Marfan Syndrome

Genetics

-FBN1

-AD; 75% inherited, 25% de novo

Clinical findings/Dysmorphic features

-CV: dilation or dissection of the ascending aorta

-Skeletal: pectus carinatum or excavatum; reduced upper to lower segment or arm span to height; scoliosis; pes planus; high palate; reduced elbow extension

-Eye: ectopia lentis (retinal detachment; in 60-70%); glaucoma; early cataracts (60%)

-Lumbosacral dural ectasia (widening/ballooning of the dural sac surrounding the spinal cord)

-Family history: pathogenic FBN1 variant or 1st degree relative with Marfan syndrome

-Major morbidity and early mortality because of cardiovascular system and dilatation of the aorta at the level of the sinuses of Valsalva

Etiology

-1:5,000-1:10,000

Pathogenesis

-Abnormal fibrillin-1 is believed to have dominant-negative activity

-Severe reduction of microfibrils in explanted tissues and in matrix deposited by cultured dermal fibroblasts

Genetic testing/diagnosis

-Major involvement of two body systems and minor involvement of a 3rd

-Sequencing of FBN1 (90-93%), Deletion/Duplication (~5%)

-No family history:

--> Aortic root enlargement (Z-score≥2) + ectopia lentis/pathogenic variant/systemic score ≥7

--> Ectopia lentis + pathogenic FBN1 variant previously associated with aortic enlargement

-Family history:

--> Ectopia lentis or systemic score ≥7 or aortic root enlargement (Z-score≥2 in those ≥20yo or Z-score≥3 in those ≤20yo)

Others

-Beta blockers/Losartan for aortic root dilation; bracing/surgery for scoliosis; annual dilated eye exam and echocardiography

-Surgical repair of the aorta is indicated once:

--> the maximal measurement approaches 5.0 cm in adults or older children

--> the rate of increase of the aortic root diameter approaches 1.0 cm per year