

Familial breast cancer genetics: the experience in Cyprus

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Breast cancer: incidence, mortality and epidemiology

Breast cancer is the most common cancer in women and in 2008 there were over 1.4 million new cases, with nearly 0.5 million deaths. The incidence is increasing even in countries with established population screening programs and in Europe breast cancer affects approximately 1 in 8 women. The epidemiology of breast cancer has been studied more extensively than any other human disease. A spectrum of risk factors is associated with the development of breast cancer, including duration of estrogen exposure, late first pregnancy and family history. In contrast higher parity and longer duration of lactation lower the risk. However in most women with breast cancer, a specific risk factor cannot be identified.

Breast cancer: familial genetics

The most important risk factor is a family history and it has been recognized for many years that about 10% of breast cancer patients present with a positive family history. The Hereditary Breast Ovarian Cancer syndrome (HBOC, MIM113705) is the most common form of inherited breast cancer and this is associated with the BRCA1 and BRCA2 genes. Germline mutations in the BRCA1 and BRCA2 genes greatly increase the risk of developing not only breast, but ovarian, and other cancers. A bewildering number of mutations has been characterized, and in Cypriot families a unique spectrum of mutations has been identified including a founder mutation in BRCA2.

The discovery of the BRCA genes has provided an important tool for identifying individuals at high risk. It is now possible to identify causative mutations in the BRCA genes and genetic testing, for susceptibility to HBOC, forms an integral part of contemporary oncological practice. Such services should be offered following genetic counseling and must respect the ethical and psychological issues pertaining to patient's welfare.

Breast cancer: pathology in BRCA carriers

Breast cancers that arise in women with BRCA1/2 mutations frequently manifest characteristic pathological and histological features, such as high histologic grade, hormone receptor negativity and aneuploidy. Despite this, women with BRCA mutations and breast or ovarian cancer, experience better survival than women without mutations, possibly due to enhanced susceptibility to chemotherapy. The genetic hallmark of BRCA deficient cells is inadequate DNA repair which leads to mutational events and eventually cancer. This property is being exploited in pharmacogenomics to design highly targeted and more effective therapies for breast tumors arising in BRCA carriers.