Noonan Syndrome

Genetics

-PTPN11 (50%, pathogenic missense variant), SOS1 (13%), KRAS (<5%), RAF1 (5%), NRAS, CBL, SHOC2, BRAF, RIT1 (5%), SOS2, MAP2K1

-AD, affected parent in 30-70%

Clinical findings/Dysmorphic features

-Short stature

-Congenital heart defect (50-80%; pulmonary valve stenosis, hypertrophic cardiomyopathy)

-Ocular abnormalities (95%; strabismus, refractive errors, amblyopia, nystagmus)

-Broad or webbed neck; feeding problems; unusual chest shape (superior pectus carinatum and inferior pectus excavatum); renal malformation

-Lymphedema, bleeding disorders, myeloproliferative disorder (risk of leukemia)

-DD of variable degree

Etiology

-1:1000 to 1:2500

Pathogenesis

-GoF mutations --> constitutive activation of the Ras MAP Kinase pathway

Genetic testing/diagnosis

-Multigene panel is test of choice for an individual suspected of having Noonan syndrome

-Significant phenotypic overlap with cardio-facio-cutaneous syndrome and Costello syndrome

Others

-Early term "Male Turner syndrome" incorrectly implied that condition is not found in females

-Pulmonary valve stenosis + increased nuclear translucency == Noonan