Developments in Clinical Practice: Follow up Clinic for BRCA Mutation Carriers: a Case Study Highlighting the "Virtual Clinic"

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Abstract

This paper highlights the need for carriers to be followed up by health professionals who understand the complexities of the *BRCA* syndrome. A *BRCA* carrier clinic has been established in London and regular follow up is an essential part of the care for families. An open door policy has been set up for patients who may meet or telephone the cancer genetic nurse specialist for support and care at any time. An example of the follow up work is discussed in the format of a case of a young woman with a *BRCA1* alteration who developed a primary peritoneal cancer following prophylactic oophorectomy. This case illustrates the work of the multi-disciplinary team caring for *BRCA* carriers.

Families who harbour deleterious genetic alterations in a *BRCA* gene react differently according to their situation. Health professionals provide time and understanding within the genetic testing programme to help individuals consider their options before proceeding to genetic testing. Once the test result is confirmed, the affected person may consider new prevention options to reduce the risk of another cancer developing. These options may be discussed with the medical team who are trained in oncology and genetics. Patients who are gene mutation carriers and who have developed cancer have a risk to develop further primaries. Gene carriers who have developed cancer are managed under different units with specialists who may not have an in-depth understanding of the *BRCA* syndrome.

The *BRCA* gene mutation carrier clinic of the Royal Marsden Hospital/Institute of Cancer Research has a threefold purpose [1]:

1. Ongoing support of gene carrier families and patients. Annual appointments are made for these patients as well as access to a "virtual telephone clinic". The latter clinic is run by the nursing team who are trained in oncology and genetics and who probably know the family well.
2. Clinical management issues: Discussions related to further surgical prevention procedures i.e. mastectomy, prophylactic oophorectomy. All information is given in the light of the current research.
3. The opportunity for family members to participate in research. Within the Carrier Clinic of the Royal

Marsden Hospital/Institute of Cancer Research there are several ongoing collaborative studies (as shown in Figure 1) and patients have the options to be involved in studies after full informed consent.

There are nearly 200 patients who have *BRCA* gene mutations who are participating in this clinic. For some people, years later, the effort of attending a clinic diminishes its attraction, especially if they are unaffected and have chosen prophylactic surgery as an option. A "virtual" clinic has therefore been established as part of the "carrier clinic". This means that there is "telephone availability" for follow up. This telephone service is managed by the nurses within the unit. It offers regular follow up support and access for gene carriers who are worried about their medical health. The service involves discussions with nurses who are trained in oncology and genetics and who have experience in working with *BRCA* gene mutation carriers.

Families with mutations in the *BRCA* genes know that they can contact the "virtual clinic" at any time for support or advice. Medical matters are acted on immediately via a link with the Consultant in charge. If a patient is already under another unit/hospital, then contact is made with the appropriate medical person accompanied by a follow up letter and appropriate investigations. In some instances, preliminary investigations such as blood tests are arranged before referral thereby providing maximum information for the specialist.

This following case is illustrative of the virtual clinic and the referral process.

The Case of Mrs X

Mrs X is a known *BRCA1* mutation carrier. She was keen to be tested as so many of her female relations had died prematurely from cancer. Information from another centre provided her with the knowledge that there was a deleterious mutation present in the *BRCA1* gene in her family. At the age of 33 she underwent predictive genetic testing and had several sessions with the Clinical Nurse Specialist and the medical team before deciding to proceed. The testing showed that she carried the pathogenic mutation identified in her family. After serious consideration, she decided to undergo prophylactic ovarian surgery. This she hoped would reduce her life time risk of ovarian cancer of 50% by about 96% and reduce her risk of developing breast cancer by 50% [2]. After serious consideration following several counselling sessions, she was referred to the gynaecologist for discussions on risk reducing surgery. She had a medical history of endometriosis and decided along with her gynaecologist to have a total hysterectomy as she was troubled by menstrual problems. Furthermore, she had two children and was adamant that she did not wish to have any more children. This operation was successful. She was followed up in the breast unit for annual screening. As part of the "virtual clinic" for gene carriers, ongoing support was available for this young lady who had a limited family support structure. On one of the regular follow up calls, she sounded depressed and was therefore invited in to the nurse who led follow up clinic. During this session, she informed the nurse that she was feeling tired and "not herself". This young lady was known well to the nurse through the predictive genetic testing programme. The nurse was concerned that there maybe something medical that needed serious consideration. Furthermore, as part of the *BRCA* clinic protocol, patients who have undergone prophylactic oophorectomy are offered a CA125 test with the knowledge that this test's predictive value in this situation is uncertain. In this particular case, the Consultant and the nurse were in discussion about the management of this young lady and a CA125 test was arranged along with a few other blood tests.

The CA125 result was elevated (130). A transvaginal ultrasound scan and another CA125 test was arranged along with an appointment to the gynaecology clinic. Unfortunately, this young woman was found to have an early stage primary peritoneal cancer. She has undergone intensive chemotherapy and is currently being followed up in the onco-gynaecology unit for her cancer care. As well, there is ongoing genetic support for this young woman when needed. She continues to be followed up in the breast unit for breast screening.

The ongoing follow up for this young woman as part of the Carrier Clinic has shown the benefits of this follow up service both from a medical management perspective and a psychological support service. It is essential that there are professionals who understand the *BRCA* syndrome in the fullest sense, including both genetic and oncological perspectives and the possible associated further cancer risks. As it is such a specialist area of knowledge, the patient is well served with qualified professionals who will liaise with the appropriate health professionals.

Acknowledgements

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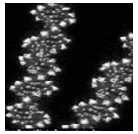
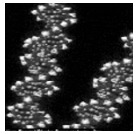
RESEARCH PROJECTS INVOLVING BRCA1 AND BRCA2 ALTERATION CARRIERS AT THE ROYAL MARSDEN HOSPITAL





DUCTAL LAVAGE STUDY

Ductal Lavage in BRCA1 and BRCA2 mutation carriers and non-carriers

What is the study for?

We are interested in looking at the fluid within the ducts of the breast as it is made by and bathes the cells that can become cancerous. It is possible that by analysing this fluid for the presence of cells and chemical markers we could identify early cases of breast cancer or use the information to give a better estimate breast cancer risk.

Who is eligible?

Women with a known alteration in a BRCA1 or BRCA2 gene and women who have tested negative for an alteration in either of these 2 genes which is known to be present in the family. Women with at least one breast unaffected by cancer.
Exclusions include pregnancy and breast-feeding within the last 12 months.

What does it involve?

Local anaesthetic cream is used to numb the nipple area. An extremely fine, flexible tube is passed into the nipple ducts, coated in anaesthetic jelly, and a few millilitres of a dilute salt solution is introduced into the duct to wash it out.

THE EMBRACE STUDY

Lifestyle study of BRCA1 and BRCA2 gene alteration carriers

What is the study for?

We know that some BRCA1 and BRCA2 gene alteration carriers get breast cancer, but we do not know what other genetic or lifestyle factors may be important. This study is trying to identify these other risk factors.

Who is eligible?

Members of families where a BRCA1 or BRCA2 gene alteration has been identified. Anyone can take part whether they have the gene or not, and even if they have not been tested.

What does it involve?

A simple questionnaire about background, medical and family history, and an optional blood test (not a "gene test").

IMPACT STUDY

This study is an international targeted prostate screening study of male BRCA1 and BRCA2 mutation carriers.

What is the study for?

Men who carry alterations in these genes are known to be at a higher risk of prostate cancer. This study aims to look at substances which may be markers for prostate cancer in the blood and urine of these men.

Who is eligible?

Men aged 40-69 who have a known alteration in either the BRCA1 or BRCA2 gene with no history of prostate cancer. We are also looking at their male relatives who do not carry this gene to compare the results.

What does it involve?

A blood and urine sample will be taken annually for a total of 5 years. People are also asked to complete a short personal history questionnaire.

EFFECTS OF RADIATION STUDY

Study to assess the effects of radiation in BRCA1 and BRCA2 carriers versus non-carriers

What is the study for?

Cancer is often treated with radiation (i.e. radiotherapy), or screening for it uses radiation. We are trying to determine whether gene alteration carriers are any more or less sensitive to radiation than those who do not carry an alteration. At present the answer to this question is unknown, and this study will help us to design future treatments.

Who is eligible?

Any woman who has a known alteration in a BRCA1 or BRCA2 gene.

What does it involve?

A one-off blood sample, and some people may be asked to give a small skin biopsy, usually from the buttock. These samples are used to study how blood and skin cells behave after irradiation.

NIPPLE ASPIRATION STUDY

Nipple aspiration in women – BRCA1, BRCA2 and p53 mutation carriers.

What is the study for?

We are interested in looking at the fluid within the ducts of the breast as it is made by and bathes the cells that can become cancerous. It is possible that by analysing this fluid for the presence of cells and chemical markers we could identify early cases of breast cancer or use the information to give a better estimate breast cancer risk.

Who is eligible?

Women with a known alteration in a BRCA 1, BRCA 2 or p53 gene under the age of 65. Women with at least one breast unaffected by cancer.
Exclusions include pregnancy and breast-feeding within the last 12 months.

What does it involve?

A sample of fluid taken from the nipple using a special pump, similar to that used for expressing milk during breast-feeding. The breast is warmed and gently massaged to move duct fluid towards the nipple. The procedure does not use a needle and has been well tolerated by women previously.

THE PROSE STUDY

Preventative surgery in carriers of BRCA1 and BRCA2 gene alterations
(PROSE stands for Prevention and Observation of Surgical Endpoints)

What is the study for?

We are trying to find out the long-term effects of preventative surgery in BRCA1 and BRCA2 gene alteration carriers. Some women choose to have their breasts and/or ovaries removed to prevent getting cancer. We want to find out exactly how much this kind of surgery reduces the incidence of cancer, and how lifestyle factors may be involved.

Who is eligible?

We want to study both women who have had preventative surgery to the breasts and/or ovaries, and those who have not. The eligibility criteria for this study are a little complicated, but most women with a known BRCA1 or BRCA2 gene will be eligible.

What does it involve?

Data about any treatment and subsequent follow-up are taken from the hospital notes. People are asked to fill in a simple questionnaire about background, medical and family history. This questionnaire is very similar to the one used in the Embrace study. If a person consents to take part in the PROSE study and has already filled in the Embrace questionnaire, there is no need to fill this in again as we can share the data.

PROPHYLACTIC MASTECTOMY STUDY

Evaluation of the effectiveness of prophylactic mastectomy (i.e. preventative removal of the breasts)

What is the study for?

We are trying to find out the long-term effects of preventative breast surgery. Some women choose to have their breasts removed to prevent cancer. We want to find out exactly how much this kind of surgery reduces the incidence of cancer in women, and how it affects their general physical health and psychological well being over time.

Who is eligible?

This is a "prospective" study. Women who are going to have preventative surgery to the breasts are eligible.

What does it involve?

Data about any treatment and subsequent follow-up are taken from the hospital notes. A questionnaire is filled in before surgery, and then at 3 months, 1, 5 and 10 years after the surgery. It asks about general health, cancer worry, body image and relationships.

OUTCOME OF BREAST CANCER TREATMENT STUDY

Study to assess the effects of radiotherapy and chemotherapy in treatment for breast cancer

What is the study for?

We are trying to find out which treatment for beast cancer gives the best results (in tumour control and cosmetic effect) in women who have had cancer due to an alteration in a BRCA1 or BRCA2 gene. We do not know whether women who carry an alteration have any significant differences in their responses to radiotherapy and chemotherapy compared to the general population of women with breast cancer.

Who is eligible?

Women who have had chemotherapy and/or radiotherapy as part of breast cancer treatment. Both women with an alteration in a BRCA1 or BRCA2 gene, and women in the general population with breast cancer are eligible.

What does it involve?

A one-off visit to the hospital. Questions are asked about what treatment was undergone, and where and when it was carried out. Photographs are taken of the breasts to evaluate the cosmetic outcome of treatment, and some people may be asked to have a small skin biopsy.

Data about any treatment and subsequent follow-up are taken from the hospital notes.

We are also interested in finding out if there are any differences in the facial and general features of women who carry a BRCA1 or BRCA2 gene alteration. If people are willing, we are taking photographs of the head and shoulders. This information may help us in future assessments of the likelihood of individuals being alteration carriers.

All photographs taken in this study will be used for study purposes only, and will not be used for teaching or in publications without an individual's written consent.