

Ductal carcinoma in situ of the breast: our experience

R. RUGGIERO, E. PROCACCINI, A. SANGUINETTI¹, C. CREMONE, S. GILI, G. DOCIMO,
L. DOCIMO, L. SPARAVIGNA, A. GUBITOSI, D. PARMEGGIANI, N. AVENIA¹

SUMMARY: Ductal carcinoma in situ of the breast: our experience.

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Aim. The ductal carcinoma in situ (DCIS) is a more and more frequent neoplasia, representing over 25% of diagnosed breast cancer in recent surveys. It is particularly interesting as concerns several aspects of which the most important are issues linked to clinical diagnosis and the difficulties of histopathological classification, with evident and important therapeutic implications.

Patients and methods. The authors report their experience about 161 ductal carcinoma in situ of the breast. Guidelines for surgical treatment are: radiological or clinical diagnosis, tumor's extension, histological classification, grading and margin status. At the present the authors prefer breast conserving surgery with tumor margin's study. They report their experience in the last seven years about sentinel lymph node biopsy.

Results. The most frequent histotype resulted comedocarcinoma (61,8%) followed by non comedo (38,2%). Local recurrence after DCIS therapy is 6,1%.

Conclusions. 80-90% of the patients currently treated for DCIS present non-palpable breast lesions at diagnosis. Breast conserving surgery is the first choice and radiotherapy and endocrine therapy are indicated for selected patients.

RIASSUNTO: Carcinoma duttale in situ della mammella: nostra esperienza.

R. RUGGIERO, E. PROCACCINI, A. SANGUINETTI, C. CREMONE,
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Obiettivo. Il carcinoma duttale in situ (DCIS) rappresenta una neoplasia sempre più frequente, rappresentando oltre il 25% dei cancri della mammella osservati in recenti casistiche. Presenta particolare interesse circa alcuni aspetti tra i quali l'approccio clinico e diagnostico e le difficoltà di classificazione istopatologica con implicazioni terapeutiche.

Pazienti e metodi. Gli Autori riportano la loro esperienza relativa a 161 casi di carcinoma duttale in situ. Linee guida per il trattamento chirurgico sono: diagnosi clinica o radiologica, estensione della neoplasia, classificazione istologica, grading e studio dei margini di sezione. L'orientamento attuale è per un trattamento chirurgico conservativo con attento studio dei margini di sezione. Viene anche riportata l'esperienza degli ultimi 7 anni circa l'impiego della biopsia del linfonodo sentinella.

Risultati. L'istotipo più frequente è stato il comedocarcinoma (61,8%) seguito dalle forme non comedo (38,2%). La recidiva locale si è attestata intorno all'6,1%.

Conclusioni. L'80-90% delle pazienti trattate per DCIS si presenta alla osservazione senza lesioni palpabili. La chirurgia conservativa rappresenta l'opzione di scelta mentre la radioterapia e la endocrinoterapia sono indicate in casi selezionati.

KEY WORDS: Ductal carcinoma *in situ* - Conserving surgery - Sentinel lymph node.
Carcinoma duttale *in situ* - Chirurgia conservativa - Linfonodo sentinella.

Introduction

The ductal carcinoma in situ (DCIS) of the breast, identified 70 years ago (1), is a more and more frequent

neoplasia thanks to the screening programs, representing over 25% of diagnosed breast cancers in recent surveys (2). It is particularly interesting as concerns several aspects of which the most important are issues linked to clinical diagnosis and the difficulties of histopathological classification, with evident and important therapeutic implications (3-6).

In fact DCIS diagnosis presents some peculiarities concerning not only its presence but its extension as well; from this point of view mammography remains the most reliable diagnostics, though combined with

Second University of Naples, Italy
Department of General and Specialistic Surgery

¹ University of Perugia, Terni, Italy
Endocrine Surgical Unit

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echo-guided microbiopsies (Mammotome®). Still today the first problem is the diagnosis of the extension of disease. The techniques which were proposed to be carried out together with mammography, didn't show particularly effective, including MR with contrast medium (7).

Aim of this work is to analyse the results of diagnostics in homogeneous population of women with DCIS and compare them with the results of the international literature, paying particular attention to the diagnosis of location and extension with current diagnostics, which can lead to the possibility of remaining disease at the surgical resection margin.

The other peculiarity of DCIS is the difficulty of the surgical and metasurgical treatment. If the paradigm according to which mastectomy cancels the possibility of DCIS relapse (of which 50% is penetrating) is true, then it is also true that it sounds contradictory thinking that it's possible to treat the penetrating types with conservative surgery and those in situ with radical surgery (8, 9). The problem lies fundamentally in the difficulty of diagnosis of multifocal and multicentric lesions and because DCIS looks like a group of diseases with different degrees of development and aggressiveness. Hence, the therapy may require an appropriate "tailoring" depending on the histological and immunohistochemical findings.

Patients and methods

From January 2001 to January 2007 we treated 161 DCIS (97 in Naples and 64 in Terni) in women aged between 28 and 71 years (mean 51,4). DCIS was diagnosed in 28 women for a palpable mass (2,2 cm) with or without nipple bleeding, in 3 cases only for hemorrhagic secretion and in 130 cases for the presence of microcalcifications at the mammography, with or without other alterations which could be pointed out by radiological exam or echography. In 28 patients with palpable mass fine needle cytology was suspicious in 19 and not indicative in 9 patients. In the group of 130 patients without palpable mass fine needle cytology was carried in 51 patients (correct diagnosis in 35 patients), core biopsy in 29 patients (4 false negative), echo-guided Mammotome® in 34 patients and surgical biopsy for other reasons in 17 patients. Excisional biopsy with metallic guide or with ROLL was carried in 101 patients to confirm diagnosis.

All the women underwent surgical treatment which consisted in lumpectomy in 11 cases, quadrantectomy in 133 and mastectomy in 17. The mastectomy was a simple one in 16 cases, skin-sparing in 2 and nipple-sparing mastectomy in 3. In 5 cases, due to the observation of involved margins after quadrantectomy, a following mastectomy was necessary. The treatment of axillary lymph nodes was also different as 2 case received no treatment, in 114 cases only the sentinel node biopsy (SNB) was carried out, and 45 women had the axillary sampling. The main indication which led to lymphectomy (SNB or sampling) was either the presence of a palpable mass or extended DCIS or G3-type comedonic DCIS. In 6 (5,1%) cases the histological exam showed the presence of lymphonodal metastasis (the only sentinel node).

Results

The most frequent histotype resulted comedocarcinoma (99 cases, 61,8%), followed by non comedo (62 cases, 38,2%). In some cases we observed of different histotypes at the same time. However we excluded from this work the DCIS cases with microinvasion. As for the nuclear ratio we observed differences in histotypes present at the same time.

The hormone receptors resulted positive in 128 cases; the positivity of *c-erb* was noticed in 10 cases.

The adjuvant treatment was modulated considering various elements:

- palpable mass or DCIS XR and its extension;
- histotype and nuclear ratio;
- free margins;
- chemotherapy (used only for one patient with metastasis at the sentinel node).

On the basis of these factors, the adjuvant radiotherapeutic treatment was proposed to the women having high-degree comedonic DCIS with palpable mass or widely extended.

At 3,7 year average follow-up, we observed 10 (6,1%) relapses of which 5 penetrating type, still found in women who underwent conservative surgery. The relapse arose in the same quadrant in 4 and in different quadrants of the same breast in 2 cases, at time interval variable between 1 and 6 years. In one case the relapse arose one year after the operation in the retroareolar ducts of the right breast in a woman who had gone through menopause and had bilateral nipple-sparing mastectomy for an extended DCIS, without adjuvant radiotherapy (RT) but with anti-aromatase hormone treatment. In 3 cases we carried out an iterative conservative surgery and in 7 a simple mastectomy or skin sparing.

Relapse after conservative surgery arose in 2 cases in women also treated with adjuvant RT and in 4 women who didn't receive such treatment. The rate of local relapse is lower for Van Nuys Prognostic Index (UNPI) 3 or 4 (5%) and higher for UNPI 8 or 9 (60%). We didn't find any new tumours at the controlateral breast.

Concerning treatment with tamoxifen or aromatase inhibitors, all women who received hormone treatment had a positivity for hormone receptors. Preference for tamoxifen treatment and LH-RH inhibitors went to premenopausal women; aromatase treatments were advised to women gone through menopause.

Discussion

About 80-90% of the patients currently treated for DCIS present non-palpable breast lesions at diagnosis.

Though mammography has 88% sensibility and a 10-60% specificity, it undervalues the real extension of these lesions in 46% of cases and often it doesn't locate multifocality.

The breast Magnetic Resonance (MR), complementary to mammography and ecography, thanks to its high sensibility (94-100%) and negative predictive value (~100%), better defines dimensions and number of the lesions, allowing to either identify or exclude multifocality, multicentricity and contralateral lesions (4). Furthermore it is the best detail methodology to evaluate those lesions already identified by the mammography, of which elevates sensibility (up to 90%) and specificity (up to 98%) (5, 6). It also values the ETC (extended intraductal component) which represents a fundamental parameter in the presurgical penetrating balance (10).

The limits of this methodology are represented by the low specificity (37-86%) and by the impossibility of predicting any possible penetrating component of the carcinoma. For this parameter is then necessary to resort to "core biopsy" (CB) which, in pre-surgical diagnosis of breast lesions, allows a reliable histological diagnosis, except for limited sampling. CB allows to have a histological diagnosis of malignancy either *in situ* or invasive at least in 95% of palpable carcinoma and in 90% of non-palpable ones (there are still uncertain cases due to malignancy represented by ductal and/or lobular atypical epithelial hyperplasia, by papillary lesions, by philloides tumour and by radial scar or sclero-elastic lesions), as well as the possibility of evaluating histotype and histological grading.

The only disadvantage is linked to the impossibility of studying the real extension of the neoplasia, which remains prerogative of excisional biopsy. As in 90% of the cases it appears with micro calcifications associated to opacity and/or a parenchyma distortion non clinically palpable, it's possible to opt for an excisional biopsy making use of three "centring" methods, besides skin mapping (9):

- metallic guide;
- colouring agent;
- ROLL: Radio-guided Occult Lesion Localization.

The advantage of ROLL is that one only intralesional injection can identify the sentinel lymph node in 97% of the cases, with a complete excision of the tumour of 87% (11).

The DCIS surgical management goes from mastectomy to local excision followed by radiotherapy, right to surgical excision (1). The type of treatment differs according to the clinico-radiological pre-surgical findings (clinically palpable lump, microcalcifications or opacity) and whether a cyto-histological data is available or not.

With the only excision the risk of relapse increases unacceptably even when the resection margins are >1 cm and the neoplasia presents a reduced degree, i.e. 1-2 degree (12), considering that for tumours <2,5 cm is possible that the micro infiltration is confirmed in 2% of the cases. The characteristics that lead towards a possible DCIS invasivity are: comedo forms, high-degree dysplasia, extended lesions, and presence of a mass (13-15).

Different is what emerges from the mastectomy and conservative surgery comparative study with RT, with superimposable local relapse percentage and survival: respectively 90% vs. 89% and 100% vs. 89%. Risk factors are: young age (<45 years), positive margins (<2 mm), missed RT, boost <9MeV, grade 3 (16). On the basis of these factors, the adjuvant radiotherapeutic treatment was proposed in those woman having high grade comedonic DCIS with palpable mass or widely extended (17-20).

The guidelines about lymph nodes of the axillary cavity are still uncertain. The lymph node axillary dissection seems to be an unacceptable over treatment, as lymphonodal metastasis are present only from 0 to 7%, being even lower in case of pure DCIS. But as 20% of DCIS present infiltrations of the basal membrane, it's now routine use to search the sentinel lymph node also in patients at the initial phase of tumore evolution (usually T < 3 cm with N0) with palpable mass and with diffuse calcification areas, keeping the dissection for positive cases only (21).

Conclusions

Ductal carcinoma in situ present some peculiarities concerning diagnosis and treatment. Important aspects are extension, histopathological classification, surgical resection, adjuvant radio- and ormonotherapy.

About 80-90% of the patients currently treated for DCIS present non-palpable breast lesions at diagnosis. Mammography has 88% sensibility and 60% specificity; magnetic resonance as complement to mammography and echography has high sensibility (94-100%) and identify or exclude multifocality, multicentricity and contralateral lesions (22-24). Core biopsy and Mammotome® microbiopsy allows a reliable histological diagnosis but for studying the real extension of neoplastic lesion is preferable remain excisional biopsy using centring methods (metallic guide, ROLL).

The DCIS surgical management goes from mastectomy to local excision; in our experience we prefer quadrantectomy with metodic control of free margins. Guidelines about axillary lymph nodes are still uncertain. We use to search the sentinel lymph node kee-

ping the axillary lymphectomy for positive case only. Adjuvant radiotherapeutic treatment was proposed to patients having high degree comedonic DCIS with palpable mass or widely extended. Patients with positive

hormone receptors received hormone treatment.

In conclusion treatment of DCIS is very difficult and it is possible the risk of overtreatment in the surgical and adjuvant management (19).

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