Lobular Carcinoma In Situ

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KEYWORDS

- Pleomorphic lobular carcinoma in situ Variant lobular carcinoma in situ E-cadherin p120
- CDH1 Core biopsy

Key points

- Lobular carcinoma in situ (LCIS) is a risk factor and a nonobligate precursor lesion.
- LCIS shows loss of E-cadherin and diffuse cytoplasmic staining for p120 catenin.
- The most frequent chromosome alteration in LCIS is deletion of 16q; the most common somatic mutations in LCIS affect *CDH1* (gene encoding for E-cadherin).
- Surgical excision can be safely spared in patients with classic LCIS diagnosed on needle core biopsy with concordant imaging and pathologic findings.
- Surgical excision is recommended for LCIS with variant or pleomorphic morphology, and for classic LCIS with discordant imaging and/or pathologic findings.

ABSTRACT

obular carcinoma in situ (LCIS) is a risk factor and a nonobligate precursor of breast carcinoma. The relative risk of invasive carcinoma after classic LCIS diagnosis is approximately 9 to 10 times that of the general population. Classic LCIS diagnosed on core biopsy with concordant imaging and pathologic findings does not mandate surgical excision, and margin status is not reported. The identification of variant LCIS in a needle core biopsy specimen mandates surgical excision, regardless of radiologic-pathologic concordance. The presence of variant LCIS close to the surgical margin of a resection specimen is reported, and reexcision should be considered.

OVERVIEW

Foote and Stewart¹ first described lobular carcinoma in situ (LCIS) in 1941 as a rare form of

mammary cancer originating in lobules and terminal ducts. They reported all the key morphologic features of LCIS that still hold true and accurate today: (1) LCIS is an incidental microscopic finding: "There is no way in which a clinical diagnosis of lobular carcinoma in situ can be made" ... "There is no way by which it can be recognized grossly"; (2) LCIS has characteristic morphologic features: "The cells lose polarity, varying in shape while maintaining surprisingly uniform size"; (3) LCIS is multifocal: "it is always a disease of multiple foci." The aforementioned features characterize the so called "classic" form of LCIS. Even though classic LCIS constitutes both a risk factor and a nonobligate precursor of invasive breast cancer, it is currently managed as a benign lesion, and does not require complete removal and/or evaluation of margin status. Hormonal chemoprevention is recommended for patients with classic LCIS. In the eighth edition of the TNM staging by the American Joint Committee on Cancer (AJCC),² LCIS is no longer staged as Tis.³

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EPIDEMIOLOGY

Classic LCIS usually is an incidental finding in a breast needle core biopsy or surgical excision specimen targeting another lesion. It is therefore difficult to estimate the actual incidence of LCIS. LCIS is identified in 0.5% to 1.5% of benign breast biopsies⁴⁻⁶ and in 1.8% to 2.5% of all breast biopsies.^{4,7} In a population-based study using data from the Surveillance, Epidemiology, and End Results (SEER) program,⁸ the incidence of LCIS in women without prior history of in situ or invasive breast carcinoma increased from 0.90 per 100,000 person-years in 1978 to 1980 to 3.19 per 100,000 person-years in 1996 to 1998.^{8,9} The increased incidence of LCIS is likely due to the increased use of mammographic screening and biopsy of mammographically indeterminate or suspicious lesions. Age-specific incidence analysis revealed that the magnitude of the increase was highest among women ages \geq 50 years, the age group most likely to participate in routine mammographic screening.⁹

CLINICAL FEATURES

LCIS occurs predominantly in premenopausal women, with mean and median age at diagnosis of 49 and 50 years, respectively (range 20s–80s).^{10–13} LCIS is multicentric in 60% to 80% of patients¹⁴ and bilateral in 20% to 60%.^{11,15,16} Classic LCIS is clinically and mammographically occult, although recent studies report an

association with grouped amorphous or granular mammographic calcifications,^{13,17} or heterogeneous non-masslike enhancement with persistent enhancement kinetics on MRI.¹⁷ LCIS variants, such as pleomorphic LCIS and LCIS with central necrosis, are usually detected mammographically due to associated pleomorphic calcifications, or can present as a mass lesion with or without associated calcifications.^{13,18–25}

HISTOPATHOLOGY

CLASSIC LOBULAR CARCINOMA IN SITU

LCIS is a proliferation centered in the terminal ductal lobular units (TDLUs), and consists of neoplastic cells that fill and expand most (>50%) of the acini (Fig. 1). Pagetoid extension into the terminal ducts with growth of LCIS cells underneath the ductal epithelium is also common. The crosssection of a duct with pagetoid involvement by LCIS has a characteristic "cloverleaf" pattern (Fig. 2). Classic LCIS is a monomorphic, dyshesive proliferation of nonpolarized cells with round to oval shape, inconspicuous cytoplasm. The nuclei are located in the center of the cells, and are small, round to oval, with smooth nuclear membrane and inconspicuous nucleoli (Fig. 3). Cell borders are indistinct. Intracytoplasmic vacuoles are common, and signet-ring cell formation can occur (Fig. 4). Mitotic activity is absent to exceedingly rare.

The cells of classic LCIS can have scant cytoplasm ("small cells" or "type A" cells)¹⁰ or be a bit larger ("large cell" type or "type B"),¹⁰ with



Fig. 1. LCIS, classic type. The acini are expanded by monomorphic, evenly spaced dyshesive cells with low-grade nuclear atypia. Magnification $\times 200$.

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