Lobular Breast Cancer

Different Disease, Different Algorithms?

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KEYWORDS

• Invasive lobular carcinoma • E-cadherin • The Cancer Genome Analysis
• Breast conservation • Mastectomy • Chemotherapy • Aromatase inhibitors

KEY POINTS

- Invasive lobular breast cancer is a biologically unique entity, distinct from invasive ductal cancer.
- The characteristic molecular features of invasive lobular carcinoma (ILC) include its largely ER-positive and low-grade nature, and loss of E-cadherin protein expression.
- Tumor biology is of key importance in designing treatment approaches.
- Harnessing the growing knowledge of the molecular features inherent to lobular cancer holds promise for the next generation of tailored therapies.

INTRODUCTION

Invasive lobular carcinoma (ILC) is the second most common histologic form of breast cancer, comprising 10% to 15% of invasive tumors.[1] ILC is now recognized as a biologically distinct disease from the more common invasive ductal carcinoma (IDC), with a unique molecular pathogenesis and consequential implications on diagnosis and treatment. An understanding of these differences is of utmost importance to tailor management strategies. Ongoing investigations of the genomic basis of breast cancer are paving the road for novel approaches to treatment of ILC.

EPIDEMIOLOGY

The mean age of diagnosis of ILC is 57 years.[2] Risk factors include age at menarche, age at first birth, and use of hormone therapy, emphasizing the role of estrogen

The authors have nothing to disclose.
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Surg Oncol Clin N Am 27 (2018) 81–94
http://dx.doi.org/10.1016/j.soc.2017.07.005
surgonc.theclinics.com

exposure in pathogenesis. This relationship is also observed for most IDCs, but is more pronounced for ILC.[3] The incidence of ILC in the Western world has generally mirrored trends in use of hormone replacement therapy, with a steep increase between 1975 and 2000 and a decline between 2000 and 2004, but now increasing since 2005 with an unclear cause.[4]

Hereditary ILC is uncommon, but may be seen as a secondary tumor in families with hereditary diffuse gastric cancer syndrome, caused by a germline mutation in the tumor suppressor gene, CDH1. ILC otherwise accounts for a minority of cancers associated with known susceptibility genes, comprising less than 10% of cancers in patients with BRCA2 mutations, and less than 5% of cancers in patients with BRCA1 or TP53 mutations.[5]

HISTOLOGY

Classic ILC is histologically characterized by discohesive cells infiltrating the breast stroma in a single-file pattern[2] with a limited host inflammatory response (**Fig. 1**A).[6] Observed loss of membranous E-cadherin staining by immunohistochemistry may be a useful adjunct to confirm the diagnosis (see **Fig. 1**B). Several nonclassic forms of ILC have also been described, distinguished by morphology (alveolar, solid, dispersed, trabecular, and mixed) and cytology (apocrine, pleomorphic, signet ring, histiocytoid, and tubulolobular).[5] These variant forms show the typical cytologic

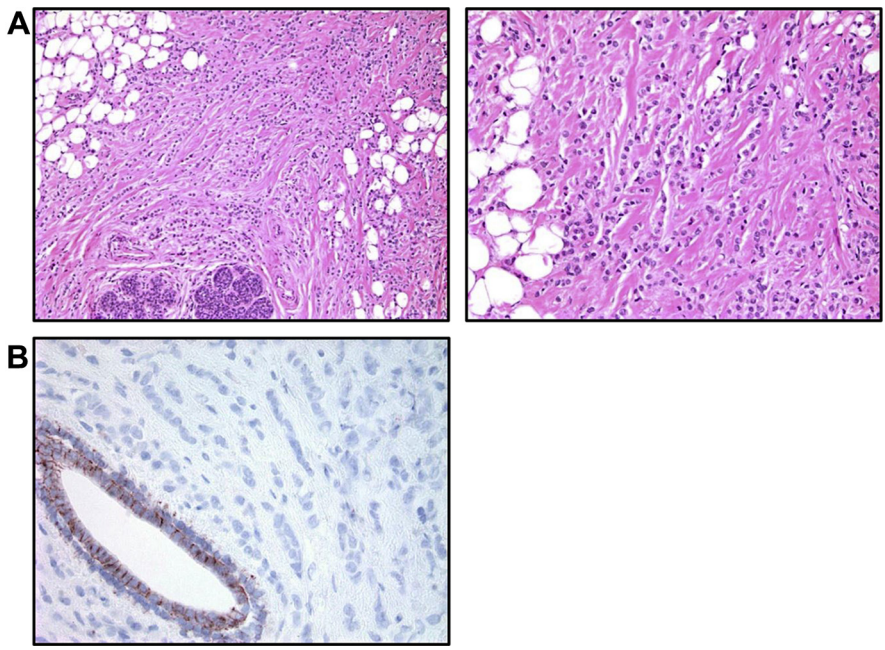

Fig. 1. (*A*) Hematoxylin and eosin staining, 10× and 20× magnifications, depicting the classic "single-file" morphology of ILC. (*B*) Immunohistochemistry of paraffin-embedded breast cancer tissue showing characteristic loss of membranous E-cadherin in lobular carcinoma. (*Courtesy of* Dr Stuart J. Schnitt, MD, Chief of Breast Oncologic Pathology, Dana-Farber/Brigham and Women's Cancer Center; Associate Director, Dana-Farber Cancer Institute/Brigham and Women's Hospital Breast Oncology Program; Professor of Pathology, Harvard Medical School.)