Letters

LCIS variants and DCIS

June 2018—We write in response to the article by Karen Lusky regarding tips to distinguish DCIS from variant forms of LCIS (April 2018). A different question might be: Is it actually important to distinguish these two in situ proliferations?

As a starting point in addressing this issue, let's compare and contrast variant forms of LCIS with classic LCIS.

Classic LCIS (and atypical lobular hyperplasia):

- Several epidemiologic studies document that the age of diagnosis for classic LCIS is 49 years.
- Classic LCIS is an incidental histologic finding.
- Classic LCIS is often multifocal and bilateral.
- The invasive carcinomas that occur following a diagnosis of classic LCIS can occur in either breast and show a variety of histologic subtypes.
- Margins are not assessed for atypical lobular hyperplasia or classic LCIS.
- Classic LCIS and atypical lobular hyperplasia lack E-cadherin expression and show a dyshesive growth pattern.
- Classic LCIS and atypical lobular hyperplasia generally express estrogen receptor.

Variant (pleomorphic) LCIS:

- Pleomorphic LCIS affects older women, generally reported to be 55–60 years of age.
- Pleomorphic LCIS presents as an imaging abnormality: pleomorphic calcifications with or without a mass.
- Pleomorphic LCIS is frequently associated with an invasive component showing similar cytologic features, strongly supporting its role as a precursor lesion. (Tari King, MD, quotes studies that show an associated invasive component in up to 60 percent of cases of pleomorphic LCIS.)

- Surgeons attempt to obtain clear margins when the diagnosis of pleomorphic LCIS is rendered.
- Pleomorphic LCIS lacks E-cadherin expression and shows a dyshesive growth pattern.
- Pleomorphic LCIS may be HER2 over-expressed/amplified.
- Some cases of pleomorphic LCIS do not express estrogen receptor.
- Pleomorphic ALH does not exist.

Now let's compare pleomorphic LCIS with DCIS:

- Same age at diagnosis (i.e. 55–60 years).
- Both usually present as an imaging abnormality: calcifications or mass.
- Excision to negative margins is attempted for both.
- The invasive carcinomas that occur following DCIS affect the same quadrant, supporting a precursor role.
- The invasive carcinomas that occur following pleomorphic LCIS affect the ipsilateral breast, supporting a precursor role.
- HER2 may be over-expressed/amplified in both pleomorphic LCIS and DCIS.

What is the natural history of pleomorphic LCIS? Stuart Schnitt, MD, is correct that there are not "a lot of data." As Sandra Shin, MD, points out, the information that is available is anecdotal. Both Drs. Shin and Schnitt suggest that these in situ proliferations were diagnosed as DCIS before 1996. We expect that is because pathologists relied on morphology (including advanced nuclear atypia, central necrosis, and ductal distortion) as well as the clinical presentation, rather than the use of immunohistochemistry, to diagnose these lesions.

The results of immunohistochemical studies using antibodies to E-cadherin corroborate the morphologic features of a dyshesive growth pattern; this is the only difference between pleomorphic LCIS and DCIS. Does loss of expression of E-cadherin solely define a disease process? Should we ignore the clinical presentation, and the frequently dense disease characteristic of so-called pleomorphic LCIS, which is similar to the features of DCIS? Does the lack of E-cadherin expression obviate the need for radiation therapy?

As Dr. Shin points out, the eighth edition of the AJCC staging manual does not include LCIS. This is because classic LCIS is accepted as an indicator of increased risk of later cancer development, and not a true cancer. The omission of pleomorphic LCIS from the staging manual is surely related to the lack of evidence as to the natural history of this disease. Carefully designed clinical studies with strict pathologic definitions are needed. Until there are data regarding the natural history and treatment that justify the separation of pleomorphic LCIS from DCIS, we will continue to diagnose these lesions as DCIS by their morphologic features, acknowledging their unusual dys-hesive growth pattern.

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predicted by more extensive disease. *Hum Pathol.* 1991;22(12):1232–1239.
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