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OCCURENCE OF CARCINOMA IN SITU IN ASSOCIATION WITH INVASIVE CANCER OF BREAST

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ABSTRACT

The objectives of this study were to find out the frequency and the pattern of carcinoma in situ occurring in association with different types of breast cancers. This study was conducted in the Department of Clinical Oncology and the Department of Pathology, King Edward Medical University / Mayo Hospital, Lahore on breast cancer patients diagnosed between 1st January 2001 and 31st December 2005. The age, menopausal status, histopathological type, grade, and presence or absence of carcinoma in situ were recorded. Histopathological features were recorded according to WHO system. Grade was recorded only when it was assigned according to the Elston-Ellis modification of Scarff-Bloom-Richardson grading system. A total of 1230 histopathologically documented invasive and non-invasive breast cancers patients were included in the study. DCIS alone was seen in seven patients (00.57%) and LCIS alone in two patients (00.16%). Invasive ductal carcinoma was seen in 998 patients (81.14%) and invasive lobular carcinoma in 96 patients (07.80%). Majority of breast cancers were grade II whereas grade I seen in 23.90% patients only. Areas of carcinoma in situ in different types of invasive cancers were seen in 328 (26.86%) patients. Majority of these patients were below 50 years of age. DCIS was present in 246 of 998 patients (24.65%) of invasive ductal carcinoma (NOS). Comedo pattern was seen in 154 of 290 (53.10%) of DCIS. LCIS was present in 38 of 96 patients (39.58%) of invasive lobular carcinoma. Carcinoma in situ of breast is a rarely diagnosed disease entity in our setting. It is seen mostly in association with invasive carcinoma of breast cancer. Ductal carcinoma in situ with comedo pattern is most frequent.

INTRODUCTION

The in situ carcinomas of the breast are either ductal or lobular. This distinction is based upon their growth pattern and cytological features. Ductal and lobular carcinomas in situ differ with regard to their anatomical distribution, morphology, biological behaviour and radiological appearance.[1]

DCIS is the most rapidly growing subgroup of breast cancer. In 1978 American College of Surgeons survey reported a frequency of <1 percent among newly diagnosed breast cancers.[2] But today, it accounts for about 21 percent of all new breast cancers diagnosed in the United States. Majority of these are detected only on imaging studies.[3] The ductal carcinoma in situ (DCIS) includes lesions that differ in their clinical presentation, histological appearance, and biological potential. They are all characterized by proliferation of malignant epithelial cells within the mammary ductal system, with no evidence of invasion into the surrounding stroma on routine light microscopic examination. DCIS are divided histologically into a variety of subtypes in different classification systems. The traditional method for classifying DCIS lesions is primarily based upon the architectural features of the tumour and recognizes comedo, cribriform, micropapillary, papillary and solid type.[4-7] DCIS carries a variable risk of an invasive event, and is considered to be a direct precursor of invasive breast cancer.

In contrast to DCIS, the histological features of LCIS show little variation and are typically characterized by a solid proliferation of small cells with small, uniform, round-to-oval nuclei, and variably distinct cell borders. The cells of LCIS are also typically oestrogen receptor-positive and rarely, if ever, show over expression of the HER 2 neu epidermal growth factor receptor.

LCIS is associated with a substantially increaseed risk of subsequent invasive breast cancer. Subsequent invasive cancers can develop in either breast, and can be either invasive lobular or ductal cancers. Almost half of subsequent lesions are of the infiltrating ductal type.[8] Therefore the LCIS is considered a risk factor for invasive carcinoma and in some cases, a precursor lesion to invasive breast cancer.

In our country the DCIS and LCIS are seldom diagnosed independently as a separate disease entity. They are mostly reported in association with invasive cancers in lumpectomy or mastectomy specimens. The frequency and pattern of in situ carcinomas in association with invasive

cancers has not been studied well. Their relationship to different types of histopathologies has also not been studied. This study was conducted to document the frequency and the pattern of in situ carcinomas in relation to different histopathologies of breast cancer.

PATIENTS AND METHODS

We conducted this study in the Department of Clinical Oncology and the Department of Pathology, King Edward Medical University / Mayo Hospital, Lahore. A proforma was designed to document the age, menopausal status, histopathological type, grade, and the presence or absence of carcinoma in situ. All this information was obtained from the medical record section. Data of patients diagnosed between 1st January 2001 and 31st Decemeber 2005 was included. Histopathological features were analysed by a careful review of medical reports and were reported according to WHO system.

Grade was assigned according to the Elston-Ellis modification of Scarff-Bloom-Richardson grading system (Nottingham combined histological grade).[9] This system evaluates the morphological features and includes, the percentage of tubule formation, the degree of nuclear pleomorphism and an accurate mitotic count using a defined field area. A numerical scoring system is used and the overall grade is derived from a summation of individual scores for the three variables and three grades of differentiation are used.

Carcinoma in situ in association with different histopathological types was identified and the pattern was grouped according to the conventional system.

RESULTS

A total of 10280 cancer patients presented at King Edward Medical University / Mayo Hospital, Lahore from the year 2001 to 2005. Female patients constituted 4935. Breast cancer was seen in 1450 (29.38%) female patients. The median age at the time of diagnosis of breast cancer was 47 years (range, 21-85). Record of menopausal status was available in 1138 patients only and in the remaining women above the age of 50 they were considered post menopausal and below 50 years were considered pre-menopausal. Pre-menopausal status was assigned to 754 (52%) patients and post menopausal status to 696 (48%) patients.

Histopathology reports of lumpectomy or mastectomy specimens were available in 1230 entries (84.83%). In the remaining patients 135 (9.31%) had cytological evidence of disease and in 85 (5.86%) no cytological or histopathological diagnostic evidence was available. All these were excluded from further analyses.

DCIS alone was diagnosed in seven patients (00.57%) and LCIS alone in two patients (00.16%). Invasive ductal carcinoma was seen in 998 patients (81.14%) and invasive lobular carcinoma in 96 patients (07.80%). Other types were seen in a few percent each (Table 1).

Table 1: *Histopathological diagnosis (n=1230).*

Noninvasive carcinoma	
Ductal carcinoma in situ	07 (00.57%
Lobular carcinoma in situ	02 (00.16%)
Invasive carcinoma	
Invasive ductal carcinoma	998 (81.14%
Invasive lobular carcinoma	96 (07.80%)
Mucinous carcinoma	29 (02.36%)
Medullary carcinoma	16 (01.30%)
Papillary carcinoma	14 (01.13%)
Tubular carcinoma	17 (01.38%)
Metaplastic carcinoma	02 (00.16%)
Inflammatory carcinoma	47 (03.82%)
Paget's disease of the nipple	02 (00.16%)

Table 2: *Grades of carcinoma (n=1230).*

Specified according to SBR system (= 435)	
Grade I	104 (23.90%)
Grade II	135 (31.03%)
Grading system not specified # (= 525)	
Grade I	108 (20.57%)
Grade II	225 (42.86%)
Grade III	192 (36.57%)
Grade unknown / not described = 270	

Grade was described according to the Elston-Ellis modification of Scarff-Bloom-Richardson grading system in 435 histopathology reports. Majority of patients 196 (45.06%) were grade II with grade I seen in 104 (23.90%) patients only. (Table 2). In 270 (21.95%) patients grade was not described. In the remaining histopathology reports grade was described without reference to SBR system and / or without reference to morphological features of tubule formation, nuclear pleomorphism and mitotic rate. Tumours were described as well, moderately or poorly differentiated, or of low, intermediate or high grade or grade 1, 2 or 3 (Table 2).

Table 3: *Area of carcinoma in situ in different types of invasive cancers.*

DCIS alone with IDC (NOS)	246/998 (24.65%)
DCIS and LCIS with IDC (NOS)	29/998 (02.91%)
DCIS with tubular carcinoma	07/17 (41.18%)
DCIS alone with ILC	38/96 (39.58%)
DCIS and LCIS with ILC	08/96 (08.33%)

DCIS = ductal carcinoma in situ, IDC = Invasive ductal carcinoma, LCIS = lobular carcinoma in situ, ILC = Invasive lobular carcinoma

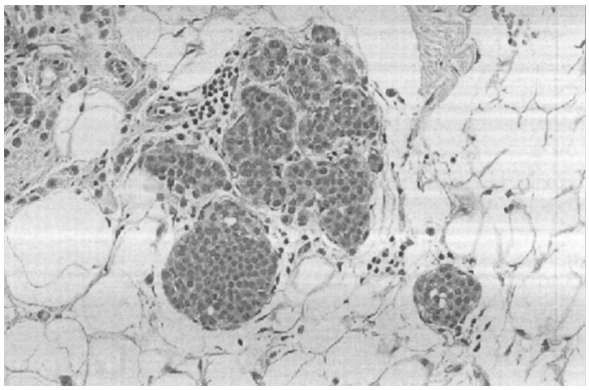

Fig. 1: *Invasive Lobular Carcinoma with LCIS Component (H&E Stain).*

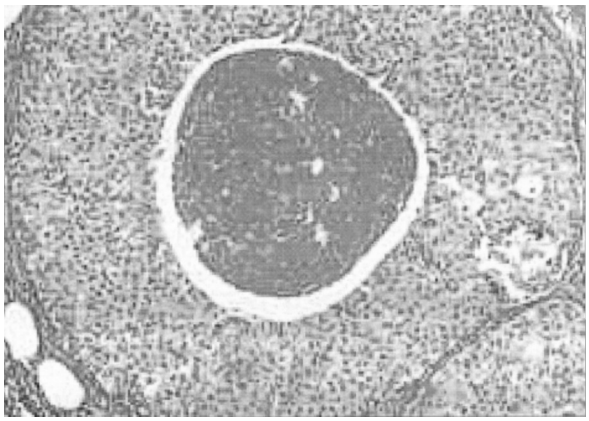

Fig. 2: *Ductal carcinoma in situ – comedo pattern (H & E Stain).*

Areas of carcinoma in situ in different types of invasive cancers were seen in 328 (26.67%) patients. Majority of these patients (64%) were below 50 years of age. DCIS was present in 246 of 998 patients (24.65%) of invasive ductal carcinoma (NOS) and in 29 (2.91%) areas with both the features of DCIS and LCIS were seen with invasive ductal carcinoma (NOS). DCIS was also seen in association with tubular carcinoma in 07 of 17 patients (41.18%).

LCIS was present in 38 of 96 patients (39.58%) of invasive lobular carcinoma and in 08 (8.33%) both the features of DCIS and LCIS were reported with invasive lobular carcinoma. LCIS as a component of invasive lesion is shown in fig.1.

Comedo pattern of DCIS was seen in 154 of 290 (53.10%) and in the remaining 136 (47.00%) it was described as non-comedo. A typical comedo pattern of DCIS is shown in figure 2. All the seven cases of DCIS in association with tubular carcinoma were described as non-comedo and were not further characterized.

DISCUSSION

Carcinoma in situ alone is rarely seen in our clinical practice. It is seen most frequently in countries where screening mammography is performed. DCIS is rapidly expanding clinical entity in the west. It accounts for about 21 percent of all new breast cancers diagnosed in the United States and the majority of these are detected during screening mammography.[3] Similarly LCIS accounts for 9.8 percent of mammographically detected malignancies.[10] Therefore, in the absence of a mass screening programme in Pakistan, the carcinoma in situ is currently seen only in association with advanced disease and is best described in lumpectomy or mastectomy specimens.

In this series DCIS and LCIS collectively have been found in 27% of lumpectomy and mastectomy specimens of invasive cancers. Presence of DCIS in mastectomy specimens has no predictive or prognostic significance. However, DCIS occurring as extensive intraductal component in invasive cancers is associated with increased risk of relapse only when lumpectomy or wide excision is performed for breast conservation. DCIS at margins of resection also confers greater risk of relapse, whereas, LCIS at margins of excision is not related with increased risk of local recurrence in breast conserving treatment. LCIS is considered to be an indicator for the risk of subsequent invasive cancer, both intraductal and lobular, in either the ipsilateral or the contralateral breast. Different DCIS lesions do not confer the same risk of local recurrence. As a result, there is continued interest in developing a classification system that predicts recurrence and possibility of progression to invasive breast cancer. Proposed classification systems for DCIS use different terminologies, all are primarily based upon nuclear grade and/or the presence or absence of necrosis and have commonly recognized three main categories of high, intermediate, and low grades.[11,14]

In this study, carcinoma in situ was not seen in patients with medullary or mucinous varieties of breast cancer. It was most frequently seen in tubu-

lar type. Significance of these findings is not known.

It is **concluded** that in the absence of mass screening programme for early detection of breast cancer the carcinoma in situ of breast is a rarely diagnosed as a distinct clinical entity. It is seen commonly in association with invasive cancer of breast. Ductal carcinoma in situ with comedo pattern is most frequently reported lesion.

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