Predictive genetics: the Maltese familial breast/ovarian cancer genetic screening programme.

Introduction: Predictive genetic testing is used to assess the future risk of an inherited disease in individuals with a family history of the disease. BRCA1 and BRCA2 autosomal dominant mutations account for 5-10% of breast cancers and for around 15% of ovarian cancers. There are also families with hereditary tumours that are wild-type for both genes.

Methods: Genetic testing was offered at the Genetics Clinic, Mater Dei Hospital, according to the National Institute for Health and Care Excellence guidelines. BRCA1 and BRCA2 gene sequencing (n=127) was outsourced. Family members of individuals having BRCA1 or BRCA2 mutations were then tested locally (Laboratory of Molecular Genetics) for the presence of the mutation found in the proband and provided with the required counselling. BRCA1/2 wild-type individuals were recruited in the ImaGenX project, together with a Sicilian hereditary breast cancer cohort, for next-generation DNA sequencing (NGS) to find other causative mutations.

Results: The prevalence of BRCA1 and BRCA2 mutations in index cases was of 12% collectively; only one case (0.8%) had a BRCA1 mutation. Another 12% of cases carried a variant of undetermined clinical significance, all in BRCA2. NGS data will be communicated.

Conclusions: Through this on-going service, affected families have been offered predictive genetic testing for the past 5 years. This allows asymptomatic individuals at an increased risk of hereditary cancer to benefit from surveillance programmes and ensure early tumour detection. Further research objectives (R.D.) will be to elucidate the role of novel genes discovered through NGS and work out their pathological molecular pathways using expression techniques.

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