Hereditary Multiple Osteochondromas

Genetics

-Gene: EXT1, EXT2 (Exostosin-1, Exostosin-2)

-AD

Clinical findings/Dysmorphic features

-Growths of multiple osteochondromas (benign cartilage-capped bone tumors that grow outward from the metaphyses of long bones)

-Osteochondromas associated with reduction in skeletal growth, bony deformity, restricted joint motion, shortened stature, premature osteoarthrosis, compression of peripheral nerves

-Median age of diagnosis is 3 yrs; nearly all affected individuals are diagnosed by age 12 years

-Low risk for malignant degeneration to osteochondrosarcoma (lifetime risk (~1%))

Etiology

-1 in 50,000 in DC

Pathogenesis

-EXT1/2 encode glycosyltransferases; mutations lead to actin accumulation and cytoskeletal abnormalities

Genetic testing/diagnosis

-Combination of sequence analysis and InDel of coding regions of EXT1 and EXT2 --> pathogenic variants in 70%-95% of affected individuals