Letter

The diagnosis and management of pre-invasive breast disease: another point of view

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I read with interest the series of articles on 'Pre-invasive breast disease' in the September and November issues of *Breast Cancer Research* [1–9]. Although each of the articles is well written, the series raises several issues and in places is contradictory.

Loss of heterozygosity (LOH) has been detected in invasive carcinomas, in ductal carcinoma *in situ* (DCIS), in atypical ductal hyperplasia (ADH) and in atypical lobular hyperplasia/lobular carcinoma *in situ* [10,11]. LOH has also been detected in much lesser frequency in ductal hyperplasia usual type, in normal breast [12] and in gynecomastia [13].

Two mutually contradictory conclusions can be drawn from this data. First, LOH studies indicate a progressive build-up of molecular abnormalities, which in some instances culminate in malignant transformation. Similar frequencies of LOH in ADH and in low-grade DCIS indicate a relationship close enough to justify merger of these entities (suggested by Pinder and Ellis [2]).

The second conclusion is that, since LOH is seen even in normal breast, it has no significance. This conclusion is supported by the distinct keratin profiles of ductal hyperplasia usual type and of ADH/DCIS [14]. Lesions called 'atypical hyperplasia' are either hyperplastic or neoplastic but are not precursory in nature, and the term ADH is best discarded (suggested by van de Vijver and Peterse [5]).

The morphological identification and distinction of ADH from DCIS is problematic to say the least. One can easily agree with van de Vijver and Peterse [5] in questioning the use of the term ADH for lesions that have the morphological features of DCIS but are smaller than 2 mm. Whatever our individual bias may be, it seems clear from the studies initiated by Page and colleagues [15] that there exists a lesion that is a marker of increased risk for breast cancer. This lesion is similar to atypical lobular hyperplasia/lobular carcinoma *in situ* and is distinct from DCIS in that cancers arising in patients with this lesion are not localized to the area of prior abnormality, but can arise anywhere in the same breast or in the contralateral breast. Although some forms of low-grade DCIS, such as micropapillary DCIS, can be multicentric, most DCIS is unicentric and cancers arising in patients with this condition seem to arise at the site of prior lesion. Whatever the molecular resemblance, this biologic behavior should be sufficient to merit the distinction of ADH from DCIS.

I agree that the term ADH is a misnomer as the lesion arises in terminal duct lobular units and not in 'true' ducts [15]. However, ADH still serves an important function of identifying a unique lesion that indicates an increase in risk for breast cancer and indicates that this risk, unlike that associated with DCIS, is bilateral. Combining ADH with low-grade DCIS, on the basis of the limited molecular data currently available, is premature.

Competing interests

None declared.

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ADH = atypical ductal hyperplasia; DCIS = ductal carcinoma *in situ*; LOH = loss of heterozygosity.

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