Intraductal Breast Cancer: Review of 183 Consecutive Cases

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The aim was to review a series of 183 intraductal breast cancer to define the diagnostic features and therapeutic outcome. Patients' average age was 54 years. Diagnostic procedures employed were clinical examination, mammography in 173 cases and fine-needle aspiration cytology in 98 cases. The sensitivity of clinical examination was 0.61, of mammography 0.74, of fine needle aspiration cytology 0.70. The sensitivity of clinical examination and mammography associated was 0.93. The surgical options adopted were: conservative surgery 80 cases, mastectomy 103 cases. Conservative surgery was followed by breast irradiation in 34 cases. Axillary dissection was performed in 122. 97 cases have been reviewed histologically. 60% of ductal carcinoma *in situ* (DCIS) were multifocal and 22% multicentric. Local recurrence, all infiltrating, occurred in the same breast after conservative surgery in 8 cases, 3 of which had received postoperative radiotherapy, and in 3 patients after mastectomy. Contralateral breast cancer was recorded in 13 cases, being synchronous in 4 (infiltrating in 3, DCIS in 1) and metachronous in 8 (all infiltrating). 3 patients died of breast cancer. The present series confirms the risk of ipsilateral cancer recurrence after conservative surgery but there are no significant differences relating to mammographic pattern, size, histological type, margin involvement and radiotherapy.
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INTRODUCTION

FINDING A ductal carcinoma *in situ* (DCIS) is getting more and more frequent owing to the widespread use of mammographic screenings [1–3]. However, there are still doubts on the choice of the most suitable surgical and radiotherapy treatment [4–7]. The aim of the present study is to review a consecutive series of 183 cases of DCIS to evaluate the most frequent clinico-radiological diagnostic features and the outcome of different treatments.

MATERIALS AND METHODS

183 cases of DCIS were diagnosed at the Centro per lo Studio e la Prevenzionea Oncologiea, Florence, and treated in the Departments of Surgery and Radiotherapy of the University and General Hospital of Careggi in Florence from 1968–1990.

Paget's disease of the nipple and 1 case of DCIS with positive axillary nodes were excluded from the evaluation. Patients were 31–83 years old with mean age of 54. The available data were the site of tumour, clinical, mammographic and cytological findings (when available), size of lesion, data and type of treatment, pathological findings, local recurrence, contralateral tumours, final status. The final status was assessed in July 1991 when 24 cases were lost at follow-up. These data were assessed at the last observation.

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The clinical, mammographic and cytological diagnostic assessment was reported as negative, suspicious and positive. Clinical examination and mammography also reported benign findings consistent with benign lesion. 173 mammograms were reviewed for this analysis. Sensitivity was defined as the ratio of suspicious/positive to total cases. 97 cases were reviewed to define histological type, nuclear grade, multifocality and multicentricity. Multifocality and multicentricity implied the presence of independent neoplastic foci of DCIS in the same quadrant as the primary lesion or in the rest of the breast, respectively.

Statistical significance of observed differences was set at a P level of 0.05 and determined by the χ^2 test.

RESULTS

Site of tumour

Tumour site was known in 169 cases and in 48.5% it was located in the outer quadrants (33% in outer upper quadrant). in 30.2% in the central quadrants , and in 20.7% in the inner ones. In 1 case the lesion covered the whole breast.

Clinical examination

The clinical examination was negative in 44 cases (24%); in 9 cases (4.9%) the only sign was nipple discharge, which in 19 cases was associated with other findings. Blood discharge was the only sign in 16 cases and there was no blood in 12. A lump was present in 125 observations (68.3%), skin retraction was the only sign in one case and in 30 cases it was associated with other findings. Nipple retraction was present in 4 cases. To sum up, 44 were infraclinical lesions and at least one symptom was present in 139 cases. Clinical diagnosis was negative in 44 cases (24%), benign in 27 (14.7%), suspicious in 38 (20.8%) and positive in 74 (40.4%). The sensitivity of clinical examination was 0.61.

Table 1. Correlation of roentgenological and pathological size*

Roentgeno-logical size (cm)	Pathological size (cm)						
	0–1	1.1–2	2.1–3	3.1–4	4.1–5	> 5	Not evaluable	Total
0–1	19	3	1				1	24
1.1–2	9	17	5				2	33
2.1–3	4	3	9				3	19
3.1–4	2	1	4	1				8
4.1–5		1	1	1				3
> 5		1		2	1			4
Not evaluable	2	1	1				2	6
Total	36	27	21	4	1		8	97

* 97 evaluable cases.

Mammography

Mammography was not carried out in 10 patients, it was not interpretable owing to dense breast in 19 and negative in 15; 2 of them showed abnormalities on galactography. Mammographic abnormalities were found in 139 cases: 12 asymmetrical increased density, 9–22–10 sharp borderline, undefined borderline and stellate opacities, respectively; 83 microcalcifications, in 9 cases associated with opacity; 3 parenchymal distortion.

Radiological diagnosis was negative in 13 cases (7.5%), benign in 12 (6.9%), suspicious in 18 (10.4%) and positive in 111 (64.2%). The sensitivity of mammography was 0.74. The sensitivity of clinical examination and mammography associated was 0.93. 7% of cases were considered benign by both exams.

Cytology

Fine needle aspiration cytology was carried out in 98 cases and in 9 cases the material was inadequate (absence of cells). It was negative in 23 cases (27%), suspicious in 24 (28.2%) and positive in 29 (34.1%). Cytological examination was inadequate in 1 out of the 28 discharge cases. It was negative in 15 cases (55%), suspicious in 2 (7.4%) and positive in 10 (37%). Suspicious/positive reports were observed with blood discharge in 7 cases and no blood in 5 cases. In 3 cases cytology was the only suspicious test that led to diagnosis. The sensitivity of fine needle aspiration cytology was 0.70.

Size

The size of a tumour was calculated from mammography whenever possible (opacity, clustered microcalcifications) or on a clinical basis. In 30 cases size was undefinable. The distribution of cases according to size was 0–1 cm in 35 cases; 1.1–2 cm in 59; 2.1–3 cm in 36; 3.1–4–cm in 12; 4.1–5 cm in 4; > 5 cm in 7. Table 1 shows the correlation between roentgenological and pathological size on 97 cases.

Treatment

7 cases had tumorectomy, 73 had wide excision or quadrantectomy associated with axillary dissection in 34 cases and 34 cases had radiotherapy (50 Gy with tangential fields and 10–14 Gy boost on the surgical bed). Total mastectomy was carried out in 15 cases, Madden's, Patey's and Halsted's mastectomy in 18–26 and 44 cases, respectively. Therefore surgery was radical in 103 patients (56.2%), conservative in 80 (43.7%), associated with radiotherapy in 34 cases, and axillary dissection was carried out in a total of 122 patients (67%). Marked decrease in radical

surgery is evident if our experience is divided into four calendar periods: 15 of 18 cases in 1968–1974, 54 of 67 in 1975–1981, 31 of 77 in 1982–1988 and 3 of 21 in 1989–1990. The curve of axillary dissection was 46.1%, 39.1%, 55.5%. Radiotherapy associated with conservative surgery in the last three calendar periods was employed in 15.4%, 45.6% and 61% of cases, respectively.

Pathology

In 55 out of 80 conservative surgery cases the final pathological margins were assessed and proved to be positive on five occasions (9%), and radiotherapy was therefore given.

97 cases (47 mastectomies; 50 conservative surgery) were reviewed to define the histological type and their distribution was: comedo in 19 cases (19.6%), solid in 14 (14.4%), cribriform in 15 (15.5%), micropapillary in 8 (8.2%), papillary in 3 (3.1%), mixed in 38 (39.2%).

The correlation between clinico-mammographic and pathological findings does not show significant differences between the different histological types, i.e. there are no radiological or clinical criteria to recognise preoperatively the DCIS histological type.

The study of multifocality and multicentricity related to each single histological type is reported in Table 2, which shows that 60% of DCIS are multifocal, 22% multicentric, 17% both multifocal and multicentric and 38% unifocal.

The distribution of 97 cases according to their nuclear grade 1–2–3 is 33.7%, 28.4% and 37.9%, respectively.

Local recurrence

The data referring to local recurrence and survival were assessed in 175 patients with minimum follow-up of 15 months (range 15–267 months, mean 105 months, median 94 months). The data for local recurrence in those cases where histological type was defined were assessed in 92 cases (range 15–254 months, mean 90 months, median 81 months). There were 11 local recurrences (6%). All were infiltrating, 3 on the chestwall after mastectomy and 8 in the same quadrant as the primary lesion after wide excision or quadrantectomy; followed by radiotherapy in 3 cases.

All local recurrences were treated with mastectomy but in one case metastasis appeared after 2 years. The patient is still alive with disease after 5 years.

Referring to radiological findings, recurrences were 1 out of 15 and 1 out of 19 when mammography was negative or non-interpretable for dense breast, respectively, 4 out of 83 in the presence of microcalcifications, and 4 out of 56 when these were not present ($P = 0.9$). The difference in the frequency of recurrence was not statistically significant ($P = 0.7$) in relation to the different histological types of the tumours.

Therefore there have been 3 local recurrences (2.9%) out of 103 mastectomies after 50, 56 and 62 months, respectively and 8 (10%) out of 80 conservative treatments ($P = 0.06$); 3 out of 34 (8.8%) conservative surgery with radiotherapy after 19, 27 and 66 months, respectively and 5 out of 46 (10.9%) without radiotherapy after 13, 24, 27, 76 and 115 months, respectively ($P = 0.7$).

In mastectomies follow-up was: range 2–254 months, mean 125 months, median 128 months. In conservative treatments with radiotherapy follow-up was: range 2–161 months, mean 53 months, median 50 months, and in conservative treatments without radiotherapy follow-up was: range 11–267 months, mean 80 months, median 70 months.

Table 2. Multifocality, multicentricity, bilaterality and nuclear grade according to histological type

Histological type	No. of cases	Not evaluable	Multi-focal	Multi-centric	Multifocal/ multicentric	Bilateral	Nuclear grade			
							1	2	3	Not evaluable
Comedo	19	4	12/15	3/10	3/10	1	2	2	13	2
Solid	14	2	8/12	0/4	0/4	1	5	7	2	—
Cribriform	15	4	9/11	1/8	1/8	1	11	4	—	—
Micropapillary	8	—	5/8	0/4	0/4	3	6	—	2	—
Papillary	3	1	1/2	0/2	0/2	—	—	2	1	—
Mixed	38	9	11/29	4/8	2/8	1	8	12	18	—
Total	97	20	46/77	8/36	6/36	7	32	27	36	2

3 recurrences occurred in the first 2 years, 7 in the first 5 years. In the 50 cases with negative final pathological margins there were 3 recurrences, none in the 5 cases with positive margins and 5 in the 25 cases where margins were not evaluated ($P = 0.1$).

Mean and median time values of recurrence appearance were 45.8 and 27 months after conservative surgery and 56 months (mean and median values) after mastectomy. Table 3 shows the frequency of local recurrence according to different parameters.

Contralateral tumours

Infiltrating contralateral tumours were observed 12 times (3 previous, 4 synchronous and 5 successive) and DCIS only one synchronous.

Survival

3 patients died of disease, all after mastectomy: 2 of metachronous contralateral infiltrating carcinoma. 11 patients died of other causes. A patient presented metastasis 10 years after Halsted's mastectomy and is still alive with disease. A patient had axillary recurrence 18 months after quadrantectomy, axillary dissection and radiotherapy. She is disease-free after 10 years.

DISCUSSION

DCIS is a problem that people involved in breast pathology have to face [1-8]. Although diagnostically the clinical, mammographical and cytological means employed in conjunction guarantee high sensitivity [8-10], the choice of therapy still presents problems not easy to solve.

Table 3. Local recurrence after conservative treatment and mastectomy according to mammographic pattern, size, final pathology margin, histological type

	No. of cases	Conservative + radiotherapy		Conservative − radiotherapy		Mastectomy	
		No. of cases	Local recurrence	No. of cases	Local recurrence	No. of cases	Local recurrence
Negative	13	4	—	1	—	8	1
Opacity undefined borderline	22	4	2	5	1	13	—
Opacity stellate	10	2	1	5	—	3	—
Microcalcifications	74	17	1	21	1	36	2
Other patterns	35	4	—	11	—	20	—
Radiologically dense breast	19	4	—	1	1	14	—
Not performed	10	—	—	1	1	9	—
0–1 cm	35	12	3	13	1	10	—
1.1–2 cm	59	12	—	14	3	33	—
2.1–3 cm	36	5	—	9	1	22	—
> 3 cm	23	3	—	4	—	16	1
Not evaluable	30	2	—	6	—	22	2
Positive margin	5	5	—	—	—		
Negative margin	50	20	1	30	2		
Not evaluable	25	9	2	16	3		
Micropapillary	8	2	1	2	—	4	1
Cribriform	15	2	—	4	—	9	1
Mixed	38	10	1	15	1	13	—
Others	36	6	—	9	—	21	—

Our series of patients covers a long calendar period and seems to confirm a tendency towards conservative treatment which has gone up to 81% in the past 2 years. Postoperative radiotherapy has also increased to 61%. Although axillary dissection has not given any contribution diagnostically or therapeutically, it was performed in 50% of the cases. This is probably due to the wish to avoid a second operation in the cases when the final histological examination of the lesion indicated the presence of infiltrating cancer. However, our experience also demonstrates that this choice is not correct [7].

The histopathological study of our cases shows a substantial prevalence of mixed forms (39%) and confirms the high percentage of multifocal (60%) and multicentric cases (22%) [11]. The frequency of nuclear grade 3 is particularly marked (76%) in the comedo histological type. The outcome of treatment does not seem to show elements, excluding axillary dissection, that might indicate a different behaviour in the future. Negative events are so few that an actuarial evaluation of the results would not mean anything. Survival does not seem to be affected by the type of surgery performed initially. The local control of the disease is worse after conservative treatment (10 vs. 2.9%). It should be noted that in all cases recurrence was infiltrating.

As regards conservative treatment, contrary to reports from other authors, our experience, owing perhaps to the limited number of cases, is not able to indicate significant elements of risk of local recurrence with reference to the histological type [2–3] or to the use of radiotherapy associated with conservative surgery [5–15]. Our indications as to conservative surgery are, at the moment, strictly related to the size of the lesion and to the possibility of performing a wide excision with free margins with good cosmetic result. Our data do not seem to indicate that the histological type can affect the choice of surgery, while in the use of radiotherapy there may have been a certain selection particularly in the last few years. Surgery without irradiation was advised for patients over 60 years of age, with tumours under 2.5 cm in size, free margin and breast favourable for mammographic examination. This might explain why we have more or less the same number of recurrences in conservative treatment with or without radiotherapy.

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Do Screening-detected Invasive Breast Cancers Have a Natural History of their Own?

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INTRODUCTION

WOMEN WITH screen detected breast cancer have repeatedly been shown [1–7] to have a lower case fatality rate (CFR) than women with breast cancers detected in an ordinary clinical setting. The question here is whether the prognosis of screen detected breast cancer also differs from that of a clinically detected cancer after correction for the length of time by which diagnosis is brought forward by screening (lead-time bias) [8]. Such differences might come about through several mechanisms:

(1) periodic screening picks up slower growing tumours more easily than the faster growing tumours; (2) breast cancers with mammographic signs that lead to the detection in screening might correspond with breast cancers with certain favourable histopathological characteristics; (3) the histopathological distinction between malignant and benign may be very difficult for the very small and never before thoroughly studied lesions detected in a screening program; (4) in women with breast cancers detected very early, a substantial proportion may not