The incidence of male breast cancer in the UK is approximately 240 new cases each year compared with approximately 40,500 new cases per year in women. Male breast cancer comprises about 1 per cent of all breast cancers worldwide. In the USA, the incidence of male breast cancer is seen to be increasing alongside that of women, and the current incidence is 0.86–1.08 per 100,000 men. As male breast cancer is rare, there are few clinical trials specifically focused on gender-orientated treatment; many clinical recommendations in male breast cancer are therefore derived from studies of female breast cancer.

The male breast is predominantly made up of rudimentary breast duct elements with their supporting stroma, admixed with adiposity and the overlying subcutaneous tissue of the chest wall. The male breast lacks lobular tissue, the lactational element in the female, which appears in the male only if there has been significant exposure to exogenous oestrogen.

**AETIOLOGY OF MALE BREAST CANCER**

Breast cancer is an age-related malignancy and the median age of diagnosis in men is in the mid-60s. A range of acquired and
inherited risk factors have been described, but many cases appear to be sporadic in origin. There is no direct association with gynaecomastia of idiopathic origin, which is a common condition in adolescence, early adulthood and the over-60s.

Hormone-related acquired aetiological factors are attributed to imbalances between oestrogen excess and testosterone deficiency; although this is a possible mechanism of action, many patients do not have detectable hormonal abnormalities from what are generally wide normal reference ranges. Recognised risk factors of male breast cancer that are related to androgen metabolism include a history of testicular maldescent, congenital inguinal hernias, orchitis from mumps or of other aetiology and previous testicular injury. Cirrhosis of the liver may predispose to this by increasing peripheral oestrogen conversion from androgens. There is also an association with male infertility. A higher incidence of breast cancer is also recognised in men who have had exogenous oestrogen exposure following gender reassignment. Patients with prostate cancer may be recommended antiandrogenic therapy or oestrogen as hormonal manipulation. Obesity increases the oestrogen–testosterone ratio and is a risk factor for male breast cancer. Prolactin is another hormone that is associated with male breast cancer, although the cause and effect of this is less certain.

Radiation exposure is linked to male breast cancer; studies from Japanese survivors of the atomic bomb suggest that the excess relative risk is eight-fold per sievert of radiation in a dose-response manner. Other environmental factors associated with male breast cancer include chronic heat exposure that might suppress testicular function; industries implicated are workers in blast furnaces and the steel industry.

A link to high-risk breast and ovarian cancer predisposition genes that affect women is described, in particular with **BRCA2** located on chromosome 13. Carriers of these high-risk breast cancer predisposition genes form less than 10 per cent of breast cancers in total. While the breast cancer penetrance in women may be in excess of 80 per cent with **BRCA1** and 60 per cent with **BRCA2**, the penetrance in men appears to be approximately 6 per cent by age 70 years.

Klinefelter’s syndrome is characterised by an XXY karyotype resulting in small testes, azoospermia and gynaecomastia. Affected men have an increased risk of breast cancer that is 50 per cent higher than the general lifetime risk of unaffected men.

**PATHOLOGY OF MALE BREAST CANCER**

The majority of male breast cancers present as symptomatic invasive disease. The early detection of the preinvasive form, ductal carcinoma in situ (DCIS), is rare in the absence of effective breast screening in men. DCIS in women formed less than 5 per cent of all breast malignancies until the establishment of the NHS Breast Screening Programme in women over the age of 50 years in the UK; it now constitutes 20 per cent of diagnoses of malignant breast cancer.

Most invasive breast cancer in men is of ductal phenotype because the male breast lacks terminal lobules. Specialised forms of invasive breast cancer described in men include medullary, tubular and mucinous subtypes, which have been reported at low frequency. Inflammatory carcinoma and Paget’s disease can occur with equivalent relative frequency in both men and women. DCIS of the male breast is mainly of a papillary subtype.

Male breast cancer is approximately 80 per cent oestrogen-receptor positive and 75 per cent progesterone-receptor positive, the relative frequency of which is not dissimilar to that of postmenopausal women. Thirty-seven per cent of male breast cancers overexpress the human epidermal growth factor receptor-2 (HER-2), 30 per cent overexpress P53, 79 per cent overexpress BCL2 and 39 per cent overexpress epidermal growth factor receptor, proportionally slightly higher in prevalence for each of these receptors than in women diagnosed with breast cancer.

**CLINICAL FEATURES**

Most male breast cancers present as a painless mass in the subareola position. The male breast disc can be asymmetric; hence as the malignant mass increases in size, the lumps can also present away from the nipple-areola complex.

Changes in the nipple-areola complex may take the form of nipple retraction (see Figure 1), inversion, ulceration or a rash. Blood-stained nipple discharge is associated with male breast cancer where there is an extensive associated intraductal component or in pure DCIS without invasion through the basement membrane that surrounds the breast epithelium. Male breast cancer may be associated with serous nipple discharge. Breast cysts in men are rare and therefore any appearances of a complex cyst or cystic change should be investigated further.

Paget’s disease of the breast is described in men and presents as a rash, inflammation or ulceration that affects the nipple. Changes to the nipple such as alteration of skin contour, shape or projection should therefore be referred for specialist assessment. Less common symptoms of male breast cancer are breast pain or itching. As male breast cancer progresses, axillary lymphadenopathy may develop and can sometimes be the initial site of presentation. Late presentation of male breast cancer with occult distant metastases is rare.

**INVESTIGATION**

There is no a practical role of breast screening in men in view of the rarity, the paucity of breast tissue and the lack of impact it would make on treatment outcome in the absence of a prolonged
detectable preclinical phase of the disease. Although mammography is described in the detection and diagnosis of breast cancer, in general this is rarely necessary. When used, the features of a carcinoma on mammography are of an irregular spiculated mass. DCIS or an associated DCIS component in male breast cancer may contain pleomorphic microcalcification.

Symptoms and the physical finding of a lump or changes associated with the nipple are the principle features of male breast cancer at presentation. The primary aim is to distinguish a breast mass with the potential diagnosis of a cancer from gynaecomastia, which is a diffuse enlargement of the male breast disc. It is of course possible that both conditions can coexist. Ultrasound of male breast cancer shows an irregular hypoechoic solid mass (Figure 2a) with posterior acoustic shadowing; on colour Doppler imaging, the mass demonstrates increased blood flow.\textsuperscript{13,14}

A tissue diagnosis is best obtained by ultrasound-guided core biopsy. This provides the histologic characteristics of the tumour as well as the oestrogen receptor, progesterone receptor and HER-2 status. Ultrasound examination should include the ipsilateral axilla (Figure 2b) and any abnormal nodes should be sampled by fine-needle aspiration or core biopsy. Magnetic resonance imaging is not usually required in the diagnosis of male breast cancer.

The options available for treatment of breast cancer in men will be discussed in the second part of this article.

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**REFERENCES**


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*Figure 2. Ultrasound image that shows (a) an irregular solid mass with internal echoes diagnostic of male breast cancer and (b) abnormal metastatic axillary lymph node with a thickened cortex*