Lobular Carcinoma in Situ: Mammographic-Pathologic Correlation of Results of Needle-directed Biopsy

The mammographic and histologic findings were reviewed in 41 consecutive cases of isolated lobular carcinoma in situ (LCIS) unassociated with any malignant diagnosis. Thirty-one needle-directed breast biopsies were performed to evaluate clustered microcalcifications. In 24 of the 31 cases, the calcifications were found in areas of benign breast disease, with LCIS representing a separate process. In the few cases in which microcalcifications were seen in association with LCIS, a greater number of similar calcifications were present in adjacent benign disease. Soft-tissue abnormalities necessitating the performance of a biopsy represented benign foci, except in one patient with LCIS in and adjacent to a fibroadenoma. The authors conclude that LCIS has no characteristic mammographic features. LCIS is detected as an incidental finding at breast biopsy, with the mammographic abnormality predominantly reflecting a benign process.

Index terms: Breast, calcification, 00.813 • Breast neoplasms, 00.327

Radiology 1991; 181:363–367

Although the concept is controversial, lobular carcinoma in situ (LCIS) is at least a marker for increased risk of development of subsequent invasive breast carcinoma (1–5). Recent data suggest that this increased risk is about 10-fold greater than that for the general population of women (6). The infiltrating lesion that develops can be either ductal or lobular carcinoma and can occur in either breast (1,6).

LCIS was first described in 1941 by Foote and Stewart (7) and Muir (8), who noted a rare form of noninvasive mammary neoplasia arising in the lobules. LCIS is seen primarily in premenopausal women and its occurrence regresses to some degree after menopause (4,9,10). The lesion is multicentric in 60%–90% of patients (11).

Early investigators noted an association between the observation of clusters of punctate microcalcifications at mammography and the presence of LCIS (12,13). The calcifications, however, were more frequently seen in benign lobules adjacent to the LCIS. Our study of LCIS detected with needle-directed biopsy was undertaken to provide a detailed correlation between the mammographic finding that prompted the performance of biopsy and the areas of LCIS that were seen at histologic examination.

MATERIALS AND METHODS

From January 1987 through July 1990, 2,184 needle-directed biopsies of occult breast abnormalities were performed at Brigham and Women’s Hospital with use of the hook-wire technique (14). Over this period of time, 437 malignancies (excluding LCIS) were detected. There were 48 cases of isolated LCIS unassociated with any malignant diagnosis, which represents results of 2.2% of all needle-directed biopsies. Forty-one of these 48 patients were selected for inclusion in this study because the preoperative mammograms, localization mammograms, and pathologic slides were available for review. In addition, the radiographs of the specimens obtained in 37 (90%) of the 41 cases were reviewed.

The biopsy specimen was fixed in formaldehyde, sectioned at 1–2-μm intervals, and embedded in paraffin blocks. A minimum of one slide was obtained per block. The area localized with the wire was sectioned in its entirety. The findings in the resulting slides were correlated with the findings on the mammograms during simultaneous analysis by a radiologist (M.R.S., T.H.F.) and a pathologist (N.W.).

The background parenchyma observed to surround the occult abnormality at mammography was classified as either fatty or opaque tissue or a composite of these two, which was defined as heterogeneous.

Abbreviations: H-E = hematoxylin-eosin, LCIS = lobular carcinoma in situ.
neous or mixed opacity. The abnormality seen at mammography was classified as one of the following: (a) clustered microcalcifications, (b) mass (either noncalcified or calcified), (c) mass with adjacent calcifications, or (d) asymmetric opacity.

RESULTS

The 41 patients with pure LCIS ranged in age from 39 to 82 years, with a median age of 50 years (mean, 52.4 years). Nineteen patients were 40-49 years of age, with the second largest group (n = 12) aged 50-59 years (Table 1).

Breast involvement with LCIS was essentially equally distributed between the right (n = 21) and left (n = 20) breast. The lesion was in the upper outer quadrant in 23 (56%) patients, with the lower inner quadrant harboring only two lesions. Lesions in 23 cases were in breasts with mixed opacity (heterogeneous), lesions in 15 cases were in breasts with opaque tissue, and lesions in three cases were in breasts with predominantly fatty tissue.

Thirty-one patients (76%) had clustered microcalcifications. Noncalcified masses were identified in three (7%), calcified masses in four (10%), and a mass with adjacent calcifications in two (5%). An asymmetric area of opacity was noted in one case (2%) (Table 2). In the two patients with a mass and adjacent calcifications, the mass was of concern for calcifications in one patient and the calcifications were of concern in the other.

The majority (n = 17) of patients with clustered calcifications alone had fine granular calcifications. The second most frequent appearance (n = 10) was of granular calcifications, with one to four elongated forms (longer than oval but not long enough to be considered linear). The number of microcalcifications in the cluster ranged from less than five to too numerous to count. Twenty-eight pa-
patients had more than 10 calcifications. Pathologic review of the 31 patients with clustered microcalcifications showed that the particles were located in terminal duct lobular units in 13. In addition, for these same 31 patients, calcifications were also identified in sclerosing adenosis (n = 6), blunt duct adenosis (n = 4), microcysts (n = 4), stroma (n = 5), and within ducts with epithelial hyperplasia (n = 9) (Fig 1).

Eighteen patients had calcifications associated with two or more different processes. In 11 patients these processes were unequivocally benign. The remaining seven patients had a few calcifications associated with areas of LCIS, with the majority of the calcifications being located in one or more of the benign entities listed above (Fig 2). These seven patients were found to have widespread or multifocal LCIS within the biopsy specimen.

In one patient, the calcifications visible at mammography were an atypical manifestation of early vascular calcification. Histologic evaluation in this case also disclosed calcification in sclerosing adenosis.

Despite the fact that multiple serial sections were obtained and areas of clustered calcifications identified, the calcifications visualized histologically were sometimes smaller than those seen at mammography. Calcifications as small as 0.02 mm in diameter were noted in terminal duct lobular units and blunt duct adenosis. Some of these calcifications could be seen on magnified images of the specimens but not on the preoperative mammograms in which larger calcifications in the same cluster were seen.

In the three patients with noncalcified masses, the mass represented a benign process and the LCIS was a separate, incidental finding. One of these noncalcified masses was well circumscribed while another was poorly defined, but both were associated with areas of fibrosis. The third lesion, a relatively well-defined noncalcified mass, was a benign tubular adenoma. Two noncalcified masses with unrelated adjacent areas of calcification were relatively well defined and represented cysts. The adjacent calcifications were associated with
sclerosing adenosis in one case and with benign ducts in the other case. Three of the four calcified masses had irregular, poorly defined margins and were associated with granular calcifications. The first was sclerosing adenosis, with calcifications identified predominantly in the terminal duct lobular units and with rare calcifications in areas of LCIS. The second was related to proliferative fibrocystic changes and sclerosing adenosis, with calcifications identified in areas of the latter (Fig 3). The third represented a hyalinized fibroadenoma. Calcifications in this case were noted in areas of proliferative fibrocystic change.

The fourth mass had slightly lobulated, partially indistinct margins and contained granular and coarse calcifications. Pathologic evaluation demonstrated a sclerotic fibroadenoma with LCIS both within the mass and in the adjacent tissues (Fig 4).

Proliferative fibrocystic changes and sclerosing adenosis were the cause of the single case of an area of asymmetry; in that case the finding of focal LCIS was also incidental (Fig 5).

The benign processes found in our patients’ biopsy specimens were varied, including sclerosing adenosis (n = 13), proliferative fibrocystic changes (n = 15), fibrocystic changes (predominantly fibrosis) (n = 3), intraductal hyperplasia (n = 2), atypical ductal hyperplasia (n = 5), lobular hyperplasia (n = 1), cysts (n = 3), sclerotic or hyalinized fibroadenoma (n = 2), benign tubular adenoma (n = 1), sclerosing papillomatosis (n = 1), and radial scar (n = 1).

**DISCUSSION**

LCIS or lobular neoplasia is identified in approximately 0.8%–3.6% of all benign breast biopsy samples (2–4,10) and represented the finding in 2.2% of needle-directed biopsies in our series. LCIS is typically multicentric and is present in 23%–35% of contralateral breast biopsy samples (4,9,15).

The malignant potential of these lesions remains controversial. The reported incidence of subsequent invasive breast cancer ranges from 17% to 37%, with a risk of approximately 1% per year (2–4,10,16). Invasive carcinoma that develops in these patients is more frequently of ductal origin than of lobular origin and is just as likely to occur in the contralateral breast as in the side of the original lesion (1,6). These findings suggest that LCIS is a marker for increased risk rather than a truly malignant lesion (2–5). It is possible therefore that cases of pure LCIS could be grouped with cases of benign rather than malignant lesions.

There is also disagreement regarding the treatment of LCIS. At our institution, treatment following the discovery of LCIS at biopsy consists of close clinical and mammographic follow-up, consistent with the belief that LCIS is a high-risk marker rather than a malignant lesion (1,17). Other treatment options include (a) ipsilateral mastectomy with mirror-image biopsy and contralateral mastectomy if LCIS is found (18) and (b) bilateral mastectomy. Since both breasts are exposed to the same risk regardless of whether the contralateral biopsy shows LCIS, bilateral mastectomy would seem to be the more logical choice if surgical treatment is elected (1).

Several authors have described mammographic features associated with LCIS. In 1966, Snyder (12) evaluated mammographic features in 27 patients (35 breasts) and considered the finding of three or more randomly grouped minute punctate or linear flecks of calcium to be indicative of LCIS. She noted, however, that the calcifications were in the neighboring lobules not actually involved with LCIS. Hutter et al (13) provided continued follow-up information on these original 27 patients and 34 others. These authors also noted that the finely stippled calcifications were rarely located in the lobular carcinoma itself but were more frequently located in adjacent lobules. The calcifications were not unique for LCIS; similar calcifications were observed in sclerosing adenosis and duct papillomatosis. They also found that four patients with LCIS did not have stippled calcifications, with three having a localized noncalcified opacity and one, an increase in diffuse nonspecific calcifications. More than one-half of the patients with LCIS had no mammographic abnormality.

Morris et al (19) reported on the usefulness of xeromammography in en bloc resection of LCIS. Results of xeromammography were positive for LCIS in three of the 16 breasts sampled for biopsy (19%).

Pope et al (20) published the most recent review of mammographic features of LCIS. Of their 26 cases, 16 represented patients in whom needle localization had been performed. The presence of calcifications prompted performance of 10 of the needle-directed biopsies, with the particles most commonly seen outside of the LCIS in adjacent benign foci. Two fibroadenomas contained foci of LCIS; a spiculated opacity was related to postinflammatory changes, and an asymmetric opacity was believed to be caused by an area of fibrosis. The precise cause of several asymmetric areas of opacity was unclear. The authors concluded that LCIS has no distinctive mammographic features.

In all of our patients, the mammographic finding that prompted performance of biopsy was a benign process. Clustered microcalcifications, the most frequently observed mammographic abnormality, were confirmed to be located in benign lesions. Eight patients were found to have calcifications associated with areas of LCIS. Seven of these patients had clustered microcalcifications; the eighth had a poorly defined calcified mass. The few microcalcifications identified in areas of LCIS in these eight patients were far outnumbered by the microcalcifications present in immediately adjacent benign foci. This suggests that those few calcifications were originally associated with preexisting benign changes and were subsequently engulfed. The location of these calcifications in benign foci supports the argument that these cases should be placed in the benign category when performing statistical analysis.

Many of the calcifications visualized at histologic examination were much smaller than those seen at mammography. It is possible that some of the larger calcifications became dislodged during processing of the material. Larger fragments of calcium may have been dragged through the tissue as it was sliced by the microtome, producing a section that was then discarded. Pope et al (20), noting a similar phenomenon, theorized that some calcifications seen at mammography may represent a superimposition of numerous tiny (5 μm-diameter) calcifications within a small volume. After confirming that the area of the clustered calcifications had been sectioned, one must presume that the smaller calcifications are representative of the process noted at mammography.

LCIS was detected both within and adjacent to a fibroadenoma in one of our patients and within two fibroadenomas in an earlier study (20). LCIS represented 65% of the “malignancies” observed in 62 cases of carcinoma within a fibroadenoma (21). The higher incidence of LCIS than ductal carcinoma in situ occurring in fibroadenomas is probably related to the common lobular origin of the epithelial components of both the fibro-
adenoma and LCIS. The coexistence of LCIS and a fibroadenoma was reported in 0.2% of cases in a series of 8,690 consecutive breast biopsy specimens (22).

In summary, our data support the conclusion that LCIS has no characteristic mammographic features. Clustered microcalcifications were the most common indication for biopsy; however, these calcifications were usually found in benign fibrocystic changes adjacent to the LCIS. When calcifications were seen in areas of LCIS there were always more numerous calcifications in adjacent benign foci, suggesting that the calcifications were engulfed by the LCIS as it developed. Soft-tissue opacities that underwent biopsy were always created by a benign process, except for the patient with LCIS in and adjacent to a fi-


References

Figure 5. Mammogram and histologic spec- imens of an asymmetric opacity in a 59-year- old woman. (a) Routine mammogram shows a 1.8 ¥ 2.3-cm, asymmetric, masslike area of opacity (arrow) in the left breast. Granular microcalcifications were scattered in this area and in other areas in the same breast. (b) Dis- torted terminal-duct lobular units are shown, some containing microcalcifications (arrow) and others, immediately adjacent, containing LCIS (arrowhead) (H-E stain; original magnification, ¥50). (c) Area of sclerosing adenosis is shown, containing focal microcalcification (arrow) (H-E stain; original magnification, ¥100).

Acknowledgments: The authors thank Carol Elliott for assistance with manuscript preparation, Suresh Mukherji, MD, for assistance with gathering case material, and Arnold S. Epstein for data tabulation.

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