Cockayne Syndrome

Genetics

-Gene: ERCC6, ERCC8 (DNA excision repair protein ERCC-6 and ERCC-8)

-AR

Clinical findings/Dysmorphic features

1) CS type I (moderate): normal prenatal growth; onset of growth delay and DD in the first 2 yrs; full manifestation: height, weight, HC far below 5th %tile; progressive impairment of vision/hearing, central/peripheral NS dysfunction --> severe disability; death in 1st or 2nd decade

2) CS type II (severe): growth failure at birth; little or no postnatal neurologic development; congenital cataracts or other structural anomalies of the eye; early postnatal contractures of spine (kyphosis, scoliosis) and joints; death usually occurs by age 7 years

3) CS type III (mild): normal growth and cognitive development or late onset

4) Xeroderma pigmentosum-Cockayne syndrome (XP-CS): facial freckling and early skin cancers (typical of XP) + intellectual disability, spasticity, short stature, and hypogonadism (typical CS)

Etiology

-Minimum incidence at 2.7 per million births

Pathogenesis

-Abnormal transcription-coupled nucleotide excision repair (preferential removal of UV-induced pyrimidine dimers and other transcription blocking lesions)

Genetic testing/diagnosis

-Gene sequencing and/or Del/Dup of ERCC6 (75%), ERCC8 (25%)

Others

-XP-CS: no skeletal involvement, no facial phenotype, no CNS dysmyelination and calcifications

-CS --> no increased cancer risk