PERSPECTIVE

Not just for women

Specific research and treatment of breast cancer in men has been neglected and deserves greater attention, says **Valerie Speirs**.

Imagine a waiting room in a busy clinic. A serious-looking doctor ushers a patient into the consulting room. The patient sits down, and the doctor delivers the sombre news: 'You have breast cancer'. Worldwide, more than 1.3 million women are diagnosed with breast cancer every year[1], so this scene is perhaps not uncommon. But this time the patient is a man. He reacts with disbelief: men don't get breast cancer; this must be a mistake. Yet breast cancer affects both men and women, with some 13,000 men being diagnosed each year worldwide. When matched for important prognostic factors (tumour size, grade and lymph-node status), the outcome of male and female breast cancer is similar[2]. But men are generally diagnosed at a later stage than women, so their survival rates tend to be lower.

Male breast cancer is rare, accounting for less than 1% of all breast cancer cases, but its incidence seems to be increasing in Western countries[3]. With epidemiological studies lacking, the reasons for this increase are unknown. Lifestyle changes over the past two to three decades have been proposed as causes, including the rise in alcohol consumption and obesity, and the decrease in exercise.

Most studies of male breast cancer have been restricted to examining small numbers of tissue samples available from histopathology archives, and information about the molecular pathways associated with its biological behaviour has been largely anecdotal. To fill this knowledge gap, in 2007, my team at the University of Leeds established the Male Breast Cancer Consortium: a collaboration with pathologists in Europe and North America to gather samples from hundreds of men with breast cancer. Similarly, following a meeting in Bethesda, Maryland, in 2008, the International Male Breast Cancer Program was launched as a cross-continental effort to pool samples, epidemiological data and clinical information.

NOT THE SAME

In the past two years, analyses of these large sample collections have shown that, despite superficial similarities in tissue appearance and hormone-receptor expression, male and female breast cancers differ at the molecular level. In November 2011, using hierarchical cluster analysis, my group reported[2] subtle differences in hormone-receptor expression in male tumours. In particular, we observed clustering of androgen and oestrogen receptors in male samples and showed that androgen-receptor expression was associated with better overall survival. These differences could open up new avenues for treating male breast cancer, such as androgen-targeting approaches, which have not previously been considered.

Molecular (or gene-expression) profiling is also starting to reveal deeper differences. Female breast cancer can now be divided into as many as ten different molecular subgroups, according to a recent paper[4]. Data published in February 2012 (ref. 5) indicate that male breast cancer has two subgroups, both of which seem to differ from the female subgroups. I hope that characterizing these subgroups — identifying the differences in tumour biology and treatment outcomes — will allow the development of targeted treatments for male breast cancer. Such targeted treatments for female breast cancer have made a huge impact, adding years to women's lives.

A 2010 study[6] suggests that male breast cancer also has a specific microRNA profile. MicroRNAs are regulatory RNAs that affect the stability and efficiency of the translation of messenger RNA, the intermediate between genes and proteins. Identifying a microRNA-specific signature in male breast cancer could provide further insight into disease pathogenesis, augmenting the results from gene-expression approaches.

At present, the treatment of male breast cancer relies heavily on what works for female breast cancer. As the subtle differences between male and female breast cancers become clear, it will be important to plan clinical trials exclusively for male breast cancer patients in order to determine optimal treatments. Building this capacity will allow formal testing of the emerging sex-specific data from gene-expression and microRNA profiling, indicating the potential usefulness of these molecules or signatures as markers of disease outcome or treatment progress.

THE NEGLECT OF MALE BREAST CANCER EXTENDS FURTHER THAN A LACK OF UNDERSTANDING ABOUT ITS BIOLOGY.

The neglect of male breast cancer, however, extends further than a lack of understanding about its biology. Men with breast cancer are often treated in the same clinic as women; if a patient is accompanied by a woman, many people (staff and patients) assume that he is there in a supporting role, rather than as a patient. Added to the stress of a breast cancer diagnosis, such social and psychological factors can be distressing. Patients or patient advocate groups should campaign to establish men-only breast cancer clinics to help address these issues. Providing information on treatment side effects that is better tailored to the needs of male patients would also help.

Finally, given the lack of public awareness, men are less likely than women to report signs of breast cancer, such as lumps in their breast tissue, so the disease is often diagnosed at a later stage when it is harder to treat. More public education is therefore needed — for example, through groups like the John W. Nick Foundation in Sebastian, Florida, a charity that promotes male breast cancer awareness — so that men know about the risks of breast cancer and the measures they can take to reduce them. Such education is also vital if society is to move away from the idea that breast cancer affects only women. ■

Valerie Speirs *is a reader in cellular pathology at Leeds Institute of Molecular Medicine, University of Leeds, UK.*
e-mail: v.speirs@leeds.ac.uk

1. Ferlay, J. *et al. Int. J. Cancer* **127**, 2893–2917 (2010).
2. Shaaban, A. M. *et al. Breast Cancer Res. Treat.* doi:10.1007/s10549-011-1856-9 (18 November 2011).
3. White, J. *et al. Breast Cancer Res.* **13**, 219 (2011).
4. Curtis, C. *et al. Nature* doi:10.1038/nature10983 (18 April 2012).
5. Johansson, I. *et al. Breast Cancer Res.* **14**, R31 (2012).
6. Lehmann, U. *et al. BMC Cancer* **10**, 109 (2010).