Branchio-Oto-Renal syndrome

Genetics

-EYA1, SIX1, SIX5

-AD; 100% penetrance

Clinical findings/Dysmorphic features

-Malformations of outer, middle, and inner ear:

--> Conductive, sensorineural, or mixed hearing impairment (>90%)

--> Abnormalities of the pinnae (external part of the ear): preauricular pits (82%), lope ear malformation (36%), preauricular tags (13%)

-Branchial fistulae and cysts

-Renal malformations (mild renal hypoplasia to bilateral renal agenesis) (67%)

Etiology

-not known

Pathogenesis

-EYA proteins are four transcriptional activators --> interact with other proteins --> normal embryologic development

-EYA1 important for inner-ear, kidney, branchial-arch development

-SIX gene family binds EYA proteins --> nuclear translocation of the resultant protein complex

-SIX1 and SIX5 function as transcriptional activators/repressors --> regulation of organogenesis

Genetic testing/diagnosis

-Diagnosis established in ind. with clinical features and/or het variant in: EYA1, SIX1, SIX5

-EYA1 (40%; of those 80% seq., 20% In/Del), SIX1 (2%), SIX5 (2.5%), >50% unknown cause

Others

-Some individuals progress to ESRD later in life