Male breast cancer: treatment options

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As male breast cancer is so rare, treatment recommendations are in general based upon data derived from clinical trials of women with breast cancer. In the second article in this series, the author looks at the available treatment options for breast cancer in men.

Men who are axillary node negative on ultrasound imaging criteria or who have an ultrasound-guided needle biopsy that is negative for metastasis are suitable for sentinel node biopsy. Patients who are sentinel node biopsy positive or proven to be node positive on preoperative assessment are recommended to have an axillary dissection. Sentinel node biopsy to select men to whom conservative surgery to the axilla can be offered reduces the risk of shoulder stiffness, seroma formation, wound infection and subsequent arm lymphoedema. An example of the gross pathology and histology of male breast cancer is shown in Figure 2.

LOCAL ADVANCED BREAST CANCER

Most patients with locally advanced breast cancer are treated by primary endocrine therapy if the tumour is oestrogen-receptor (ER) and progesterone-receptor (PgR) positive. Patients who do not respond to endocrine therapy or those with ER-negative locally advanced breast cancer may be treated by primary chemotherapy if medically fit. With a good response, the tumour may be downsized to allow simple mastectomy or modified radical mastectomy. Where significant defects require to be resected in spite of primary medical therapy, resurfacing of the chest...
A myocutaneous flap might be required. Hair-bearing skin from the back or the abdomen may be used, which provides a similar appearing skin surface to the surrounding chest wall tissue.

**ADJUVANT THERAPY**

Adjuvant chemotherapy improves overall survival and reduces the risk of recurrence in patients with breast cancer of moderate and poor prognostic type. Clinical indications for chemotherapy include larger tumours of high-grade type, the presence of lymphovascular invasion, lymph-node positivity, ER- and PgR-receptor negativity and human epidermal growth factor receptor-2 (HER-2) positivity. Patients with tumours larger than 2cm, particularly if grade III, are offered chemotherapy even if node negative.

Although there are limited trial data to support the role of adjuvant chemotherapy in men, there is general agreement that patients with stage II disease are offered adjuvant chemotherapy. Most adjuvant chemotherapy regimens incorporate the use of an anthracycline such as epirubicin or doxorubicin, in conjunction with cyclophosphamide, and some regimens include 5-fluorouracil.

Systemic chemotherapy incorporating an anthracycline as above combined with a taxane is usually recommended in men who are hormone-receptor negative. HER-2-positive cancers are treated with trastuzumab (Herceptin) with the taxane component but not with the anthracycline component because of possible potentiation of adverse effects. A total of six cycles of chemotherapy is usually given as two- to three-weekly cycles while trastuzumab is usually scheduled three-weekly for one year.

Radiotherapy is often delivered to prevent local recurrence, but less is known about the impact on survival rates. The case for post-mastectomy radiotherapy is more established in patients with larger tumour size (greater than 3cm, node involvement, high-grade tumours, multifocality and extensive lymphovascular invasion). Several studies have found that radiation reduces the risk for local recurrence, but its impact on overall survival remains controversial. Radiotherapy is usually incorporated to control locally advanced ulcerating disease or as adjuvant therapy after surgical resection.

**ENDOCRINE TREATMENT**

Most cases of male breast cancer are ER positive and the adjuvant endocrine treatment of choice is tamoxifen, which is usually given for five years.

The use of aromatase inhibitors in men remains controversial, as 20 per cent of circulating oestrogen in men is produced by the testis, which is independent of the aromatase enzyme system. Complete inhibition of oestrogen may therefore not occur in the absence of an orchietomy or with concomitant use of a gonadotrophin-releasing hormone analogue. In spite of these theoretical considerations, aromatase inhibitors are commonly used in men, with successful outcomes.

**METASTATIC BREAST CANCER**

Common sites of distant metastases include bone, lung, liver, brain, and the cervical and mediastinal lymph node groups. Systemic therapy in patients with ER-positive disease is endocrine in the first instance. In metastatic disease, hormonal therapy is as effective as chemotherapy in patients who are ER positive. Disease recurrence in spite of previous tamoxifen therapy is usually retreated with tamoxifen if a reasonable interval from therapy has elapsed.

Kantarjian et al. found that orchietomy was not additive to treatment response with hormonal therapy, but others have reported adjunctive benefits of orchietomy or gonadotrophin-releasing hormone agonists. The efficacy of the aromatase inhibitors in men with metastatic breast cancer remains controversial. Various case reports have shown some benefits in men with metastatic disease.

Chemotherapy with second-line agents may be used as necessary depending on systemic treatment exposure at initial diagnosis and treatment. The role of trastuzumab in metastatic male breast cancer may be of benefit either as part of first-line treatment or in retreatment.
important that tissue histology and the cancer biomarkers ER, PgR and HER-2 are re-evaluated where possible upon relapse in metastatic disease to guide endocrine and biological treatments.

CONCLUSIONS
Male breast cancer is rare and treatment recommendations are in general based upon data derived from clinical trials of women with breast cancer. Invasive carcinoma is more common than DCIS and most invasive carcinoma in men is of invasive ductal type. Men have high rates of ER and PgR positivity and are amendable to response with endocrine treatments. Limited data are available for determining which patients might benefit from radiation therapy after mastectomy for male breast cancer that is detected early.

In metastatic disease, hormonal therapy is as effective as chemotherapy in patients who are ER positive as first-line treatment. Combined multimodal therapy including chemotherapy is used upon disease progression in men with hormone-insensitive breast cancer. Future investigation to help delineate pathologic markers to influence breast cancer treatment and prognosis in men would better define clinical management plans.

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REFERENCES