Original Study

Pleomorphic Lobular Carcinoma in Situ Diagnosed by Breast Core Biopsy: Clinicopathologic Features and Correlation With Subsequent Excision

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Abstract

Pleomorphic lobular carcinoma in situ (PLCIS) is a variant of LCIS with high grade morphologic features. However, the number of case series are limited, and the natural history and optimal clinical management are not well-defined. We report the largest breast core biopsy series of PLCIS which included 37 patients with PLCIS diagnosed on core biopsy. Upgrade rate to invasive carcinoma on excision was 60%, which was multifocal in 46%. Over one-half of our cohort had a family history of breast cancer.

Introduction: Pleomorphic lobular carcinoma in situ (PLCIS) is a variant of LCIS with high-grade morphologic features. The number of case series studying PLCIS is limited, and clinical management of patients with PLCIS is controversial. We report a breast core biopsy (BCBx) series of PLCIS. **Materials and Methods:** We reviewed 37 cases of PLCIS with or without microinvasion diagnosed by BCBx. PLCIS was defined as dyscohesive cells showing acinar expansion and loss of immunohistochemical membranous expression of e-cadherin or beta-catenin with nuclear pleomorphism with at least 2- to 3-fold variation in nuclear size, membrane irregularities, and variably prominent nucleoli. Clinical information and findings on excision were evaluated. **Results:** Thirty-one (84%) patients presented with mammographic calcifications, 4 (11%) presented with ultrasound findings, 1 (3%) presented with magnetic resonance imaging enhancement, and 1 (3%) with combined imaging abnormality. The mean patient age was 62.3 years. Nineteen patients (51%) had a family history of breast cancer. Microinvasion was present on BCBx in 9 (24%) of the 37 patients. Excision, available in 34 patients, demonstrated invasive carcinoma in 24 (65%), which was multifocal in 11 (46%). Twenty-three patients with PLCIS without microinvasion on BCBx, and without known history of ipsilateral invasive cancer, underwent excision; 14 of these patients demonstrated invasive carcinoma, representing an upgrade to invasive carcinoma of 60%. **Conclusion:** We report the largest BCBx series of PLCIS and confirm its aggressive biology and frequent association with multifocal invasive lobular carcinoma, as well as frequent presentation in patients with a family history of breast cancer. Our results support excision to negative margins.

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Introduction

Lobular carcinoma in situ (LCIS) of the classic type is predominately considered to represent a risk factor for the subsequent development of invasive carcinoma. It typically presents as an incidental finding, it is often bilateral and multifocal, and the subsequent breast cancer risk is in both breasts. Further, the majority of invasive carcinomas that develop after a diagnosis of LCIS are invasive ductal carcinomas. Hence, clinical management of LCIS is generally focused on risk-reduction strategies.

Pleomorphic LCIS (PLCIS) is an aggressive variant of LCIS characterized histologically by pleomorphic cytologic features along with a higher risk of concurrent invasive disease when compared with classic LCIS.[1] PLCIS is more often hormone receptor-negative, human epidermal growth factor receptor 2-positive, and has a higher Ki67 proliferative index when compared with classic LCIS.[2] As a result of high-grade cytologic and biomarker profile, it is

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sometimes mistaken for high-grade ductal carcinoma in situ (DCIS). PLCIS was first described in the 1990s, and its recognition was facilitated by the advent of e-cadherin immunohistochemistry demonstrating loss of expression in PLCIS, characteristic of lobular lesions.[3,4] However, detailed information on the natural history of PLCIS is limited.

The most recent National Comprehensive Cancer Network guidelines acknowledge that PLCIS may have a similar biologic behavior to that of DCIS, and surgical excision is recommended if PLCIS is diagnosed on a core biopsy; however, these guidelines do not make a firm recommendation regarding whether excision to clear margins is necessary. The guidelines contain a statement that clinicians may consider complete excision with negative margins, but this may lead to high mastectomy rates without proven clinical benefit.[5] Currently, there is no consensus regarding management of PLCIS. One survey of 358 surgeons reports that about one-half would not perform re-excision of a margin that was positive for PLCIS.[6] The role of radiation therapy for patients with PLCIS is also unsettled, and the most recent National Comprehensive Cancer Network guidelines state there is no data to support use of radiotherapy at this time. This is somewhat contested, though, as some literature suggests potential benefit in these patients.[5,7]

PLCIS is rarely diagnosed on breast core biopsy, and the number of reported case series are few, hence the rate of upgrade to invasive carcinoma upon excision is not well-characterized. In the present study, we report one of the largest series of PLCIS diagnosed on breast core biopsy. We characterize clinical and pathologic features of these cases along with findings on excision. We hope our findings will better define the clinical and pathologic aspects of PLCIS and add to the body of literature that can help shape future practices regarding the most appropriate management for PLCIS.

Materials and Methods

We retrospectively identified 37 cases of PLCIS diagnosed on breast needle core biopsy. Cases were identified through a search of the computer database of surgical pathology reports from 2006 through 2017 at Montefiore Medical Center and Lifespan Medical Center. Only patients who had their initial breast core biopsy performed and/or slides reviewed at our hospitals were included in the study. Cases with a diagnosis of either PLCIS alone or PLCIS with microinvasion were included in the study, where microinvasion was the most advanced lesion. Cases with invasive carcinoma larger than microinvasion on the core biopsy were not included. Clinical information including patient age, imaging, clinical findings, and demographic information were obtained by review of the electronic medical record. Pathology reports and results of surgical resections were reviewed.

PLCIS was defined as a population of dyscohesive cells showing acinar expansion and loss of immunohistochemical membranous expression of e-cadherin and/or beta-catenin characteristic of LCIS, along with nuclear pleomorphism with at least 2- to 3-fold variation in nuclear size, nuclear membrane irregularities, and variably prominent nucleoli (Figure 1).[8] Additionally, the presence of comedo-type necrosis and classic LCIS was documented. In select cases, a cytokeratin immunostain was performed to evaluate for invasion (Figure 2). Cases of florid LCIS with comedo-type necrosis but without nuclear pleomorphism were not included in the study.

Differences in the presence of associated invasive carcinoma between African American and white patients was compared using the Fisher exact test. This study was approved by the institutional review boards of both Montefiore Medical Center and the Lifespan Medical Center.

Results

Our study included 37 women who underwent breast needle core biopsy demonstrating PLCIS with or without microinvasion. In all patients, the indication for the core biopsy was an imaging abnormality on either a mammogram, ultrasound, or via magnetic resonance imaging (MRI). Specifically 31 patients (84%) presented with calcification seen on mammogram, and core biopsy in 30 of these patients demonstrated calcification within foci of PLCIS. In 1 patient with a core biopsy done for calcification, microscopic examination of the slides did not demonstrate any calcification. One patient, who presented with a calcium-containing mass on mammogram, demonstrated only PLCIS with calcification on core biopsy, although subsequent excision revealed a 5-mm invasive lobular carcinoma. Four patients (11%) presented with a mass or distortion on ultrasound, 3 of whom demonstrated PLCIS with microinvasion on core biopsy. Core biopsy in the fourth patient demonstrated only PLCIS without subsequent invasion on excision. One patient, with a known diagnosis of invasive lobular carcinoma, had an MRI that revealed abnormal enhancement in a separate quadrant. Core biopsy of the MRI abnormality revealed PLCIS without microinvasion. Two additional patients in our series also had a separate breast core biopsy diagnosis of invasive lobular carcinoma in the ipsilateral breast as follows; 1 patient with PLCIS had a subsequent abnormal MRI, and a core biopsy revealed invasive lobular carcinoma in a quadrant separate from her known PLCIS. One patient with a core biopsy diagnosis of PLCIS with microinvasion had a core biopsy diagnosis of invasive lobular carcinoma in the ipsilateral breast; however, further details are not available.

Family history was available in 30 patients, of whom 19 (63%) had a family history of breast cancer, and 10 of these 19 had a family history of breast cancer in a first-degree relative (mother or sister). The mean age of all patients was 62.3 years with a range of 41 to 86 years. Ten (27%) patients were African American, 21 (57%) were white, and race was not available in 6 patients (Table 1).

Breast core biopsy showed PLCIS without microinvasion in 28 (76%) patients and PLCIS with microinvasion in 9 (24%) patients. Results of subsequent resection were available in 34 of the 37 patients, including conservative surgery in 21 and mastectomy in 13. Invasive carcinoma was identified in the resection specimen in 24 (71%) of 34 patients. The invasive carcinoma was invasive lobular carcinoma in all but 1 patient, who had invasive ductal carcinoma. In 1 of the 9 patients with microinvasion on the initial core biopsy, there was no residual invasive carcinoma on the excision. However, the remaining 8 patients with microinvasion on the initial core biopsy demonstrated invasive foci within the surgical resection specimen. Of the 28 patients with PLCIS without microinvasion on their initial core biopsy, 25 (64%) had follow-up excision demonstrating invasive tumor foci in 16 (Table 2). Twenty-three of these 25 patients had no known invasive carcinoma in the ipsilateral breast prior to resection, and, among these 23 patients, invasive carcinoma was identified in 14, representing an