CHARGE syndrome

Genetics

-CHD7 (Chromodomain-helicase-DNA-binding protein 7, 8q12.1)

-AD

Clinical findings/Dysmorphic features

-Coloboma, heart defects, choanal atresia, retarded growth and development, genital abnormalities, ear anomalies

-Unilateral/bilateral coloboma of iris, retina-choroid, and/or disc with or without microphthalmos (small eye) (80%-90%)

-Cardiovascular malformations (75%-85%): conotruncal anomalies (Tetralogy of Fallot, interrupted aortic arch, perimembranous ventricular septal defect, double-outlet right ventricle, truncus arteriosus), AV canal defects, aortic arch anomalies, ASD, VSD, PDA

-Unilateral/bilateral choanal atresia or stenosis (nose closed) (50%-60%)

-Growth and developmental delay

-Cryptorchidism in males; hypogonadotropic hypogonadism in both males and females

-Abnormal outer ears, ossicular malformations, Mondini defect of the cochlea and absent or hypoplastic semicircular canals (>90%)

-Cranial nerve dysfunction --> hyposmia or anosmia; unilateral/bilateral facial palsy (40%); impaired hearing, and/or swallowing problems (70%-90%)

-Tracheoesophageal (TE) fistula

Etiology

-At least 1:10,000

Pathogenesis

-Majority of variants are nonsense and frameshift throughout gene --> haploinsufficiency

-CHD7 with role in early embryonic development --> chromatin structure and gene expression

Genetic testing/diagnosis

-CHD7 only known gene (accounts for 60-70%)

Others

-Empiric risk to sibs of a proband is approximately 1%-2% (germline mosaicism)

-20-25% mortality in the first year