Cleidocranial Dysplasia Spectrum Disorder

Genetics

-Gene: RUNX2 (Runt-related transcription factor 2; 6p21)

-AD (high proportion de novo)

Clinical findings/Dysmorphic features

-Skeletal dysplasia with clinical continuum ranging from classic CCD (1) delayed closure of the cranial sutures, 2) hypoplastic or aplastic clavicles, 3) dental abnormalities) to mild CCD to isolated dental anomalies without the skeletal features (most with classic form and normal ID)

-Wide-open fontanelles at birth (may remain open throughout life)

-Clavicular hypoplasia (narrow, sloping shoulders that can be opposed at the midline)

-Dental anomalies (supernumerary teeth, eruption failure of permanent teeth)

-Increased risk of developing recurrent sinus infections, recurrent ear infections leading to conductive hearing loss, upper-airway obstruction

Etiology

-1 in 1,000,000

Pathogenesis

-RUNX2 is TF involved in osteoblast differentiation and skeletal morphogenesis; osteoblast differentiation during intramembranous ossification and chondrocyte maturation during endochondral ossification --> pathogenic variants in RUNX2 result in haploinsufficiency

Genetic testing/diagnosis

-X-ray: clavicular hypoplasia, open sutures, wormian bones (extra bone pieces within a suture), poor or absent sinus pneumatization, hypoplastic scapulae, wide symphysis pubis and sacroiliac joints, large femoral neck and epiphyses, pseudoepiphyses of the metacarpals and metatarsals, deformed and short middle phalanges, osteopenia

-RUNX2: 70% of cases (Seq: 60%; Indel: 10%)

Others

-Cleido=Clavicula; women with CCD have increased rate of Caesarian section in childbirth