

BREAST CARCINOMA-IN-SITU: AN EMERGING PROBLEM IN SINGAPORE

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ABSTRACT

Breast carcinoma-in-situ constitutes 4.1% of 707 breast cancers diagnosed between 1988 and 1990. Among these 30 patients, intraductal carcinoma-in-situ (DCIS) outnumbers lobular carcinoma-in-situ (LCIS) by 9-fold. They are mostly symptomatic - 87% present as breast lumps and/or nipple discharge, with 52% of lumps exceeding 2cm size. Three patients were detected by screening mammography and it is expected that more breast carcinoma-in-situ will be detected through mammographic screening. Two-thirds of the patients had mastectomy while the rest had lesser procedures. The different surgical procedures and adjuvant therapy instituted for the patients are reflections of the differing opinions regarding optimum therapy for carcinoma-in-situ and the differing rationale for DCIS and LCIS lesions.

Keywords : Breast Cancer, Intraductal carcinoma, Lobular Carcinoma-in-situ, Mastectomy

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INTRODUCTION

Breast carcinoma-in-situ has become a clinical problem because of increased mammographic examination. It has been reported in a national survey among 1029 physicians that there has been a three-fold increase of doctors referring their patients for screening mammography⁽¹⁾.

This imaging tool has detected pre-invasive breast cancers with increasing frequency during the past 15-20 years. However, therapeutic knowledge lags behind technology as the best treatment option for breast carcinoma-in-situ is still in a state of flux. Since local tumour control and survival for intra-ductal carcinoma-in-situ (DCIS) approaches 95% with mastectomy, surgeons face the paradox of advocating conservative procedure for invasive cancers and advising aggressive approach for non-invasive lesion⁽²⁻⁴⁾.

It is interesting to note that in all the past 3 publications on breast carcinoma in Singapore, not a single case of breast car-

cinoma-in-situ was diagnosed out of 649 women⁽⁵⁻⁷⁾. Will Singapore experience the same trend shown in Western countries as more and more patients are referred for screening mammography by their family physicians and by the Polyclinic Well-Women Clinic? Although some feel that mammography is not as useful in Asian women because of their smaller and denser breasts, better mammographic machines and improved nutrition may have to be taken into consideration. Meanwhile, this study serves to document the pattern of pre-invasive breast cancer among local women. It also draws the attention of clinicians to the current controversies.

MATERIAL AND METHOD

A computerised printout of all cases of breast carcinoma diagnosed at Tan Tock Seng Hospital and Singapore General Hospital between 1988 and 1990 was provided by the Pathology Department. The list was used to trace the patients' case records from which data were collated for both intraductal and lobular breast carcinoma-in-situ. All invasive carcinoma were excluded; as also were those invasive cancers with co-existent carcinoma-in-situ.

The following generally accepted criteria were used to diagnose breast carcinoma-in-situ

1. Intraductal carcinoma-in-situ

In general ductal carcinoma-in-situ is characterised by the proliferation of malignant epithelial cells confined to the mammary ductal system without light microscopic evidence of invasion through the basement membrane into the surrounding stroma.

2. Lobular carcinoma-in-situ

The entire lobule and/or terminal ducts are distended with neoplastic cells. These cells are smaller than those seen in ductal carcinoma-in-situ and are loosely cohesive. They have round to oval nuclei with small nucleoli.

RESULTS

During the period of study, 707 invasive breast cancers and 30 carcinoma-in-situ cases were diagnosed and treated in the two largest hospitals in Singapore. Among the pre-invasive cancers, the majority (27 cases) were the intraductal carcinoma (DCIS). Two patients had lobular carcinoma-in-situ (LCIS) and one had co-existent DCIS and LCIS. The youngest patient was 29 years while the oldest was 79 years - the age distribution being: 21-30 years (2), 31-40 years (2), 41-50 years (11), 51-60 years (8), 61-70 years (3), 71-80 years (4).

Only 3 patients had truly subclinical, nonpalpable lesions detected by screening mammography through the Well-Women

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Clinics in the government polyclinics. The rest presented with either breast lump, nipple discharge or axillary lymphadenopathy (Table I). Among those with breast lumps, 52.4% were more than 2cm size (Table II).

Table I - Clinical Presentation

Breast lump	19
Breast lump with discharge	2
Nipple discharge alone	5
Axillary lymphadenopathy	1
Asymptomatic (screening mammography)	3

Table II - Size of lesions presenting as lumps

Size of Lump	Number
<1cm	2
<2cm	8
<5cm	7
>5cm	4
Total	21

The 3 patients diagnosed through screening mammography had DCIS lesions. Another 11 patients had mammography as part of pre-operative workout because they were clinically suspected of having breast cancer on the basis of their age. The mammogram reports of these 14 cases showed that 12 had features suggestive of malignancy whereas 2 were thought to have benign-looking microcalcifications.

Twice as many patients underwent mastectomy as those undergoing wide excision or sector mastectomy (Table III). Among those who had conservative surgery, one 48-year-old woman had sector mastectomy showing multiple foci of DCIS but she refused further mastectomy and opted for irradiation instead. No adjuvant therapy was offered to 13 DCIS patients, 9 of whom had mastectomy while 4 had wide excision/sector mastectomy. The latter procedure was done for lesions which were less than 2cm. Adjuvant chemotherapy was administered to 4 DCIS patients while 7 were treated with adjuvant tamoxifen. Postoperative irradiation in addition to tamoxifen was given for one DCIS patient, and one other DCIS patient with axillary nodal disease had chemotherapy and tamoxifen as well as radiotherapy.

Table III - Surgical Procedure

Mastectomy	20	(1 patient had concomitant DCIS/LCIS)
Wide Excision/ Sector Mastectomy	9	(including 1 LCIS patient)
Microdochectomy	1	(LCIS patient)

Among the LCIS patients, one had wide excision alone. Another was diagnosed after microdochectomy was performed for nipple discharge but she refused further surgery. Unfortunately, she developed invasive intra-ductal carcinoma one and a half years later. Mastectomy was then performed and as the axillary nodes were free of disease, no adjuvant therapy was added. The patient with the unusual concomitant LCIS and

DCIS was treated with mastectomy, postoperative radiotherapy and tamoxifen.

The mean follow-up was 21.4 months (range 7-24 months) and at the time of review, no recurrence or malignant development was detectable in any of the patients.

DISCUSSION

The American College of Surgeons National Survey in 1978 showed that only 0.84% of 24,000 new breast cancers were intraductal carcinoma-in-situ (DCIS)⁽⁸⁾. The prevalence rose in the 1980s when routine X-ray screening gained widening acceptance. More occult breast cancers were being detected and of these, 40-78% were the non-invasive carcinoma-in-situ type rather than the micro-invasive variety^(3,9). As a result, DCIS increased from 0.8% - 5% breast cancers to the current prevalence of 15-20%. LCIS constitutes another 2.5%-6%⁽¹⁰⁾. Our study indicates that presently the incidence of breast carcinoma-in-situ is about 4.1% in Singapore.

In our study, DCIS outnumbers LCIS by 9 times and this is far more than the 4-fold difference in Western series^(3,9). Presently, almost all our DCIS are symptomatic (presenting with breast lumps and/or nipple discharges), whereas in Western studies, the asymptomatic DCIS is the rule. This differentiation is important as it influences the extent of surgery^(11,12).

The dramatic increase in mammographic pick-up is due to the fact that DCIS tends to precipitate calcium into the ductal lumen and this manifests as microcalcifications^(10,13). On the other hand, LCIS do not undergo necrosis or have extracellular secretions⁽³⁾ and so there are no distinctive features. However, X-ray calcification are still the main reasons for biopsy. These are almost always in the benign breast tissue while LCIS actually lies outside the radiologically-suspicious areas^(3,14). Hence, in the clinical setting, LCIS is often an unexpected histological finding on biopsy of so-called benign lesions⁽³⁾.

Another paradoxical phenomenon is that mammography has caused a shift towards detection of small invasive cancers but not for the non-invasive intra-ductal cancers⁽⁹⁾. A recent report from Netherlands revealed 51% were 50mm or larger and the authors declared that size distribution was independent of the mode of detection⁽⁶⁾. Similarly, among the cases from the UK Guildford Breast Screening Unit, the average size of 38 DCIS lesions was 21mm⁽¹¹⁾. In our series with only three screening mammography, the average size was 24.4mm for DCIS lesions and 35mm for LCIS.

The main concern with DCIS is that an estimated 30% will eventually develop into invasive cancer in six to nine years⁽¹⁰⁾. Since malignancy tends to be largely limited to the ipsilateral breast, total mastectomy would be curative in over 95% patients^(2,9). Our study shows that two-thirds of our DCIS patients had mastectomy. The one patient with concomitant DCIS and LCIS also underwent mastectomy. It would appear that our surgeons are inclined to this philosophy of total eradication.

It has been suggested that asymptomatic, screen-detected DCIS have a more indolent behaviour than symptomatic lesions, and that multicentricity (20%) is related to tumour size^(2,12). Only 6% mastectomy specimens of DCIS patients revealed coexistent invasive carcinoma in other parts of the breast⁽⁹⁾. Hence Lagios et al recommended excision alone for DCIS detected by mammography, when lesions are 25mm or less, when excised specimens show histologically negative margins; if postoperative mammograms are clear of residual calcifications, and if breast is suitable and patient is agreeable for mammographic and clinical follow-up⁽¹²⁾. Old women should undergo only wide excision since invasive cancer takes years to develop^(10,13).

Using the criteria⁽¹²⁾ proposed, it would mean that 13 patients instead of 8 women who had sector mastectomy or wide excision in our series would be suitable for conservative sur-

gery. The others who had mastectomy were 8 patients whose breast lumps exceed 2.5cm, 7 had nipple discharge and one case had axillary spread. There was one patient who had multiple foci of DCIS and refused mastectomy. It is worthwhile noting that a recent meta-analysis showed that salvage mastectomy for recurrence following local excision is not associated with a worse prognosis -1.7% mortality for DCIS treated with primary mastectomy compared with 2.3% mortality following mastectomy for recurrence⁽¹⁰⁾.

The need for irradiation following excision remains conjectural until the results of the NSABP B-17 randomised trial are published. It will take a few more years for the study to be completed as accrual only terminated in December 1990^(1,15). A subset analysis from the NSABP (Protocol 6) suggests that compared with lumpectomy alone, adjuvant irradiation reduces local recurrence for DCIS by three-fold (23% vs 7%). But the report admits that the sample size is too small to warrant a definite conclusion⁽¹⁶⁾. We notice that among our patients, there was no uniform policy regarding adjuvant therapy. Patients were randomly given irradiation following mastectomy (one case), adjuvant chemotherapy (4 cases including one screen-detected), adjuvant tamoxifen (7 cases), radiotherapy and tamoxifen (2 cases, including the DCIS/LCIS patient) and irradiation with chemotherapy and tamoxifen (one case of segmental mastectomy for DCIS with axillary nodal spread).

On the other hand, LCIS is a 'marker lesion' and represents a field change in which the entire breast tissue is at risk of developing carcinoma^(3,10). With LCIS, multicentric lesions occur in 50%-80% cases while bilateral breast involvement is found in 20%-45% patients^(3,10). Invasive cancer will occur equally in both breasts in 25-30% affected women, though it may take 15 years or more to develop cancers^(3,9,10).

Interestingly, when invasive disease develops after LCIS, it is usually an infiltrative ductal carcinoma (50-60% cases), as is the case in one of our patients^(3,10). So obviously, LCIS cannot be simply considered an intermediate development from pre-invasive to malignant disease⁽¹⁰⁾.

Therefore, it is clear that the rationale for unilateral mastectomy (even with biopsy of the opposite breast) is flawed^(3,9). Logically, bilateral mastectomy is the proper, effective and definitive therapy but the emotional price is high. Hence, local excision with close follow-up is a reasonable alternative^(3,9,10). We have very limited experience with LCIS as it is uncommon in our series.

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CONCLUSION

Breast carcinoma-in-situ is not a single entity for there are two distinct types, DCIS and LCIS which behave differently. Surgeons and oncologists are particularly interested in their progression to invasive cancer and in whether these changes can be predicted by histopathology, oncogene expressions, or tumour markers⁽¹⁾. At the present moment, there are still unanswered questions concerning optimal therapy for these patients. We predict carcinoma-in-situ will continue to increase in the 1990s and surgeons should follow closely the trials comparing conservative surgery with surgery that includes adjuvant radiation and hormonal therapy^(7,11,12,14).

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