Ehlers-Danlos syndrome vascular (type IV)

Genetics

-COL3A1 (2q31)

-AD; penetrance ~100%

Clinical findings

-Usually no soft, doughy, stretchy skin/abnormal scars/large-joint hypermobility (vs. cEDS)

-Major criteria: arterial rupture, intestinal rupture, uterine rupture during pregnancy

-Minor criteria: thin, translucent skin, easy bruising, thin lips and philtrum, small chin, thin nose, large eyes, aged appearance of hands, small joint hypermobility

Etiology

-1:200,000

Pathogenesis

-COL3A1 encodes the proα1(III) chain of type III procollagen --> major structural component of skin, blood vessels, hollow organs

-Majority of identified pathogenic variants result in single amino-acid substitutions for glycine in the Gly-X-Y repeat of the triple helical region of the type III procollagen molecule

-Pathogenic variants in COL3A1 --> structural alteration of type III collagen --> intracellular storage/impaired secretion of collagen chains

Genetic testing/diagnosis

-Sequence analysis of COL3A1 (95%), then gene-targeted deletion/duplication analysis (~1%)

-Abnormalities in synthesis and mobility of type III collagen chains on biochemical analysis of type III procollagen from cultured fibroblasts when vEDS is suspected

-Individuals with COL3A1 null variants have 15y delay in onset of complications and improved life expectancy