Portrait of invasive lobular carcinoma of the breast

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According to the most recent SEER cancer statistics review, pure invasive lobular carcinoma (ILC) makes up 8% of histological breast cancer diagnoses, compared to 68% invasive ductal type (IDC) and 14% combined infiltrating (=invasive) ductal and infiltrating (=invasive) lobular carcinoma. During recent years, epidemiologists have described an increasing frequency of ILC, and have related this finding to the use of hormone replacement therapy in postmenopausal women [1].

ILC is characterised by small, round cells that are bland in appearance and have scant cytoplasm, which infiltrate the stroma in single file and surround benign breast tissues in a targeted manner. Infiltration typically does not destroy anatomic structures or incite a substantial connective tissue response. By virtue of their distinctive growth pattern and biology, lobular carcinomas often fail to form distinct masses [2]. The detached pattern of growth in single cell files ("Indian files") is believed to be related to the loss of the cell adhesion molecule E-cadherin. Using immunohistochemistry, E-cadherin is known to be absent in ILC. There is controversy whether ILC should be graded in the same way as IDC, but when grading is given for ILC, it is mostly well (G1) or moderately well (G2) differentiated. ILC has been subclassified histologically into several subtypes: a classic type with linear strands of tumour cells infiltrating the stroma (30–70%), a solid type with large sheets of cells (4–22%), an alveolar type separated by delicate fibrous septa (4–19%), or a mixed type (13–29%). Similarly, a *pleomorphic* type has been described, with a worse prognosis, which is similar to the classic type except that nuclear pleomorphism is considerably accentuated.

The following clinical characteristics in the diagnosis of ILC (compared to IDC) may be related to the histological features described above: localisation of ILC is particularly difficult because its margins are difficult to detect by palpation (clinically as well as intraoperatively) and by imaging. While mammography is often unable to visualise ILC, breast ultrasound and/or breast MRI may be able to show areas of tumour involvement. Given these difficulties with localisation and margin detection, it is not surprising that rates of mastectomy compared to breast-conserving surgery in ILC are slightly higher than for IDC. Despite this, there is general agreement that ILC may be treated by breast-conserving surgery (followed by breast irradiation) provided that clear margins are achieved.

Several large series have compared clinical and pathologic features of ILC to IDC and found essentially similar results [2–5]. Numbers given here are from the largest series by Arpino and colleagues [2]. Median age at diagnosis for ILC is a few years above that for IDC (% above 50 years is 80% for ILC versus 70% for IDC). Tumour size in ILC is somewhat larger than for IDC ($T > 2$ cm: 54% for ILC versus 48% for IDC; >5 cm: 14% for ILC versus 9% for IDC). Hormone receptors (ER and/or PgR) are more often positive in ILC (92%) than in IDC (81%). There is no difference in nodal involvement between ILC and IDC.

While there has long been controversy about the overall prognosis of ILC compared to IDC, more recent series with prolonged follow-up observation have revealed interesting patterns. While in early years prognosis of ILC is somewhat better than for IDC, this trend is reversed in later years: After about 6 years, relapse of ILC catches up with IDC. After about 10 years of follow-up, mortality of ILC catches up with IDC. These trends have been observed in two large series with long follow-up [3,4]. These patterns are seen in both ER-positive as well as ER-negative cancers and are therefore not a mere reflection of the fact that ILC is more often ER-positive than IDC.

Local recurrence and contralateral recurrence of ILC have been found to be increased in several retrospective series, a finding which could not be confirmed in a large series of prospectively observed patients included in 15 adjuvant trials of the International Breast Cancer Study Group (IBCSG) [3]. In any event, it should be stressed that the rates of local recurrence do not justify the routine performance of mastectomy for ILC. Similarly, ILC histology does by

no means justify the performance of a contralateral prophylactic mastectomy. Relapse patterns of distant disease are somewhat different for ILC compared to IDC. ILC recurs more frequently with bone metastases, GI-metastases and meningeal metastases, and less frequently with lung metastases.

In terms of treatment, ILC is not a good candidate for neoadjuvant chemotherapy because pCR-rates are much lower for ILC (3%) than for IDC (15%) [5]. Choices of adjuvant systemic treatments for ILC are based on similar criteria as for IDC. For metastatic ILC, endocrine treatment is the first choice. This is based on its usual ER-positivity, its low-grade histology, as well as its usually prolonged natural history. While overall ILC is HER2-positive in only 8%, the pleomorphic variant is more often HER2-positive (30%) [6]. Such cancers may respond to trastuzumab combinations. When ILC has become resistant to endocrine treatment, palliative chemotherapy may be attempted.

Conflict of interest statement

No conflict of interest to declare.

References

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