Blepharophimosis, ptosis, and epicanthus inversus (BPES)

Genetics

-FOXL2 (3q23) is only gene associated with BPES

-AD; 50% de novo

Clinical findings/Dysmorphic features

-Complex eyelid malformation invariably characterized by four major features:

1) Blepharophimosis (horizontally narrow palpebral fissure, from canthi to canthi),

2) Ptosis (drooping of the upper eyelid)

3) Epicanthus inversus (fold over canthi comes from below)

4) Telecanthus (increased distance between the medial canthi of the eyes with normal inter-pupillary distance)

-BPES type I: + premature ovarian failure (POF), BPES type II: only the four major features

Etiology

-unknown

Pathogenesis

-FOXL2 protein belongs to the large family of winged-helix/forkhead transcription factors

-Haploinsufficiency of FOXL2 (82% of pathogenic variants are LoF)

-FOXL2 is a transcriptional repressor of granulosa cell differentiation

-Mutations cause accelerated differentiation of granulosa cells and secondary depletion of the primordial follicle pool

Genetic testing/diagnosis

-FOXL2 sequencing: 75%, Deletion/Duplication: 10-15%, Regulatory region: 5%