



CONSEJO GENÉTICO Y CÁNCER

Shirley Hodgson

Professor of Cancer Genetic

St George's Hospital Medical School Genetic Counselling and Cancer. Londres, Inglaterra

There is a rapidly-increasing awareness of the importance of inherited factors in cancer susceptibility, which is reflected in a great increase in referrals to cancer genetics services for genetic advice and screening. The issues that need to be addressed in managing this demand are:

- How effective are screening and prophylactic measures in high-risk individuals in reducing cancer morbidity and mortality?
- How is risk assessed?
- How should referrals be ascertained, prioritised and managed?

Genetic counselling is a process by which a family tree is determined and from it a risk assessment made and communicated to the patient of

- the chance that there may be a genetic susceptibility to specific types of cancer in certain individuals in the family;
- whether a genetic test for such a susceptibility may be possible in that family;
- the risk to the consultand of developing specific cancers, and what can be done to reduce that risk;
- what can be done to ascertain and counsel other members of the family in a similar way.

There are several important factors to bear in mind:

- the need for confidentiality, particularly in view of the fact that data about relatives of the consultand will need to be obtained and recorded;
- the importance of obtaining confirmation of the diagnosis in affected individuals;
- the need to obtain written consent from these affected relatives by an approach from the consultand before such information is obtained;
- the need to respect genetic information about an individual and to release it only with that individual's consent, other than in exceptional circumstances when the interests of a relative may over-rule a person's desire not to release such information.

The most common reasons for referral to a cancer genetics centre are a family history of breast/ovarian or colorectal cancer. The vast majority of people referred to such centres in the UK are female, and most have children. Their reasons for attending are largely to assess and reduce the risks of cancer to themselves and their families.

Approximately 5% of breast and colorectal cancers are due to inherited mutations in highly-penetrant, dominantly inherited genes: BRCA1 and BRCA2 in the case of breast/ovarian cancer and APC (causing familial adenomatous polyposis, FAP) and the genes causing hereditary non-polyposis colorectal cancer (HNPCC). FAP is the only one of these conditions that can be diagnosed clinically with ease, so that the assessment of risk for the other genes is based on an evaluation of the pedigree. There is a number of computer packages that can assess risk: for example, the "Cyrillic" program which assesses the risk of a BRCA1 or BRCA2

mutation being present in a family. Unfortunately there are several pitfalls with such a program, such as the fact that often information about unaffected relatives is not factored in, and that in families where familial clustering of cancer is due to low-penetrance genes rather than strongly-penetrant ones risk estimates may be inaccurate.

In families where it is thought that a mutation in a highly-penetrant gene may be present in affected relatives of the consultand, one or more of these relatives may be contacted by the consultand, to ask if they are willing to be seen and to give a blood sample for mutation testing. If a mutation is detected, the affected person is seen and their results discussed with them. If they are happy to release the information to the consultand, the consultand is offered "predictive test counselling". This is a process whereby they are informed of their risk of inheriting the mutation, what the cancer risks are in mutation carriers, and what surveillance and prophylactic measures can be instigated to reduce their risk. Insurance/employment issues are discussed, and the likely emotional response to the genetic information.

It is usual to establish whom the consultand would like to inform about their test result, and how other at-risk relatives may be contacted and managed. In the case of BRCA1 and BRCA2 carriers, breast and ovarian cancer screening can be offered, by annual mammography from age 35 years, and annual vaginal ultrasound and serum CA125 estimations. Prophylactic mastectomy and oophorectomy can be discussed. In the case of FAP, annual endoscopic surveillance (sigmoidoscopy and colonoscopy) should commence from the early teens with prophylactic colectomy when florid polyposis has developed. In HNPCC, 2-yearly colonoscopies are recommended from age 25 years, with endometrial, ovarian and urinary tract surveillance in certain individuals. Prophylactic surgery such as subtotal colectomy if a cancer is detected can be discussed.

In the majority of families, however, no mutation is likely to be detected, and the family will be assigned to a moderate- or low-risk category depending on the extent of their family history of cancer. Low-risk individuals can be reassured and released from surveillance, and moderate-risk individuals may be offered screening for cancer; but such surveillance protocols are still being evaluated and evidence for their efficacy is being accumulated.

These protocols need to be developed on a national basis, ensuring consistency of management across the country and allowing long-term evaluation of their effect.