E16. Diagnosis and management of *in situ* diseases

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In situ malignant lesions (CIS) are currently named *in situ* duct carcinoma (DCIS/DIN) and *in situ* lobular carcinoma (LCIS/LIN). In spite of the classical classification it is wondered whether this distinction is actually correct as most neoplastic lesions arise within the terminal duct lobular unit (TDLU).[1] At present, by convention, the distinction is based on cytology and/or on the lack/presence of an adhesion molecule (i.e. e-cadherin).[2] Lobular lesions are devoid of e-cadherin. Both lesions (so called duct and lobular) spread along the duct of the pertinent lobe. Cytology of both lesions is, classically, of luminal type, but apocrine,[3] myoepithelial[4] and endocrine[5] differentiation can be seen. The fact that both lesions (lobular and ductal) share similar origin is shown by hybrid cases,[6] which are the result of different combinations of the two lesions. Both types of CIS can be graded according to their cytology and extension. Accordingly LCIS can be graded into LIN I, II and III[7] and DCIS can be graded as DCIS/DIN I, II and III.[8]

Pleomorphic *in situ* lobular carcinoma is LIN III and it is frequently apocrine in nature and may show central necrosis.[9] Necrosis per se does not indicate high grade lesions. LIN II can occasionally display necrosis.[10]

LIN is very frequently a multifocal and multicentric disease,[11] similar to DCIS/DIN g1.[12] On the contrary, DCIS/DIN g3 is a unicentric unilobar disease.[13] Therefore, it seems that LIN and DCIS g1 are similar lesions that spread widely throughout the breast tissue and are frequently bilateral. This is probably the result of a germline mutation that affects, at the same time, multiple lobes from both breasts. A somatic mutation leads to the development of DCIS g3 which is a localised disease limited to one lobe.

DCIS/DIN

Mammography is the standard of care for the detection and diagnosis of DCIS whereas other breast imaging such as sonography, scintimammography, MRI and positron emission tomography have been previously shown to be unreliable.[14]

Recently, however, it has become evident that the diagnosis of intraductal cancer is feasible with MRI using diagnostic criteria different from those that are used to diagnose invasive cancer.[15] Since the mammographic image is a representation of the underlying histology in DCIS, they can vary substantially. MRI is more likely to detect high grade DCIS because of a significantly higher vessel density with or without necroses and the enhancement pattern in breast MRI has been shown to correlate with the biological profile of DCIS. Probably, MRI detects a different subset of DCIS than mammography does. Those cases do not exhibit calcifications and therefore, will remain mammographically occult.[15]

The choice between breast conservation and mastectomy in the treatment of DCIS involves extensive discussion among the patient, surgeon, radiologist, medical oncologist and radiation oncologist. The combination of oncologic surgical principles with plastic surgical techniques may help to avoid poor cosmetic results after wide excision and may increase the number of patients who can be treated with BCT. The goals of BCT are total removal of the lesion. There is general consensus that a 2–3 mm margin is adequate if adjuvant radiation is to be administered.

Axillary dissection and sentinel lymph node biopsy (SNB) have no role in the management of DCIS; however, SNB may be considered in certain situations (larger lesions, palpable, high-grade disease).

Three prospective trials have shown that adding radiation after BCT statistically decreases a patient's risk of developing recurrent breast cancer.[16]

To date no subset of patients has been identified that does not benefit from radiation therapy when undergoing BCT for DCIS.

The 5-year results of the Eastern Cooperative Oncology Group and North Central Cancer Treatment Group prospective trial revealed a breast cancer relapses rate of 6.8% ipsilateral and of 3.5% contralateral.

This study selected patients with lower intermediate grade DCIS < 2.5 cm treated with excision (margins >3 mm) without radiation.[17]

Further follow up is needed to have long-term results.

Adjuvant therapy with tamoxifen was studied in two prospective trials in DCIS. These studies have shown a modest reduction in the risk of ipsilateral or contralateral events in ER positive DCIS.

To compare the effectiveness of anastrozole with that of tamoxifen in preventing recurrences after surgery and

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breast irradiation in DCIS, NSABP conducted the B 35 trial which closed the accrual in June 2006 and the results are now awaited.

Recently, the MD Anderson Cancer Centre began a trial of neo-adjuvant transtuzumab for DCIS.

LCIS/LIN

Since most LCIS do not present as a mass nor contain microcalcifications, mammography and ultrasound do not appear to have a role in diagnosing LCIS. Reliable diagnosis may not be possible even with MRI and LCIS is often an incidental finding on core needle biopsy (CNB) performed for breast abnormalities or indeterminate calcifications.

However, accurate diagnosis may be difficult for the small amount of tissue extracted during the procedure.

The significance of LIN diagnosed at CNB remains unclear. [18]

The need for excisional biopsy is controversial. The data in the literature, often retrospective, are confusing and contradictory and a multidisciplinary discussion is essential to determine the management of LIN. Available data suggest that associated high risk lesions increase the risk of upgrade. [18]

Finding LIN at CB associated with calcifications or masses at mammography suggest the necessity of an excisional biopsy. [19]

Pathological reporting and management based on excisional specimen will depend on the associated pathology.

If LIN is only seen in an excision biopsy then no further excision is required even if it is at margins, but it must be a multidisciplinary team decision.

Radiotherapy and endocrine therapy are not recommended but patients should be encouraged to participate in clinical trials.

Conflict of interest statement

None declared.

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