DICER1-Related Disorders

Genetics

-Gene: DICER1 (Endoribonuclease Dicer; 14q32.13)

-AD; 80% inherited

Clinical findings/Dysmorphic features

-Familial tumor susceptibility syndrome --> increased risk for pulmonary pleuroblastoma (PPB; neoplasm that arises during lung development or shortly after birth); ovarian sex cord-stromal tumors; cystic nephroma; thyroid gland neoplasia

-Less common: ciliary body medulloepithelioma; botryoid-type embryonal rhabdomyosarcoma of the cervix; nasal chondromesenchymal hamartoma; renal sarcoma; pituitary blastoma

-Majority of tumors in individuals < 40 years

Etiology

-unknown

Pathogenesis

-DICER1 encodes RNase III enzyme --> miRNA and siRNA biogenesis --> cleaves precursor double stranded RNAs into active forms

-LoF germline pathogenic variants in DICER1 + somatic pathogenic variants --> production of defective mature miRNAs from the 5' (5p) end of the miRNA hairpin

Genetic testing/diagnosis

-Dicer sequencing: 65%