

## Lobular Carcinoma in Situ in Sclerosing Adenosis

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### Abstract

The initial presentation of breast malignancy as noninvasive carcinoma in an area of sclerosing adenosis is unusual. Especially, lobular carcinoma in situ in sclerosing adenosis sometimes can be a potential source of confusion with invasive lobular carcinoma. We report a case of lobular carcinoma in situ presenting in adenosis exhibiting patterns akin to invasive lobular carcinoma, thus leading to potential misdiagnosis. Overall architecture of the lesion as seen at lower power and immunohistochemistry can be useful to distinguish between sclerosing adenosis with lobular carcinoma in situ and infiltrating lobular carcinoma.

**Key Words:** Lobular carcinoma in situ, sclerosing adenosis, immunohistochemistry

### INTRODUCTION

The pathologic features of lobular carcinoma of the breast have already been well characterized. The cytologic spectrum of the in situ forms have been identified<sup>1</sup>: namely, type A (or classical), type B (or pleomorphic), less common signet ring cells and myoid forms. Moreover, a variety of invasive growth patterns have been illustrated on numerous occasions in recent years.<sup>2-5</sup> The presence of lobular carcinoma in situ within foci of sclerosing adenosis or adenosis tumor is not surprising and until currently, several patients who had extensive sclerosing adenosis with ductules containing cells characteristic of lobular carcinoma were documented in world literature.<sup>6-9</sup> We have found this combination in a 52-year-old postmenopausal woman and microscopic appearance raised the possibility of an invasive lobular carcinoma. Therefore, it seems worthwhile to document this aspect of lobular carcinoma in situ because of the potential source of confusion with invasive carcinoma.

### CASE REPORT

A 52-year-old postmenopausal Korean woman presented with a 10-year history of right breast mass. Previously, core needle biopsy was done and the diagnosis of invasive lobular carcinoma was made in an other hospital.

Mammography showed an irregularly marginated mass involving subareolar area without distortion of surrounding breast parenchyma (Fig. 1). On ultrasonography, an oval shaped hypochoic nodule with microcalcification can be seen (Fig. 2). Left breast was unremarkable on mammography.

We were asked for a reviewing of microscopical finding of core needle biopsy of this patient and concurred on that diagnosis, which was invasive lobular carcinoma. Right modified radical mastectomy including axillary node dissection was done on the basis of that diagnosis and disclosed a 1.8 cm-sized pinkish, gray bulging out multinodular mass in the central portion of the breast.

Microscopically, a multinodular mass was a confluence of foci of sclerosing adenosis, resulting in a grossly discrete lesion, namely adenosis tumor. At low power, the lobular ducts were disarrayed and organized into concentrically swirling patterns. Increased numbers of lobular ducts along with an increase in the density of intralobular fibrous tissue were noted. Some of the lumina of the ductules were dilated and some were attenuated or obliterated. Even though the

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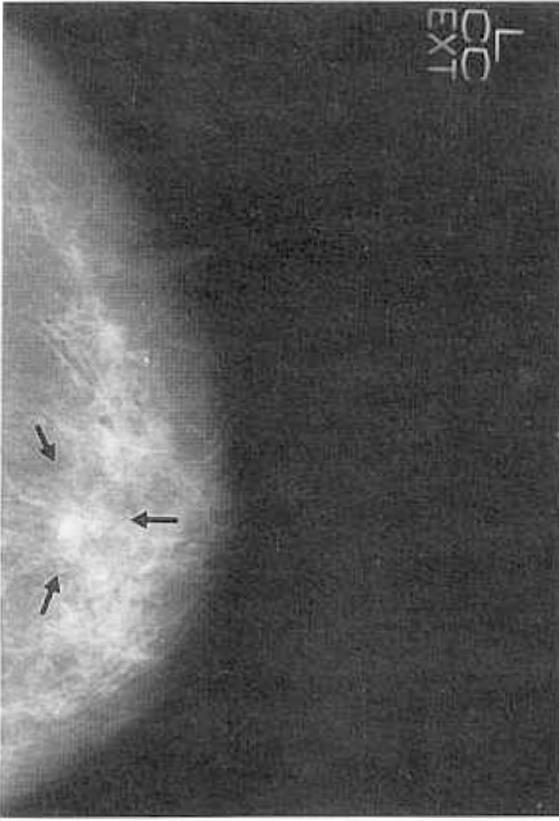


Fig. 1. Mammography shows an irregularly margined mass involving subareolar area.

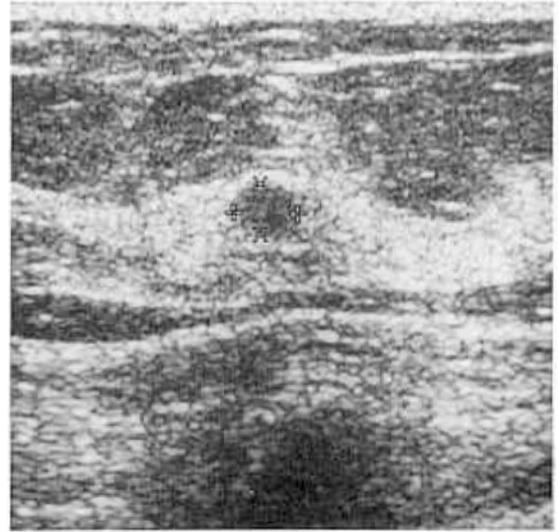


Fig. 2. Ultrasonography shows an oval shaped hypoechoic nodule with microcalcification.

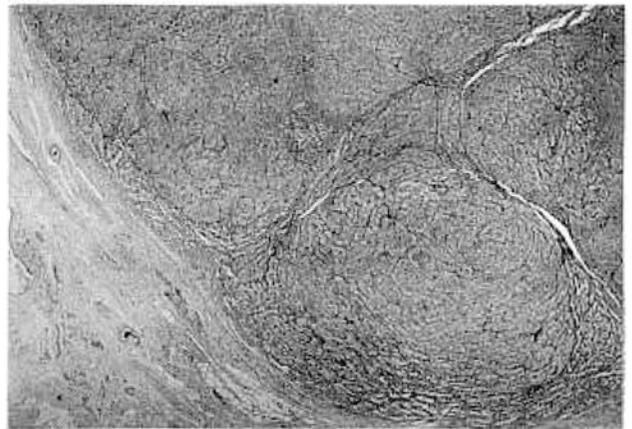
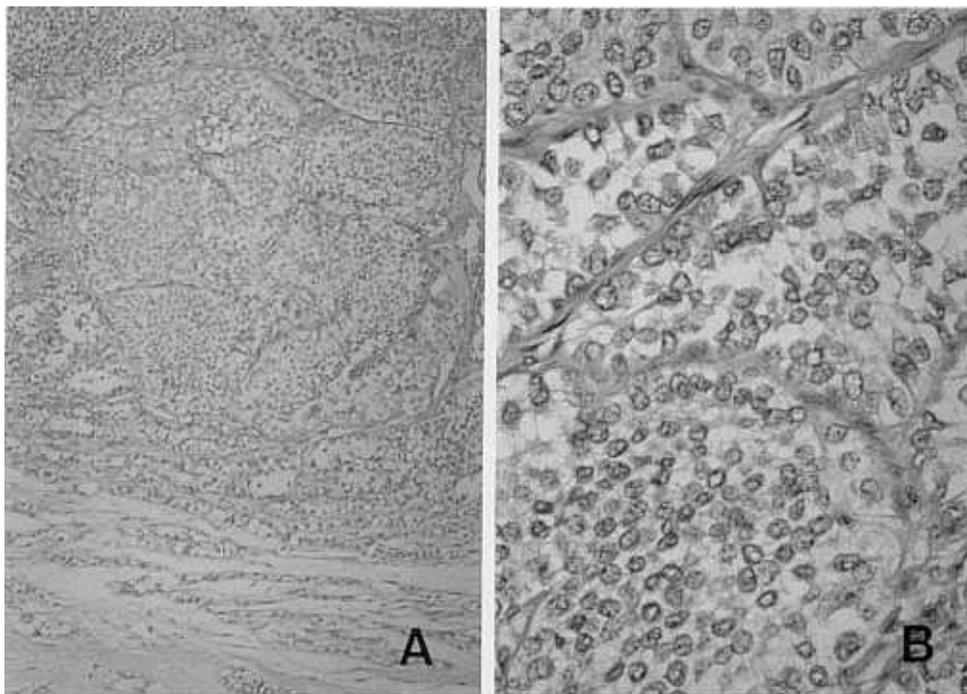


Fig. 3. At low power, relatively well delineated pushing margin and lobular nature of sclerosing adenosis can be noted (H and E,  $\times 40$ ).

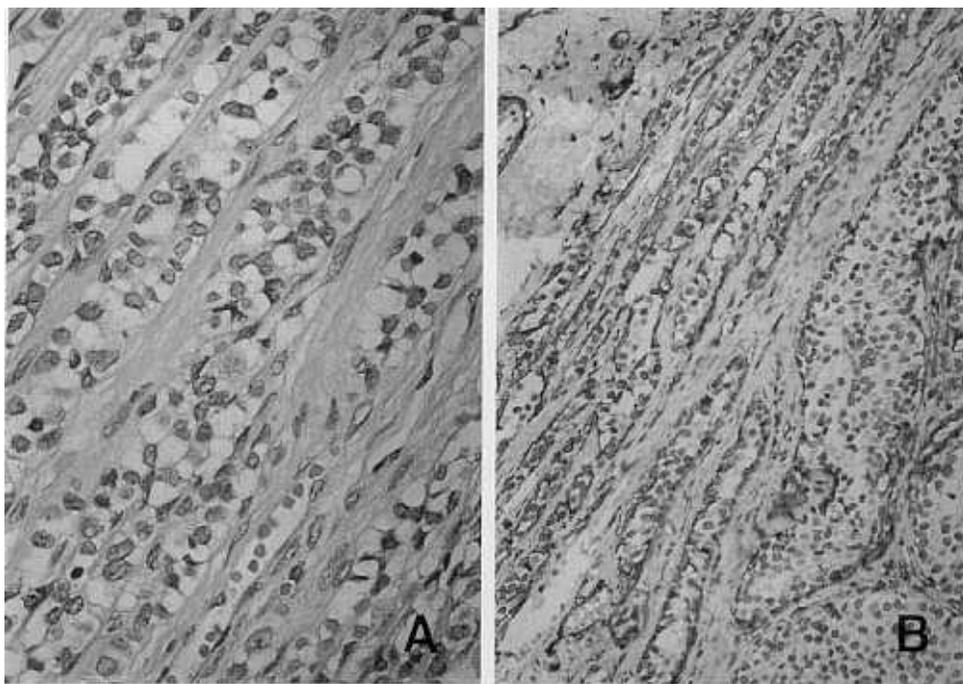
normal double layer of ductules appeared to be preserved, myoepithelial cells were more plump or spindly shaped compared to those of the normal ductules. Moreover, myoepithelial cells were highlighted in the section stained for smooth muscle actin. As noted in ultrasonography, microcalcifications were present in areas of sclerosing adenosis. Among the conglomerated foci of sclerosing adenosis, the largest one cut a conspicuous figure. This lesion had relatively well delineated pushing margin and showed lobular nature of sclerosing adenosis at low power (Fig. 3). The mass was composed of tightly packed ductules separated by thin fibrous septa (Fig. 4A). Ductules along the margin were compressed by the expansile growth so that a convex rim was formed. Normal epithelium of ductules were completely replaced by a population of small, uniform, rounded cells with powdery or clear cytoplasm, which is characteristic of cells of lobular carcinoma (Fig. 4B). Interestingly, many elongated cords of cells were embedded in the layer of circumferentially oriented

fibrous tissue along the margin (Fig. 5A). This mimics the single file pattern of invasive lobular carcinoma.

Immunohistochemistry using a monoclonal antibody to smooth muscle actin showed regularly outlined basal lamina of the involved ducts, as well as an uninterrupted myoepithelial layer (Fig. 5B). This case showed positive immunoreactivity for cytokeratin, estrogen receptor and progesteron receptor and negative for both chromogranin and neuron specific enolase. Putting these findings together, our diagnosis was lobular carcinoma in situ in preexisting sclerosing adenosis.



**Fig. 4.** (A) The mass is composed of tightly packed ductules separated by thin fibrous septa (H & E,  $\times 400$ ). (B) Normal epithelium of ductules are completely replaced by a population of small, uniform, rounded cells with powdery or clear cytoplasm, which is characteristic of cells of lobular carcinoma (H & E,  $\times 400$ ).



**Fig. 5.** (A) Many elongated cords of cells are embedded in the layer of circumferentially oriented fibrous tissue along the margin (H & E,  $\times 400$ ). (B) Regularly outlined basal lamina of the involved ducts, as well as an uninterrupted myoepithelial layer are discernible (smooth muscle actin immunohistochemical stain,  $\times 200$ ).

Table 1. Noninvasive Carcinoma in Adenosis: Previous Reports

| Author         | No. of patients | Mean age (yr) | LCIS/DCIS          | Separate foci of in situ carcinoma | Follow-up (yr)* |
|----------------|-----------------|---------------|--------------------|------------------------------------|-----------------|
| Fechner (1981) | 5               | 52            | 5/0                | 5                                  | NA              |
| Nielsen (1987) | 5               | 44            | 1/3/1 <sup>†</sup> | 3                                  | A and W (4)     |
| Chan (1987)    | 1               | 32            | 0/1                | 0                                  | NA              |
| Eusebi (1989)  | 7               | 40            | 5/2                | 3                                  | A and W (4)     |
| Oberman (1991) | 9               | 43            | 7/1/1 <sup>†</sup> | 0                                  | A and W (3)     |
| Jung (1999)    | 1               | 52            | 1/0                | 0                                  | A and W (2)     |
| Total          | 28              |               | 19/7/2             | 11                                 |                 |

\* Mean years of follow-up, NA, not available.

<sup>†</sup> One patient had both DCIS and LCIS in adenosis.

A and W, alive without recurrence; DCIS, Ductal carcinoma in situ; LCIS, Lobular carcinoma in situ.

No carcinoma was present elsewhere in the involved breast in mastectomy specimen. Thirteen axillary lymph nodes were available from the specimen and were free of the tumor as expected.

This patient is alive and well without recurrent neoplasm after a follow up interval of 2 years.

## DISCUSSION

The initial presentation of breast malignancy as noninvasive carcinoma in an area of sclerosing adenosis is unusual. In contrast, patients with carcinoma elsewhere in the breast also may have areas of neoplastic involvement of adenosis. Since sclerosing adenosis is a lesion derived from the mammary lobule, it is not surprising that lobular carcinoma in situ (LCIS), as in this case and previous reports, is the most common neoplasm to present in adenosis.<sup>6-9</sup> Twenty seven patients which have been previously reported with noninvasive carcinoma presenting in adenosis in addition to the present case have been collected (Table 1).<sup>6-10</sup>; they are 19 LCIS, 7 ductal carcinoma in situ (DCIS), and 2 with both LCIS and DCIS. Forty percent of the reported cases had separate foci of in situ carcinoma apart from areas of adenosis. None of these patients, regardless of treatment, had recurrent neoplasm in either breast, although the follow-up intervals are brief. This suggests that the localized character of the carcinoma in this situation implies a remarkably favorable course.

Considering previously mentioned microscopic

findings, first of all, sclerosing adenosis with predominant epithelial hyperplasia should be ruled out. Even though the underlying architectural framework of sclerosing adenosis is discernible in this case, all the ductules are distended by uniform abnormal cells and are without lumens. In addition, most of myoepithelial cells appear to be attenuated rather than hypertrophied and spindle-shaped, as shown in sclerosing adenosis.

In diagnostic pathology practice, the greatest problem occurs in differentiating this case from invasive cancers that have small, uniform neoplastic cells with round nuclei arranged in small or large nests. In this context, these particular infiltrating cancers are regarded as carcinoid tumors of the breast or solid variant of infiltrating lobular carcinoma.<sup>9</sup> In case of carcinoid tumors, they are almost always poorly demarcated and the cell cords tend to invade adjacent normal structures. Moreover, immunohistochemically, they are typically positive for cytokeratin, chromogranin and neuron specific enolase. However, this case showed cytokeratin-positive, and both chromogranin and neuron specific enolase-negative.

As Fechner suggested the term confluent or solid variant of infiltrating lobular carcinoma, that is characterized by multilayering of neoplastic cells arranged in irregularly shaped solid nests.<sup>2</sup> Such nests are sometimes in continuity with a classic single file pattern of cytologically identical cells.

As Eusebi et al. recommended, we performed immunohistochemistry using a monoclonal antibody to smooth muscle actin to distinguish between LCIS within sclerosing adenosis and solid variant of invasive

lobular carcinoma.<sup>7</sup> Regularly outlined basal lamina of the involved lobular ducts, as well as an uninterrupted myoepithelial layer can be appreciated in this case, which clarifies the noninvasive character of this neoplasm.

As mentioned previously by Fechner,<sup>2</sup> a focus of sclerosing adenosis has an overall organization even though the lesion is involved by LCIS. Even in the tangential sectioning, the tendency to peripheral distension of ductules is usually recognizable. Conversely, the nests of infiltrating carcinoma are haphazardly arranged and do not suggest organization. Overall organization of adenosis feature is discernible in this case.

As noted at the outset of this presentation, the major problem of this uncommon presentation of noninvasive carcinoma is distinguishing it from invasive carcinoma and defining appropriate treatment. Especially, the distinction of noninvasive carcinoma from invasive carcinoma is more difficult with involvement of adenosis by LCIS than DCIS. As has been noted by others, we found that identification of myoepithelium was most helpful in resolving difficult case. However, careful inspection usually reveal that underlying adenosis pattern in which glandular units are surrounded by a basement membrane, myoepithelial cells and stroma. These elements can be highlighted with PAS-alcian blue or reticulin stain and by immunohistochemical demonstration of laminin, type IV collagen, and actin.<sup>7,11</sup>

LCIS is usually diagnosed in premenopausal women as an incidental finding in a breast biopsy performed for other indications. The risk of subsequent development of an invasive carcinoma after treatment with biopsy alone is estimated to be approximately 20% to 30%, with a 10% to 15% risk in each breast.<sup>12</sup> The current concept of LCIS as a marker of increased risk for developing breast cancer rather than as a site of origin for cancer is supported by the findings that if an invasive cancer subsequently occurs, 50% to 65% of the time it will be of ductal rather than lobular histology and that all breast tissue is at equal risk.<sup>12</sup> Even though, this patient underwent modified radical mastectomy on the basis of the diagnosis which was invasive lobular carcinoma, the limited data available in this patient group support the

concept that observation of LCIS is a reasonable treatment option since the risk of breast cancer is distributed throughout all breast tissue and is similar to the lifetime contralateral breast cancer risk of the patient with non-LCIS breast cancer. Thus, if surgery is elicited to treat LCIS alone, the preferred choice is bilateral total mastectomies. Nevertheless, the number of patients reported is too small, and the follow-up interval too brief, to permit recommending any unique form of treatment.

This is an interesting case of LCIS presenting in sclerosing adenosis exhibiting patterns akin to invasive carcinoma, thus leading to potential misdiagnosis.

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