In-situ and lobular, but not as we know it

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A 54-year-old woman presented with suspicious micro-calcifications in the right breast upper outer quadrant on a screening mammogram (Figure 1). Relevant family history included breast cancer diagnosis in a maternal grandmother in her late 40s and in the patient’s mother in her 70s. Approximately 6 years prior to presentation the patient had undergone stereotactic biopsies of micro-calcifications in right breast upper outer quadrant.

Histology at that stage revealed benign fibrocystic change with micro-calcification. Stereotactic core biopsies in the new 9 mm area of radiologically indeterminant micro-calcification now showed features of pleomorphic lobular carcinoma in-situ (PLCIS). Subsequent hook-wire localisation excision of this area found a residual 3.5 mm area of low grade PLCIS (Figure 2), with clear resection margins.

Figure 1. Screening mammogram work-up view showing 9 mm cluster of micro-calcifications in right breast upper outer quadrant
PLCIS, originally described in 1996, consists of lobular cells with marked pleomorphism and large eccentrically placed nuclei. These cells are cytologically more discohesive than in classic LCIS (CLCIS). Additional findings of central necrosis, calcifications and negative staining for E-cadherin are frequently present.

Central necrosis and calcifications are otherwise rarely seen in classic LCIS, but are common in ductal carcinoma in-situ (DCIS). PLCIS may be associated with an infiltrating pleomorphic carcinoma which has similar cytologic appearance and a poor prognosis. Compared with CLCIS, PLCIS shows significantly higher Ki67 index, lower oestrogen receptor and progesterone receptor expression, and higher incidence of HER2 gene amplification. The histologic features, biomarker profile, and genomic instability suggest a more aggressive behaviour of this form of LCIS. Multi-focal disease is also reported.

There is a lack of high quality, extensive follow-up in patients with PLCIS. Current recommendations are to treat these patients more like patients with DCIS than with LCIS. Patients thus require excision to clear margins with consideration of post-operative irradiation. Axillary lymph node biopsy or dissection is not necessary in the management of LCIS. If however a pleomorphic invasive component is present, axillary staging should be performed, followed by systemic therapy where indicated.

The benefit of selective oestrogen receptor modulators (SERMs) in patients with PLCIS is undefined, as subset analysis of patients with PLCIS is not possible from the major breast cancer chemoprevention trials. LCIS is not typically tested for hormone receptor expression.

Figure 2. (left pane) Pleomorphic epithelial cells with eccentric nuclei and abundant cytoplasm; (right pane) Some duct spaces show central comedo-type necrosis and micro-calcification; (lower pane) The atypical cells are negative staining for E-cadherin
Despite the lack of data in PLCIS, the current recommended approach parallels that for pure DCIS with mastectomy or lumpectomy plus radiotherapy, followed by a SERM.

In summary, pleomorphic LCIS is a less known entity that requires more aggressive treatment than with classic-type LCIS. Multidisciplinary discussion involving radiologists, pathologists, breast surgeons and oncologists is indicated in optimal management of these patients.

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