BRCA1 and BRCA2 Hereditary Breast and Ovarian Cancer

Genetics

-BRCA1 and BRCA2 (Breast cancer type 1 and 2 susceptibility protein; 17q21 an 13q12.3)

-AD

Clinical findings/Dysmorphic features

-BRCA1: Breast, ovarian, prostate cancer

-BRCA2: Breast, ovarian, prostate and pancreatic cancer

Etiology

-Prevalence of BRCA1/2 pathogenic variants in the general population: 1:400 to 1:500

Pathogenesis

-LOF of BRCA1 --> defects in DNA repair/transcription, abnl centrosome duplication, defective G2/M cell-cycle checkpoint regulation, impaired spindle checkpoint, chromosome damage

-LOF of BRCA2 --> defects in double-strand breaks repair (hypersensitivity to ionizing radiation)

Genetic testing/diagnosis

-Suspected in individuals with personal or family history (1st-, 2nd-, or 3rd-degree relative) of any of the following: 1) Breast cancer diagnosed < 50 years; 2) Ovarian cancer; 3) Multiple primary breast cancers (in one or both breasts); 4) Male breast cancer; 5) Triple-negative (estrogen receptor-negative, progesterone receptor-negative, HER2 negative); particularly when diagnosed < 60 years; 6) Combination of pancreatic cancer and/or prostate cancer (Gleason score ≥7) with breast cancer, and/or ovarian cancer; 7) Breast cancer diagnosed at any age in an AJ individual; 8) > 2 relatives with breast cancer (one < 50); 9) >3 relatives with breast cancer at any age; 10) Previously identified BRCA1 or BRCA2 pathogenic variant in family

-BRCA1 (66% of cases; 80% seq, 10% InDel); BRCA2 (34% of cases; 80% seq, 10% InDel)

Others

1) Breast: 12% in general pop. – 46-87% in BRCA1 / 40-84% in BRCA2

2) Ovarian: 1-2% in general pop. – 40-63% in BRCA1 / 17-27% in BRCA2

3) Male breast: 0.1% in general pop. – 1.2% in BRCA1 / 9% in BRCA2

4) Prostate: 6% in general pop. – 9% in BRCA1 / 15% in BRCA2

5) Pancreatic 0.5% in general pop. – 1-3% in BRCA1 / 2-7% in BRCA2