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Ductal carcinoma in situ (DCIS) in Karachi

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Original Article

Ductal Carcinoma in Situ (DCIS) in Karachi

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Abstract

Objective: To study the frequency of ductal carcinoma in situ (DCIS) in a large pathology series. DCIS is a proliferation of non-invasive, malignant epithelial cells within the ductolobular system of the breast. It is a heterogeneous entity with several morphologic variants that differ in gross appearance, growth pattern, cytologic features, mammography, and malignant potential.

Methods: The data of The Aga Khan University' Pathology Department, diagnosed on the basis of histopathology, during a 6-year period (1st January 1998 to 31st December 2003) was reviewed, all cases of DCIS studied, and data was analyzed with the help of analytical software SPSS.

Results: Thirty-eight cases of DCIS were reported to the Aga Khan University Pathology Department, during a 6-year period (1998 to 2003), comprising approximately 1% of all breast cancers reported to the unit in the same period. The mean age of the patients at diagnosis was 48.95 years (CI 95% 44.6; 53.3). Approximately half the cases occurred in the 45-54 year age group (figure 1). Two cases (5.3%) were recurrences with previous lumpectomy scars. Comedo necrosis was observed in five (13.2%) cases, whereas 33 (86.8%) cases were non-comedo type. The clinical presentation was a palpable mass (92.1%), nipple discharge (5.3 %) or clinically occult lesions diagnosed on mammography (2.6%). Approximately half the patients presented with a grade 2 disease. Atypical ductal hyperplasia was observed in a third of the cases, predominantly associated with a grade 1 and 2 disease. The estrogen and progesterone receptor status was studied in 12 (31.6%) cases. Estrogen positivity was observed in 11 (91.7%) cases and progesterone positivity in 7 (58.3%) cases. Microcalcification was observed in four (10.6%) cases.

Conclusion: The cases reported in this study are the indolent grade 1 or 2 cases with a non-comedo pattern, and a positive estrogen and progesterone receptor status. If untreated, only 40% of these innocuous forms of DCIS become invasive over a time span of approximately 25-30 years. In Pakistan we are missing the more aggressive forms of DCIS which have a shorter transition to invasive carcinoma (JPMA 55:199;2005).

Introduction

Ductal Carcinoma In Situ (DCIS) is a proliferation of malignant epithelial cells within the ductolobular system of the breast that do not show light microscopic evidence of invasion through the basement membrane into the surrounding stroma. DCIS is a heterogeneous entity with several morphologic variants that differ in gross appearance, growth pattern, cytologic features, appearance on mammography, and malignant potential. It is a part of a spectrum of proliferative ductal lesions of the breast that extend from epithelial hyperplasia without atypia to microinvasive carcinoma.

There are various classification schemes for DCIS, the simplest classifies it into two major subtypes based on the presence or absence of comedo necrosis.[1-4] There are several other classifications based on histological structure, nuclear grade, comedo-type necrosis, cytonuclear differentiation, or various combinations of these factors. The optimal classification scheme remains controversial. Nuclear grade, comedo-type necrosis, tumour size, and the width of the tumour margin are all important predictors of the probability of local recurrence after breast conservation treatment for DCIS.[5-12] Nuclear grade and necrosis, are the basis of the Van Nuys classification.[6]

Comedo necrosis type of DCIS is diagnosed when at least one duct in the breast is filled and expanded by large, markedly atypical cells and has abundant central luminal necrosis. The partially calcified necrotic material is recognized on mammography as linear and branching calcifications. Prominent periductal fibrosis may render the lesion clinically palpable, and the resulting distortion of breast parenchyma presents some difficulty in excluding microinvasion. Noncomedo necrosis type includes the cribriform, micropapillary, and solid types, with combinations of the various histologic patterns. Necrosis if present, is less prominent than in the comedo necrosis type and not as prone to calcification. Differentiation of the noncomedo necrosis type from atypical ductal hyperplasia may be difficult.[13-15]

Methods

The data of The Aga Khan University Pathology Department, diagnosed on the basis of histopathology, during a 6-year period (1st January 1998 to 31st December

2003) was reviewed and studied. The demographic details of the registered pathology data were precise and complete. Items such as age, sex, name, address, telephone numbers and nature of surgery were well recorded at the reception counter. A single medical registration number was given to each in-patient and different specimens of the patient given separate sub-identification numbers and data updated. All cancer cases, both the in-patient and the outpatients were also given a specific cancer registration number and information updated with subsequent visits. It was thus possible to recognize duplicate examinations of the same patient. This required a well-trained staff available at all the 59 collection points of this University lab, throughout the country and also of the registration staff at the main lab. Awareness of the legal and academic requirements of accuracy of demographic data was a part of the training of the collection staff. Validity checks and random retrace of cases was conducted for follow-up and for confirmation of the information recorded.

Internal and external quality checks were used for diagnostic pathology as well as the pathology-based cancer data. External quality assurances for diagnostic pathology were maintained by the College of American Pathologists (CAP) surveys. Internal quality control and standardization of the diagnosed data was maintained by using prompt and adequate fixation, grossing as per standard protocol and using histochemical stains, immunohistochemical techniques and biological markers as and when required.

ISO 9002 certified the clinical pathology lab in 1999. Consensus diagnosis of all doubtful cases at the daily departmental consultation conferences improved the quality of diagnosed data. Assistance and technical help of Armed Forces Institute of Pathology (AFIP) Washington DC was taken for confirmation of challenging cases. Immunohistochemistry was used for malignancies, which necessitated cellular typing and sub-typing. Computerized and manual validity checks for the cancer data were also performed as per recommendations of International Agency for Research on Cancer (IARC) and International Association of Cancer Registries (IACR).[16,17] This involved factors influencing comparability i.e. classification and coding. The data are classified using the International Classification of Diseases-Oncology (ICD-O2) and computerized using a customized version of Canreg-3.[18] This software includes facilities for detecting duplicate registrations of the same cancer and for performing checks on the validity of the entered data. The data was re-checked with the help of the AKUH laboratory database using SNOMED coding and the Canreg-3 database of the Karachi Cancer Registry.[19] The variables that were recorded were the hospital patient-number date of incidence, name, age, sex, address, topography, morphology, grading and staging. The data was analyzed with the help of analytical software EPI-Info incorporated into Canreg-3 and SPSS database.

Results

Thirty-eight cases of DCIS were reported to the Aga Khan University Pathology Department, during a 6-year period (1998 to 2003). This comprises approximately 1% of all breast cancers reported to the unit in the same period. The mean age of the patients at diagnosis was 48.95 years (CI 95% 44.6; 53.3). Approximately half the cases occurred in the 45-54 year age group (Figure). The left breast was involved in 15 (39.5%), the right breast in nine (23.7%) and both breasts 2 (5.3%) cases. Laterality was not known for 12 (31.5%) cases. Two cases (5.3%) were recurrences with previous lumpectomy scars.

Comedo necrosis was observed in five (13.2%) cases, whereas 33 (86.8%) cases were non-comedo type. In the latter the spectrum of histological architecture was cribriform in 7 (21.0%), solid in 2 (6.3%), micropapillary in 8 (24.1%), and combinations in 16 (48.5%) cases. Non-comedo necrosis was observed in 2 (5.3%) cases. The clinical presentation was a palpable mass (92.1%), nipple discharge (5.3%) or clinically occult lesions diagnosed on mammography (2.6%).

Approximately half the patients presented with a grade 2 disease. (Table 1) Atypical ductal hyperplasia was observed in a third of the cases, predominantly associated with a grade 1 and 2 disease (Table 2). Fibrocystic disease was observed in 13.2% of the cases.

Table 1. Histological grade of DCIS at diagnosis.

Grade	Frequency	Percent	Cumulative percent
Grade I	8	21.1	21.1
Grade II	16	42.1	63.2
Grade III	10	26.3	89.5
Unknown	4	10.5	100.0
Total	38	100.0	

The estrogen and progesterone receptor status was studied in 12 (31.6%) cases. Estrogen positivity was observed in 11 (91.7%) cases and progesterone positivity in 7 (58.3%) cases (Table 3). Microcalcification was observed in 4 (10.6%) cases, 2 (5.3%) cases each associated with comedo necrosis and non-comedo necrosis.

Discussion

In the developed countries, DCIS was a relatively

grade 2 disease. (Table 1) Atypical ductal hyperplasia was observed in a third of the cases, predominantly associated with a grade 1 and 2 disease (Table 2). Fibrocystic disease was observed in 13.2% of the cases.

Table 2. Association of histological grade of DCIS with atypical hyperplasia.

Grade	Atypical hyperplasia	Percent	Cumulative Percent
Grade I	6	54.6	54.6
Grade II	3	27.3	81.9
Grade III	2	18.1	100
Total	11	100.0	

The estrogen and progesterone receptor status was studied in 12 (31.6%) cases. Estrogen positivity was observed in 11 (91.7%) cases and progesterone positivity in 7 (58.3%) cases (Table 3). Microcalcification was observed in 4 (10.6%) cases, 2 (5.3%) cases each associated with comedo necrosis and non-comedo necrosis.

Table 3. Estrogen-progesterone receptor status.

Status	Estrogen-Receptor (# 12) %	ProgesteroneReceptor (# 12) %
Weak +	50.0	0.0
Intermediate +	25.0	50.0
Strong +	16.7	8.3
Negative	8.3	41.7

Discussion

In the developed countries, DCIS was a relatively uncommon disease, until recently, representing only about 1% of all newly diagnosed cases of breast cancer.[20] The presentation was a palpable mass or discharge from the nipple. In 1998, DCIS accounted for about 18% of all newly-diagnosed invasive plus noninvasive breast tumors in the United States.[21] In contrast during 1997, more than 36,000 new cases of DCIS, representing 17% of all new breast cancers, had been diagnosed.[22] This figure has shown a dramatically increase, almost all the cases are diagnosed by mammography and are clinically occult. The frequency of DCIS in Pakistan is low, to date approximately 1%, and drastically low in comparison to the present status of DCIS in developed countries.

In the US 92.0% of all newly diagnosed patients with DCIS have non-palpable lesions.[22] Ironically, in the present series, 92.1% of DCIS presented with breast lumps and a mere 2.6% were diagnosed on mammography. High quality mammography is capable of finding a range of asymptomatic non-invasive lesions that cannot be palpated. These are often smaller, of lower nuclear grade, and show much subtler changes.

The considerable effect of modern mammography can be appreciated by the experience at the Breast Center in Van Nuys. During the first three years of operation (1979-81), with only a single outdated mammography unit available and no full time radiologist, an average of five cases were found each year, 16% of which were non-palpable and detected mammographically. In 1982, with four new state of the art mammography units and a full time radiologist specialising in mammography, the number of new cases increased dramatically. Fifty-eight cases were diagnosed in 1997, 11 times the number found in the first year of operation.[23]

In the best scenario, the most common mammographic finding is microcalcification and this was observed in a very insignificant (10.6%) number of cases in the present study. This calls for capacity building in terms of machines and manpower, for the detection of the most innocuous cases. Good mammography, is expensive, requires state of art mammography machines and radiologists specialising in mammography capable of exceptional attention to detail. The need for expert radiological interpretation cannot be overemphasized and is sadly deficient in Pakistan.

The cases reported in this study are the largely indolent grade 1 or 2 cases with a non-comedo pattern, and associated atypical ductal hyperplasia. The estrogen and progesterone receptor status was studied in a third of the cases, the estrogen status was positive in almost all these cases and two thirds exhibited a progesterone positivity.

If untreated, these innocuous looking forms of DCIS (low nuclear grade, small celled without necrosis, positive estrogen and progesterone receptor status, and a negative c-erbB2) may never cause a clinical problem. Only about 40% of untreated low-grade lesions become invasive over a time span of approximately 25-30 years.[25]

In Pakistan we are missing the more aggressive forms of DCIS which have a shorter transition to invasive carcinoma.This justifies the feasibility of breast screening for the detection of DCIS in a low resource setting, atleast in the high risk groups. Planning for appropriate capacity building is necessary to provide affordable, readily available, state of art mammography.

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