sensorineural hearing loss (cause lies in the inner ear or sensory organ (cochlea and associated structures) or the vestibulocochlear nerve (cranial nerve VIII))

Etiology

-DFNB1: ~50% of congenital severe-to-profound AR nonsyndromic hearing loss in the US

-14:100,000

Pathogenesis

-Homozygous or compound heterozygous for GJB2 pathogenic variants (99%)

-Compound heterozygous for one GJB2 pathogenic variant and one of three large deletions that includes sequences upstream of GJB2 and a portion of GJB6 (<1%)

Genetic testing/diagnosis

-NBS

-Sequencing of GJB2: >99%, Deletion/Duplication: <1%

-Common GJB2 pathogenic variants: 35delG Caucasians; 235delC Asians; 167delT, del35G and Cx30 gene deletion in AJ; Val37Ile in Thailand

Others

-Rare patients can have AD Cx26 hearing loss which can include skin findings: palmar-planter keratoderma, KID syndrome (keratitis-ichthyosis-deafness)