Practical Approach to the Management of Breast Cancer

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Introduction

Breast cancer has become the commonest cancer affecting women in Hong Kong since 1994. The number of new cases rises by an average of 6.4% every year in the last decade, a trend faster than the growth of all other cancers in women including colorectal and lung cancer. Almost 60% of cases are seen in the age group between 40 to 60 years. However, age-adjusted incidence rises with increasing age which does not drop after the age of 70. Patients under the age of 40 constitutes about 10% of all breast cancers.

First Presentation of Breast Cancer

According to the multidisciplinary breast conference database at the Hong Kong Sanatorium and Hospital, almost 80% of patients noticed a painless lump in their breast accidentally, either during bath, massage or felt by their partner. The first medical visit they pay is usually to their family doctor, or gynaecologist.

To differentiate a benign from malignant breast lump, the usual criteria of hard consistency and irregular edge apply. However, the picture is often confused when a painless mobile lump occurs in a relatively young patient, or a plaque of thickening in a lumpy breast in women in their thirties and forties. Slow growing cancer such as tubular or mucinous carcinoma can mimick a fibroadenoma on physical examination. Fibrocystic breast change with sclerosing adenosis or excessive fibroadenoma on physical examination. Fibrocystic breast change with sclerosing adenosis or excessive fibrous stroma, or deep seated cyst beneath hyperplastic breast tissue can produce irregular hard thickening mimicking a malignant growth.

What to Choose for Imaging of a Palpable Breast Lump

Most doubtful lumps on physical examination could easily be clarified on breast ultrasound, with high resolution probe of 10 -13 MHz. Benign solid lumps are usually seen as flattened homogeneous hypoechoic mass with well defined echogenic rim around it. Cysts are usually anechoic with posterior wall enhancement. Any tall shaped hypoechoic lesion with heterogeneity, highly irregular outline, microlobulated or serrated edge, or posterior wall shadowing calls for suspicion and warrants further investigation. Breast ultrasound is superior to mammogram in diagnosing breast cancer in palpable lump, as shown in the multidisciplinary breast conference data (91% vs 77%).

Our young patients usually have dense breasts with little intraparenchymal fat, therefore forming a distinct layer of subcutaneous and retromammary fat, sandwiching a compact layer of breast parenchymal tissue. On ultrasound, the normal breast parenchyma appears as a layer of light coloured echoes, while the normal fat layer appears as a darker layer. Abnormal growth, be it solid or cystic, benign or malignant, stands out as a darker shadow inside the lighter background of breast parenchyma. On mammogram, glandular tissue is lighter (“whiter”) in colour and fatty tissue is dark. Abnormal lesions all appear as whiter opacity on mammogram. Therefore it would be easily masked in a background of “white” glandular layer. This explains the non-visualisation of some benign or malignant lumps in dense breasts, even if they are palpable.

However, when intramammary fat content increases in obese patients, or postmenopausal women, these appear as patchy dark shadows inside the breast parenchyma. Abnormal tumour growth may then become masked by such shadows on ultrasound but become better visualised on mammogram. The accuracy of mammogram increases with more fatty content of the breasts, therefore its diagnostic accuracy increases with age. It is also supported by evidence from our Multidisciplinary Breast Conference database.

Place of Mammogram in Breast Cancer Diagnosis and Management

Early breast cancer that is too small to cast a shadow on ultrasound, may appear as microcalcifications or architectural distortion on mammogram. Microcalcifications are seen in about 40% of all breast cancers, and become the earliest sign of cancer even before they form a mass. Microcalcifications can be visualised even in dense mammograms and form the basis of early detection that brings about impact on mortality reduction in many screening programmes.

In our experience, screening mammogram detects 12% obviously benign macro or microcalcifications that do not need further intervention. For indeterminate lesions that require biopsy, 1 out of 4 is confirmed cancer. For a palpable lump that already shows a malignant picture on ultrasound, mammogram is essential before contemplating breast conserving surgery, to exclude any nonpalpable multicentric growth that produces early mammographic signs such as suspicious microcalcifications or architectural distortion.
When to Use MRI Breasts

With improved technology in magnetic resonance imaging, MRI breasts provides additional information on the breasts when findings are equivocal on ultrasound or mammogram. This often occurs in patients with severe fibrocytic breast change that casts multiple ill-defined shadows in ultrasound, and mammogram often shows dense breast tissue only. We have experience in detecting extensive DCIS that do not form microacifications and multicentric tumours that are difficult to be differentiated from benign breast change by ultrasound or mammogram. Indeed recent study conducted at Yale University showed that 28% of planned lumpectomy breast cancer cases changed their plan of management to mastectomy because of additional findings in MRI. Unfortunately, the false positive rate of MRI is between 35 to 40% in reported series in literature and therefore is yet to be evaluated as a necessary investigation for all breast cancer undergoing surgery.

At the present time, imaging of breast by MR is recommended for equivocal lesions by other imaging methods, and as a routine screening procedure in addition to mammogram and ultrasound in BRCA1&2 gene mutation carriers but not replacing them. In fact, cancer detected with malignant microcalcifications are not all seen on MRI.

Importance of Triple Assessment

Apart from clinical diagnosis based on physical examination and imaging diagnosis based on ultrasound and/or mammogram, cytohistological assessment is an important part in the trio.

Fine needle (FNA) or core needle biopsy (CNB) should always be considered in the triple assessment of palpable breast lumps. Mucinous carcinoma, which notoriously gives a benign appearing picture simulating fibroadenoma on physical and ultrasound examination, would easily be missed without a cytology arm of assessment. It is therefore a routine to biopsy using at least a fine needle (FNA) for young women with presumably palpable fibroadenoma, if the lump is to be observed.

For nonpalpable breast lesions which are seen on ultrasound, radiology opinion should be sought as to the degree of suspicion whether needle biopsy is needed. One should avoid excessive biopsy of all ill defined hypoechoic lesions which are often seen in fibrocytic breast change. In short, the need for such biopsy should be guided by radiology recommendation.

The choice between fine or core needle biopsy lies with the clinician. Both carry a high accuracy of over 90% as seen in our Multidisciplinary breast conference data. FNA is simple, carries no subsequent scar, and has few complications apart from occasional bruising. CNB needs local anaesthetic, has a small nick wound, and has a small rate of intraparechymal bleeding that may mask the original tumour. However, it provides information on the presence of invasion and grading of tumour that help preoperative planning of surgery. As there is a small false positive rate in FNA, we will perform mastectomy based on core needle biopsy result but not FNA.

For nonpalpable lesions that are indeterminate in picture, higher tissue yield and increased accuracy can be achieved with the use of ultrasound or mammogram guided (stereotactic ) vacuum assisted biopsy (VAB). Its use in removing benign tumours by piecemeal is faced with a recurrence rate of around 12-16% which should be explained to the patient before the procedure and that a FNA diagnosis to confirm its benign nature should be done before the attempted mammotomy removal (guidelines from American Society of Breast Surgeons).

Staging of Breast Cancer

When a lump or nonpalpable lesion is diagnosed as breast cancer, staging procedure could be simple chest x-ray, abdominal ultrasound and blood test, to look for distant metastasis. Breast ultrasound and mammogram may have already provided information on gross nodal status in the axilla and local region. If there is obvious nodal involvement proven on cytohistology, more detailed staging procedure such as PET-CT fusion scan, whole body MRI, or CT thorax and abdomen and bone scan could be performed.

Principles of Breast Cancer Treatment

Surgery is still the main treatment that brings about cure of breast cancer. This applies to early stage disease in stage 0,1 and 2. However, for stage 3 disease, neoadjuvant drug therapy should be considered before definitive surgery for upfront control of micrometastasis which becomes highly probable. It can also render locally advanced disease more operable, and in selected cases, may be able to downsize tumour to avoid mastectomy. For stage 4 disease, cure is unlikely and the main treatment is systemic drug therapy for control of disease. In this situation, surgery and radiotherapy are palliative measures to prevent complications.

Surgical Treatment of Breast Cancer

Surgery of breast cancer can be divided into two parts: breast and ipsilateral axilla.

Randomised studies have proven that breast conserving surgery coupled with irradiation has equivalent outcome as mastectomy in terms of local recurrence and survival. It should be reminded that the purpose of breast conserving surgery is to avoid long term psychosocial sequelae of mastectomy. Local mammoplasty procedures are often employed to restore an aesthetically intact breast and to facilitate subsequent mammogram surveillance. It should be offered as an option to suitable patients. According to our Multidisciplinary Breast Conference database, about half of breast cancer patients can be treated with breast conserving surgery. From medical viewpoint,
case selection is based on relative tumour size to breast volume, tumour location (medial especially medial-lower quadrants may create more difficulties in local mammoplasty), safety of breast irradiation in patients with autoimmune skin disorders and cardiac disease. Age of patient, presence of axillary lymph nodes or histological type of cancer are not contraindications to breast conserving surgery.

For those that require mastectomy, the option of immediate or delayed breast reconstruction should be offered. From our experience, immediate reconstruction is preferred as the cosmetic outcome is much better, allowing for skin sparing, or even areolar or nipple sparing techniques in mastectomy, and the patient will not suffer from a period of physical loss of breast. There is ample evidence in the medical literature that reconstruction will not mask local recurrence or cause undue delay in subsequent systemic treatment.

For the treatment of regional lymph nodes, level I and II dissection has been the conventional approach as a staging and treatment procedure. For those with palpable axillary nodes and confirmed involvement by FNA, this is still the standard procedure. With detection of earlier stage disease through population based screening, sentinel node biopsy is invented in the early nineties as an axillary staging procedure for early stage cancer. The aim is to avoid unnecessary axillary dissection that carries long term morbidity such as upper limb lymphedema. It has been shown to carry the advantage of enhanced pathology in diagnosing micrometastatic spread in axilla and has a high accuracy rate of over 95% in large medical centres in staging of the axilla. Ongoing randomised trials have shown no deleterious effect or excessive local axillary recurrence over conventional axillary dissection.

The Trend in Breast Cancer Management

Launch of regular breast cancer screening programmes worldwide leads to detection of breast cancer at an earlier stage. This allows for more breast conserving surgery to be performed and the physical stigma of cancer surgery to women can be reduced.

Breast cancer is a heterogeneous disease. With more understanding of breast cancer biology and research into targeted therapy, treatment can be more individualised and treatment sufferings can be reduced.

Adjuvant Systemic Therapy for Early Breast Cancer

Randomised trials have shown improved survival with the use of adjuvant drug therapy after breast cancer surgery for stage 2 and selected stage 1 cancers. Age of patient, tumour size, tumour grade and nodal status are important determinants on the need for adjuvant drug therapy. Factors such as oestrogen and progesterone receptors, c-erbB2 receptors are predictive factors for the effectiveness of certain targeted therapy and chemotherapy.

As adjuvant therapy, patient treatment should be individualised. Decisions will also take into account the patient’s past medical health, balancing the benefits and risk of individual drug therapy against the documented evidence of gain in survival.

The use of drug therapy after breast cancer surgery is to eliminate any possible micrometastasis which may be harbouring in the body and disseminated at the time of presentation of disease. Unfortunately, there is no known test which can predict the presence of these micrometastasis. Hopefully, development in gene signature can solve this problem in future. Until such time, our recommendations for such treatment is based on current available medical evidence.
Table 1. Triple Assessment of breast lump

- Clinical diagnosis
- Imaging diagnosis
- Cytopathological diagnosis
If concordant, >95% accuracy in diagnosis of the underlying nature

Table 2. Multimodality treatment of breast cancer

**Surgery:** main treatment for curable cancer

**Systemic drug therapy:** adjuvant or neoadjuvant, to treat micrometastasis; main treatment for metastatic cancer

**Radiation therapy:** reduce local recurrence and translate into survival gain

Table 3. Systemic drug therapy for breast cancer

- **Chemotherapy**
  - Anthracycline, taxane
  - Navelbine, gemzar
  - Xeloda oral

- **Hormonal therapy**
  - Tamoxifen
  - Aromatase inhibitor: arimidex, femara, aromasin

- **Biological therapy (targeted at receptors)**
  - HER-2 receptor: Herceptin, Lapatinib
  - Angiogenesis Inhibition: Avastin

References

1. Hospital Authority Hong Kong Cancer Registry 2005.