Neurofibromatosis type 2

Genetics

-Gene: NF2; (Neurofibromin-2/Merlin; 22q12.2)

-AD

Clinical findings/Dysmorphic features

-Benign nerve tumors (schwannomas, meningiomas, ependymonas, astrocytoma)

-Hallmark is bilateral acoustic/vestibular schwannoma: onset age 18-24 yrs, hearing loss, tinnitus, balance problems

-Cataracts, mononeuropathy, café-au-lait (fewer than in NF1)

Etiology

-Prevalence of NF2 is 1:60,000; birth incidence of 1:33,000

Pathogenesis

-Merlin may coordinate processes of growth-factor receptor signaling and cell adhesion

-NF2 is a tumor suppressor, 2nd hit leads to complete LOF when one germline mutation present

Genetic testing/diagnosis

-NF2 sequencing (75%), dup/del including CMA testing (10-15%)

->400 pathogenic variants: mostly missense, nonsense, splicing variants and small deletions

Others

-Somatic mosaicism is frequent: 30% of ind. with de novo NF2 variant have somatic mosaicism