

Ductal carcinoma in situ (DCIS) of the breast: thirty-two consecutive cases under 50 yrs detected by mammography: treatment and results



Ann. Ital. Chir., LXX, 4, 2000

A. Cappellani, M. Di Vita, A. Zanghì,
M. Majorana, L.W. D'Angelo, E. Lo Menzo

Università degli Studi di Catania
Dipartimento di Chirurgia
Sezione di Chirurgia Generale e d'Urgenza
Servizio autonomo di Chirurgia Generale e Fisiopatologia
Chirurgica
Direttore Prof. A. Cappellani
Centri di Diagnostica senologica M. Majorana –
L.W. D'Angelo

Introduction

The observation of the DCIS variant of breast cancer is of great interest for the different aspects compared to invasive cancers. First of all the documented greater incidence of multicentricity, multifocality and bilaterality, the strong trend to local recurrence (LR), the poor radiosensitivity and the uncertain responsiveness to hormonal therapy. All these characteristic were already observed in the past in those cancers with extensive intraductal component (EIC), that can actually be considered as an evolutive stage of "pure" intraductal carcinoma. The histologic features (comedo or non-comedo carcinoma) have an impact in the overall prognosis, negative in the former and positive in the latter [1]. In each case the possibility of an early diagnosis of an intraductal carcinoma offer significantly high advantages with regard to the overall survival and disease free survival.

The early diagnosis by mammographic screening allows a different approach to the carcinoma of the breast. The frequent observation of small and non invasive carcinomas modified all the data of this tumors [2, 3, 4, 5, 6, 7].

In fact the incidence of DCIS has raised from 2.9% in 1975 to 25-30 % in 1998 of the breast cancer [8]. DCIS is mainly observed in premenopausal women with cancer diagnosed mammographically than in postmenopausal ones (25-50% vs 15-25%) [2-6].

The advancement of annual mammography at forty years

Abstract

Thirty two consecutive cases of ductal carcinoma in situ of the breast in women under fifty are presented. Diagnostic procedure, pathological aspects, treatment and outcome are reported.

All the patients had their cancer diagnosed by mammography. The tumor was marked by stereotactic or ultrasound guided localization. Lumpectomy without axillary node dissection was the surgical treatment of thirty lesions with good cosmetic results; radiation therapy was advised in all of these cases. In two cases mastectomy with immediate reconstruction was performed because of the multifocality of the cancer none of the patients experienced local or distant recurrence.

This experience emphasizes the importance of mammographic screening for women 40 years of age, in fact this approach allowed the diagnosis of a large number of DCIS.

A correct definition of the problem and a multidisciplinary therapeutical approach is warranted to prevent the high local recurrence rate reported in the past.

Key words: DCIS carcinoma in situ, breast cancer.

old permitted the observation of a large number of DCIS as reported by most authors [9, 10].

The treatment of DCIS was also modified: mastectomy is not any more the gold standard of treatment [10, 11, 12] and, at the present time, the "dilemma" is between lumpectomy with or without radiation therapy [12].

The results from eight years of experience with this approach demonstrated a survival over 98% for both options [12].

In our experience we observed thirty-two cases detected by mammography in asymptomatic pre-menopausal women, treated preferably by lumpectomy with RT (26/32 L + RT, 4 L alone, 2 Mastectomies).

Materials and methods

The indication for mammogram in women over 40 years of age and younger when at high risk for familiar breast cancer is well known from a long time but it is very difficult to pursue due to the large amount of resources needed for a real screening program.

The model that we were able to use is a protocol defined "diagnostic anticipation" obtained with the active collaboration of the women reached by our outpatient services and who decided to adhere to the protocol.

Consequently we were able to observe a high global rate of cancer in women under 50 (9.8%) and a higher rate in women under fifties with familiar risk (at least one 1st grade relative or two of 2nd or 3rd with breast cancer) (31/175, 17%).

Over a three year period, from January 1996 to December 1998 at the Department of Surgery- General Surgery II- University of Catania, and affiliated radiology centers, 4821 mammographic examinations were performed on 2652 women. 680 of them were under 50 years of age (651 between 40 and 50). Among these women we noted 32 cases of Ductal carcinoma in situ. Also the incidence of DCIS was higher than expected with a global rate of 4.7% and a 47% of all breast cancers observed in this age group. In the group of women at high familiar risk DCIS was present in 7.4% of them and represented 42% of all cancers. In this age group, we also reported, 35 infiltrating carcinomas.

Has to be noted that the women examined (175) were at high familiar risk, so it was more easier to obtain their participation to a protocol of diagnostic screening.

In the group of women with familiar risk 31 cancers were found, 13 intraductal and 18 invasive.

The mean diameter of the lesion was 1.1 cm for both invasive and intraductal cancers.

The 32 DCIS were in the age group between 32 and 50 years old (mean age 43). We don't present DCIS with minimal invasion that we consider and treat as invasive cancer. The size of tumor varied between 3 and 21 mm (mean 0.8 mm).

Mammography showed micro-calcifications alone in 9 patients, micro-calcifications associated with distortion of glandular structure (3) or spiculated (5), round (5) or oval (4) masses in 17 patients.

In the absence of micro-calcification we observed a round or oval mass in eight cases, and in five a spiculated one. These findings were variably associated with different diameter of lesion as listed in Tab. I.

Fine needle aspiration, ultrasound guided in 4 and stereo-

taxic guided in 6 patients, was performed, achieving a cytological diagnosis in 9 cases. In 1 case material was only suggestive for a borderline lesion.

The lesion, previously localized by a wire, was removed under local anesthesia, with cosmetic incision, and with an hystological distal free margin of 1 centimeter; placement of clips on the bed of the tumor, inking and orienting of the margin of tumor and X-ray examination of specimen were performed in all cases.

The presence of multiple foci of microcalcifications required mastectomy in two women. Definitive pathological examination showed micro-invasive foci in other two patients, which were excluded from this study. These two women subsequently underwent to axillary dissection and no node involvement was found.

Clear margins were obtained in the 25 women with pure intraductal carcinoma treated by lumpectomy, so re-excision was not needed. Axillary node dissection was not performed on patients with "pure" DCIS. Radiotherapy instead was advised and accomplished in all patients undergone to conservative surgery, except one that refused treatment.

Two patients deserted the follow up, of the remaining none of them presented local or distal recurrence. Only one presented an invasive tumor of the contralateral breast after one year.

We obtained an excellent or good cosmetic results in all patients.

Pathologic examination demonstrated 14 comedo-carcinomas, 5 cribriform, 7 micropapillary and 6 solid ones. The distribution of the neoplasms with regard to the diameter of lesion is listed in Tab. II.

The mutations c-erbB-2 and p53 were observed rarely in our patients with DCIS (respectively 3 and 5 of 32) while 73% of patients with infiltrating tumors were positive.

Discussion

Ductal carcinoma in situ of the breast has been for many years an occasional finding. The treatment of choice was the mastectomy for its high multicentricity and multifocality, and the supposed poor sensitivity to radiotherapy. The LR observed in patients treated with

Tab. I

Diagnostic patterns	< 5 mm	5-10 mm	10-20 mm	> 20 mm	total
microcalcifications	3	6	0	0	9
microcalcifications + distortion	2	10	4	0	16
Parenchyma distortions	0	1	0	0	1
masses	0	2	1	0	3
cysts	0	0	1	2	3
total	5	19	6	2	32

conservative therapy with clearly free margins ranged from 10 to 63% [13, 14, 15, 16, 17, 18, 19]. These results in women with non invasive cancer were surely a good reason for considering the mastectomy the gold standard for treatment of DCIS.

Tab. II

Hystology	< 5 mm	5-10 mm	11-20 mm	> 20 mm	total
comedo	1	11	2	0	14
cribriform	2	1	2	0	5
micropapillary	1	3	1	2	7
solid	1	4	1	0	6
total	5	19	6	2	32

Presently many authors suggest that all the data of the DCIS had been examined in a non correct way especially in terms of hystological results and interpretation; in fact in many papers microinvasive tumors were considered DCIS as well the "pure" ones.

The problem of multi-centricity, multi-focality or multiplicity remains related to the size of the tumor and to its extension beyond optic limits.

In the series of Gallagher and Fisher almost all the DCIS were palpable with mean diameter from 2.2 cm [to 1.6 cm [14, 20]. In the Arnesson's series the mean diameter was 0.6-1 cm but most of the patient had their diagnosis by mammography. Although these authors treated their patients with lumpectomy alone or with radiation therapy the rate of recurrence was clearly depending on the size of the tumor; in fact the Fisher's and Gallagher' series reported a LR rate of 23% -57% and Arnesson of 17% [14, 20, 21, 22].

This is one of the most important reasons for understanding the different approach of small ductal carcinoma in situ detected by mammography. There is evidence that the recurrence is related to the micro-invasion and to the extension of the tumor and a lesion occupying 25 mm or more of breast tissue has a great likelihood to be multicentric [24]. This point will be discussed later.

Also a not accurate definition of marginal clearance can be related to recurrence, being these mostly "marginal recurrence". Howard, Fisher and Silverstein observed 100% of marginal recurrence, Solin 60%, Kurtz 67%, Recht 86%, Zafrani only 33% [20, 23, 27, 28, 29, 30, 31].

The recurrence rate in the breast is higher in patients with comedo (11%) than for those with non comedo [12, 26]. Although Schwartz treated patients with DCIS mammo-graphically detected by lumpectomy alone [32]. a large scale trial was reported by NSABP, B-17, that showed a significant reduction of breast recurrence in women treated with lumpectomy and radiotherapy from 31% to 13%, more significant in low risk group [12].

Also Solin observed a reduction in the rate of LR in patients undergone to radiotherapy [28].

Instead, in the series of Hetelekidis, that consisted of 59 patients with very small DCIS treated by excision alone, the global rate of LR was 10% at 5 years. Only 19 patients with tumors less than 5 low power fields (L.P.F), free margins more than 1mm and Nuclear Grade I or II had not LR after excision alone. In the rest of the patients the rate of LR was 15% at 5 years [33].

The importance of margin width is emphasized also by Silverstein, who did not observed lower rate of recurrence with postoperative RT when tumor is excised with margins of 10 mm or more; RT is beneficial when margin width is less than 1 mm [16].

More recently Fisher attenuated the sense of these remarks, observing only a "slight or borderline influence" of margin status on the frequency of LR at 8 years, advising anyway to obtain excision of DCIS with free margins of section [12].

The last problem is related to the microinvasion.

In the past many authors referred to carcinoma with microinvasion as carcinoma in situ. Microinvasion was used to indicate an outlying of no more than 1 mm in no more than 2 foci [16] or microscopic invasion in no more than 10% of examined ductal surface [25] or simply invasive cancer for no more than 1 mm [26]. This concept includes the possibility of reaching lymphatic or blood vessels with metastatic spreading. Such a definition can justify axillary dissection and the finding of positive nodes. Currently this is not considered carcinoma in situ anymore, being this a tumor not outlying the basal membrane [34]. The use of terms as ductal carcinoma in situ with microinvasion and "pure" is not useful any more.

Ductal carcinoma in situ with microinvasion is an invasive tumor and must be treated as such (lumpectomy, axillary dissection and radiation therapy), and should be considered an invasive cancer with Extensive Intraductal Component (EIC) [35].

A definition of intraductal carcinoma correctly restricted to tumors that have no evidence of micro-invasion at all can spare a patient a useless node dissection, and all its sequelae, as recognized by all the leading organizations and Institutes for Cancer care.

Our trend is to treat all DCIS, in absence of multicentricity mammographically detected, with lumpectomy. Mandatory is the assessment of the resection margins with frozen sections of the margin. The lesion, often preoperatively localized by wire must be suddenly marked with china and a radiogram has to be taken. In case of a non-free margin of section, a re-excision has to be performed at the time of the primary operation or during a second procedure.

After the publication of the B-17 trial, the patient should undergo to breast irradiation and assume Tamoxifen for at least five years. Obviously all of them have to undergo yearly mammographic follow up.

Conclusions

The incidence of Ductal Carcinoma in situ of the breast is steadily raising. Women under fifty years of age are at higher risk for this particular neoplasm.

A careful and serious evaluation of pathological aspects can spare these women from a mutilating over-aggressive treatment.

The role of radiotherapy has not been entirely established yet, but there is a strong evidence that the RT is able to significantly reduce the incidence of recurrences and to improve the disease-free survival.

Consequently, in the absence of prognostic factors of absolute value, the gold standard treatment for patients with carcinoma in situ of the breast is a wide local excision followed by radiotherapy.

A careful pathological examination will provide the information that, along with a prolonged follow up, will permit a better typing of the neoplasm in the following years aiming towards an optimal therapeutic strategy.

We conclude underlining the fundamental principle that prevention is the best therapy and that all women over forty must undergo yearly mammographic examination, so that we can diagnose cancers in an early and possibly pre-invasive stage.

Riassunto

Gli autori presentano la loro esperienza su 32 pazienti al di sotto dei 50 anni con carcinoma duttale in situ diagnosticato mammograficamente. Il tumore, localizzato preoperatoriamente mediante apposizione stereotassica o ecoguidata di repere metallico è stata trattata mediante lumpectomy in 30 casi ed in due con mastectomia a causa della multifocalità delle lesioni. In nessun caso è stata eseguita la linfoadenectomia ascellare. Tutte le pazienti sono vive e senza evidenza di ripresa di malattia.

L'esperienza degli AA mette in rilievo l'importanza della diagnostica mammografica precoce nelle donne al di sopra dei 40 anni, che consente la identificazione di una elevata percentuale di carcinomi in situ, nonché di una corretta definizione dei termini del problema e di un approccio terapeutico multidisciplinare allo scopo di evitare l'alto tasso di recidive locali descritte in passato.

References

- 1) Zanghì M., Cappellani A., Di Vita M., Zanghì A., Lo Menzo E, Majorana M.: *Il carcinoma infraclinico della mammella*. Arch e Atti Soc It Chir, vol. 2:477-93, 1997.
- 2) Hillner B.E., Essner R., Brenner R.J., Giuliano A.E.: *Nonpalpable versus palpable invasive breast-conserving surgical management*. Am Surg, 62:395-399, 1996.
- 3) Osteen, R.T.: *Breast cancer*. In Steele G.D., Winchester D.P.,

Menck H.R. et al. (eds.): *National cancer data base: annual review of patient care*. 1993. Atlanta, GA, American Cancer Society, 10-19, 1993.

- 4) Nystrom L., Rutqvist L.E., Wall S. et al.: *Breast cancer screening with mammography: Overview of Swedish randomized trials*. Lancet, 341:973-978, 1993.
- 5) Stacey-Clear A., Mc Carthy K.A., Hall D.A. et al.: *Breast cancer survival among women under age 50: Is mammography detrimental?* Lancet, 340:991-994, 1993.
- 6) Kerlikowske K., Grady D., Barclay J et al.: *Positive predictive value of screening mammography by age and family history of breast cancer*. JAMA, 270:2444-2450, 1993.
- 7) Cody H.S. 3d: *The impact of mammography in 1096 consecutive patients with breast cancer, 1979-1993: equal value for patients younger and older than age 50 years*. Cancer, 76(9):1579-84, 1995.
- 8) Gennaro M., Pizzamiglio M., Andreoni G., Greco M., Sacchini V.: *Carcinoma intraduttale della mammella: stato dell'arte ed orientamenti futuri*. Chirurgia, 12:53-65, 1999.
- 9) Arnesson L.G., Vitak B., Manson J.C., Fagerberg G., Smeds S.: *Diagnostic outcome of repeated mammography screening*. World J Surg, 19(3):372-7, 1995.
- 10) Ernster V.L., Kerlikowske K.: *Breast screening in women aged 40-49 years*. Lancetm, 11;354(9182):947-8, 1999.
- 11) Arriagada R., Le M.G., Rochard F., Contesso G.: *Conservative treatment versus mastectomy in early breast cancer: patterns of failure with 15 years of follow-up data*. Institut Gustave-Roussy Breast Cancer Group. J Clin Oncol, 14(5):1558-64, 1996.
- 12) Fisher E.R., Dignam J., Tan-Chiu E., Costantino J., Fisher B., Paik S., Wolmark N.: *Pathologic findings from the National Surgical Adjuvant Breast Project (NSABP) eight-year update of Protocol B-17: intraductal carcinoma*. Cancer, 1;86(3):429-38, 1999.
- 13) Schwartz G.F.: *Subclinical ductal carcinoma in situ of the breast: Selection for treatment by local excision and surveillance alone*. Breast J, 2:41-44, 1996.
- 14) Gallagher W.J., Koerner F.C., Wood W.C.: *Treatment of intraductal carcinoma with limited surgery: Long term follow up*. J Clin Oncol, 7:376-380, 1979.
- 15) Price P., Sinnott H.D., Gusterson B.: *Ductal carcinoma in situ. Predictors of local recurrence and progression in patients treated by surgery alone*. Br J Cancer, 61:869-872, 1990.
- 16) Silverstein M.J., Lagios M.D., Martino S., Lewinsky B.S., Craig P.H., Beron P.J., Gamagami P., Waisman J.R.: *Outcome after invasive local recurrence in patients with ductal carcinoma in situ of the breast*. J Clin Oncol, 16(4):1367-73, 1998.
- 17) Lagios M.D.: *Duct carcinoma in situ : pathology and treatment*. Surg Clin North Am, 70:853-871, 1990.
- 18) Silverstein M.J., Lagios M.D., Groshen S., Waisman J.R., Lewinsky B.S., Martino S., Gamagami P., Colburn W.J.: *The influence of margin with on local control of ductal carcinoma in situ of the breast*. N Engl J Med, 13;340(19):1455-61, 1999.
- 19) McCormick B., Rosen P.P., Kinne D., Cox L., Yahalom J.: *Duct carcinoma in situ of the breast: an analysis of local control after conservation surgery and radiotherapy*. Int J Radiat Oncol Biol Phys, 21(2):289-92, 1991.

- 20) Fisher E.R., Leeming R., Anderson S., Redmond C., Fisher B.: *Conservative management of intraductal carcinoma (DCIS) of the breast. Collaborating NSABP investigators.* J Surg Oncol, 47(3):139-47, 1991.
- 21) Arnesson L.G., Smeds S., Fagerberg G., Grontoft O.: *Follow up of two treatment modalities for ductal carcinoma in situ of the breast.* Br J Surg, 76:672-675, 1989.
- 22) Arnesson L.G., Smeds S., Fagerberg G.: *Recurrence-free survival in patients with small breast cancer. An analysis of cancers 10 mm or less detected clinically and by screening.* Eur J Surg, 160(5):271-6, 1994.
- 23) Silverstein M.J., Waisman J.R., Gamagami P., Gierson E.D., Colburn W.J., Rosser R.J., Gordon P.S., Lewinsky B.S., Fingerhut A.: *Intraductal carcinoma of the breast (208 cases). Clinical factors influencing treatment choice.* Cancer, 1;66(1):102-8, 1990.
- 24) Lagios M.D., Westdahl P.R., Margolin F.R., Roses M.R.: *Duct carcinoma in situ. Relationship of extent of noninvasive disease to the frequency of occult invasion, multicentricity, lymph node metastases, and short-term treatment failures.* Cancer, 50:1309-1314, 1982.
- 25) Rosner D., Lane W.W., Penetrante R.: *Ductal carcinoma in situ with microinvasion: a curable entity using surgery alone without need for adjuvant therapy.* Cancer, 67:1498-1503, 1991.
- 26) Rosen P.P.: *Lobular carcinoma in situ and intraductal carcinoma of the breast.* Monogr Pathol, (25):59-105, 1984.
- 27) Howard P.W., Locker A.P., Dowle C.S., Ellis I.O., Elston C.W., Blamey R.W.: *In situ carcinoma of the breast.* Eur J Surg Oncol, 15(4):328-32, 1989.
- 28) Solin L.J., Kurtz J., Fourquet A., Amalric R., Recht A., Bornstein B.A., Kuske R. et al.: *Fifteen-years results of breast conserving surgery and definitive irradiation for the treatment of ductal carcinoma in situ of the breast.* J Clin Oncol, 14:754-763, 1996.
- 29) Kurtz J.M.: *Assessment of the risks associated with the breast-conserving treatment of ductal in situ carcinoma.* Strahlenther Onkol, 170(1):60-2, 1994.
- 30) Recht A., Connolly J.L., Schnitt S.J., Harris J.R.: *Therapy of in situ cancer.* Hematol Oncol Clin North Am, 3(4):691-708, 1989.
- 31) Zafrani B., Vielh P., Fourquet A., Mosseri V., Durand J.C., Salmon R.J., Vilcoq J.R.: *Conservative treatment of early breast cancer: prognostic value of the ductal in situ component and other pathological variables on local control and survival. Long-term results.* Eur J Cancer Clin Oncol, 25(11):1645-50, 1989.
- 32) Schwartz G.F., Finkel G.C., Garcia J.C., Patchefsky A.S.: *Subclinical ductal carcinoma in situ of the breast.* Cancer, 70:2468-2474, 1992.
- 33) Hetelekidis S., Collins L., Silver B., Manola J., Gelman R., Cooper A., Lester S., Lyons J.A., Harris J.R., Schnitt S.J.: *Predictors of local recurrence following excision alone for ductal carcinoma in situ.* Cancer, 15;85(2):427-31, 1999.
- 34) Bassett L.W., Jahan R., Fu Y.S.: *Noninvasive carcinoma.* In Bassett-Jackson-Jahan -Gold, *Diagnosis of the disease of the breast*, ed. Saunders Company, Philadelphia, p. 44, 1997.
- 35) Rosen P.P.: *Rosen's Breast Pathology.* Lippincott-Raven, Philadelphia-New York, 1997:261.

Commento

Commentary

Prof. Ercole CIRINO

Ordinario di Chirurgia Generale
Università di Catania

Il lavoro presentato da Cappellani e Coll. rappresenta un interessante contributo nello studio dei carcinomi intraduttali della mammella, che offrono ancor oggi molti spunti di riflessione. Il messaggio espresso dagli Autori è di anticipare mammograficamente la individuazione di questi tumori nelle donne oltre i quaranta anni, annualmente seguite con tale metodica.

Interessante e minuziosa è l'analisi della problematica e dei risultati ottenuti con terapia multidisciplinare conservativa.

The paper presented by Cappellani and Coll. is an interesting contribute to the study of ductal carcinomas in situ of the breast. These tumors still offer a great number of problems to debate.

The aim of authors is to emphasize the importance of a yearly mammographic examination of women over 40ies for an earlier diagnosis of such tumors.

Interesting and detailed is the analysis of the problem and of results obtained with multidisciplinary conservative approach.

Autore corrispondente:

Dott. Antonio ZANGHÌ
Viale A. Doria, 55
95125 CATANIA

