Atypia and lobular carcinoma in situ: High-risk lesions of the breast

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INTRODUCTION

Benign lesions of the breast are generally categorized into three groups: nonproliferative, proliferative without atypia, and proliferative with atypia. (See "Overview of benign breast diseases".)

Proliferative lesions with atypia include atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), and lobular carcinoma in situ (LCIS). These lesions are considered high risk because they are associated with an increase in the patient's future risk of developing breast cancer [1]. While there is evidence to suggest that these lesions may be nonobligate precursor lesions [2], they are generally managed as risk indicators rather than precursor lesions, as not all patients will develop cancer, and the cancers that do develop subsequently may occur in either breast and not necessarily at the site of the atypia. Therefore, when these high-risk lesions are discovered, the focus should be on careful surveillance and consideration of risk reduction strategies. Flat epithelial atypia (FEA) is also an atypical proliferation, but this lesion does not appear to convey an elevation in risk beyond that of any associated proliferative lesions present.

The diagnosis, pathology, and management of patients with ADH, ALH, LCIS, and FEA will be reviewed here. Ductal carcinoma in situ (DCIS) is discussed elsewhere. (See "Breast ductal carcinoma in situ: Epidemiology, clinical manifestations, and diagnosis" and "Ductal carcinoma in situ: Treatment and prognosis" and "Pathology of breast cancer".)

ATYPICAL HYPERPLASIA

Atypical hyperplasia (AH) includes both atypical ductal hyperplasia (ADH) and atypical lobular hyperplasia (ALH).

Atypical ductal hyperplasia

Diagnosis — ADH is usually diagnosed by core needle biopsy (CNB) as the target lesion on biopsy of mammographic microcalcifications.

Histology — ADH is characterized by a proliferation of uniform epithelial cells with monomorphic round nuclei either filling part, but not all, of the involved duct or completely filling the duct(s) but measuring <2 mm or involving <2 ducts. ADH shares the cytologic and architectural features of low-grade ductal carcinoma in situ (DCIS) but is of limited extent [3].

Management

After core needle biopsy — Following a diagnosis of ADH by CNB, the standard of care is to perform an excisional breast biopsy to exclude the possibility of an associated malignant lesion [4]. Analysis of a larger tissue sample may result in an upgrade to DCIS or invasive breast cancer in 10 to 20 percent of cases depending on the gauge of the needle used at percutaneous biopsy, the number of cores procured, if the targeted microcalcifications are present in the samples, and the presence of residual microcalcifications or an associated mass lesion on imaging studies [5,6]. Several models have been proposed to predict the likelihood of upgrade upon surgical excision; however, their use has not yet been widely adopted [7-10].

Several studies have identified factors associated with a lower risk of upgrade, including no mass lesion, removal of at least 50 percent of the calcifications seen mammographically, no necrosis, and ADH involving only one or two terminal duct lobular units [11,12]. For women with ADH who met these criteria, upgrade rates were only 3 to 5 percent [12-14]. However, criteria vary between centers [14], and prospective validation of these criteria is lacking. Thus, it would be premature to omit surgical excision for ADH on CNB outside of a clinical trial.

After surgical excision — If ADH is diagnosed on an excisional biopsy, no additional surgery is indicated. Re-excision is generally not indicated when ADH is present at the margin. The only exception may be if the ADH is only present at the margin, is bordering on reaching criteria for diagnosis as DCIS at the margin, or there is concern that the imaging target was not completely excised; in these situations, a re-excision merits consideration.

Atypical lobular hyperplasia

Diagnosis — ALH is usually an incidental finding on breast biopsies performed for other reasons (eg, abnormal mammogram, breast mass).

Histology — ALH is characterized by a proliferation of monomorphic, evenly spaced, dyshesive cells filling, but not expanding, the involved lobule. ALH can also involve ducts. ALH shares cytologic and architectural features with lobular carcinoma in situ (LCIS) but is quantitatively lesser in extent [3].

Management

After core needle biopsy — The reported risk of upgrade to DCIS or invasive carcinoma following a diagnosis of incidental ALH on CNB is very low (<3 percent), and any upgrades are usually to very small, low-grade invasive carcinomas [15-17].

Thus, incidental, radiologic-pathologically concordant ALH diagnosed on CNB no longer requires excision, provided excision is not indicated for the targeted lesion. Examples of this scenario include if the radiologic target is a well-circumscribed mass and pathology shows a fibroadenoma with adjacent ALH, or if the radiologic target comprises microcalcifications and the pathology shows calcifications associated with apocrine cysts and adjacent incidental ALH. Localized excisional breast biopsy is recommended for discordant lesions [4].

After surgical excision — If ALH is diagnosed on an excisional biopsy, no additional surgery is indicated. Re-excision is not indicated when ALH is present at the margin.

Future breast cancer risk and its reduction — AH confers a moderate increase in the risk of subsequent breast cancer (relative risk 3 to 5) [18-25]. The magnitude of increase is similar between ADH and ALH, both with a relative risk of approximately 4 compared with patients who do not have atypia [1]. Although some studies have shown that the risk of developing breast cancer is higher with ALH than ADH, the data are conflicting [21,22,26,27].

AH is associated with a generalized, bilateral increase in breast cancer risk [28], although there is a slight preponderance of ipsilateral breast cancers. In a report from the Nurses' Health Study, 56 percent of cancers that developed in women with AH occurred in the ipsilateral breast [22]. The cumulative incidence of breast cancer over 30 years approached 35 percent.

Data on the effect of family history of breast cancer in women with AH are conflicting. Older studies showed that a family history of breast cancer substantially increased the breast cancer risk in women with AH [26,28]. However, several retrospective studies have now found that family history was a risk factor for breast cancer independent of type of benign breast disease found on a breast biopsy (nonproliferative, proliferative, or atypical hyperplasia) and that the presence of atypia did not further increase the breast cancer risk [21,28]. (See "Overview of benign breast diseases".)

Patients with both ADH and ALH should be offered active surveillance and options of chemoprevention. (See 'Strategies of reducing breast cancer risk' below.)

LOBULAR CARCINOMA IN SITU

The term "lobular neoplasia" refers to a spectrum of proliferative changes within the breast lobule that includes both atypical lobular hyperplasia (ALH) and lobular carcinoma in situ (LCIS). Although both lesions are associated with an increased risk of invasive breast cancer, the magnitude of risk associated with LCIS is much greater than with ALH [29]. Because of this difference and the implications for treatment, most experts continue to separate the two entities rather than using the all-encompassing term "lobular neoplasia." ALH has been discussed above. (See 'Atypical lobular hyperplasia' above.)

Epidemiology — LCIS is an uncommon finding, as suggested by autopsy studies [30-33]. The true incidence in the general population is unknown, due to a lack of clinical and mammographic signs. Differences in diagnostic criteria and patient populations undergoing biopsy have led to wide variations in the reported incidence [34-38]. As an example, in one report that included 5000 women undergoing breast biopsies between 1930 and 1972, 3.6 percent of "benign" lesions were LCIS [35]. However, some of the lesions in this series would be classified as ALH by others [34]. In later reports that used stricter diagnostic criteria, LCIS was noted in 0.5 percent of otherwise benign breast biopsies performed for clinical abnormalities [34,38].

A higher prevalence of LCIS (2.3 percent) was noted in a review of 6287 breast biopsies performed because of a mammographic abnormality; LCIS accounted for 9.8 percent of mammographically detected lesions classified as malignancies [39]. Because there are no specific mammographic findings associated with LCIS [40,41], the calcifications that prompted a biopsy may have been associated with benign proliferative processes (eg, adenosis) adjacent to the LCIS, rather than within the lobules involved by LCIS (picture 1) [40].

The mean age at diagnosis is between 44 and 46 years of age, and 80 to 90 percent of cases occur in premenopausal women [34-38,42,43]. While this may be related to the increased number of benign breast abnormalities requiring biopsy in premenopausal women, it is also likely that LCIS is dependent upon hormonal influences; LCIS cells are strongly estrogen receptor (ER) positive [44,45]. Incidence rates in postmenopausal women have steadily increased over the last two decades [46], perhaps due to the widespread use of screening mammography.

Diagnosis — LCIS almost always represents an incidental finding that is diagnosed on a breast biopsy performed for some other reason, such as an area of fibrocystic change or a

fibroadenoma [47]. In most instances, LCIS is not identified clinically, mammographically, or by gross pathologic examination.

Histology — LCIS is a noninvasive lesion that arises from the lobules and the terminal ducts of the breast. The histologic features differ between classic and nonclassic forms of LCIS. This difference is an important one because it impacts management. (See 'Management' below.)

Classic LCIS — Classic LCIS is characterized by a solid proliferation of small cells, with small, uniform, round-to-oval nuclei and variably distinct cell borders (picture 1). The cells typically show cytologic dyshesion. The cytoplasm is clear to lightly eosinophilic; occasionally, the cells contain intracytoplasmic vacuoles that may be large enough to produce signet ring cell forms. Rarely, cases are difficult to classify as either ductal carcinoma in situ (DCIS) or LCIS, as there is some cytologic overlap in the features of low-nuclear-grade DCIS with a solid growth pattern and LCIS.

The cells of LCIS are typically ER positive, rarely show overexpression of human epidermal growth factor receptor 2 (HER2) and have a very low proliferative rate.

LCIS is usually present in the terminal duct lobular units and distends and distorts the involved spaces; the extralobular ducts may also be involved. The growth within these ducts may be either solid or pagetoid (ie, the LCIS cells are insinuated between the duct basement membrane/myoepithelial cells and the native ductal epithelial cells).

Pleomorphic LCIS — Pleomorphic LCIS, originally described in 1996, consists of larger cells that demonstrate marked nuclear pleomorphism [48] but otherwise demonstrate the same characteristics of cytologic dyshesion and intracytoplasmic vacuoles as classic LCIS. Pleomorphic LCIS often demonstrates central necrosis and calcifications, which are otherwise rarely seen with LCIS but are more commonly associated with DCIS [49].

Recognition of the pleomorphic lobular phenotype is critical because the nuclear features, necrosis, and calcifications can make the differentiation from DCIS challenging. Furthermore, pleomorphic LCIS can be associated with an infiltrating pleomorphic lobular carcinoma, in which the infiltrating tumor cells have the same morphologic appearance as the in situ component [50-52].

Florid LCIS — Florid LCIS is characterized by marked distension of the involved ducts and lobules, typically by the cells of classic LCIS, such that the lesion becomes mass forming. Often there is central (or comedo-pattern) necrosis within the involved spaces, which may calcify. Florid LCIS may present as an image-detected mass or as microcalcifications. When diagnosed on core needle biopsy (CNB), excision is indicated [53].

Management

After core needle biopsy — Incidental classic LCIS with radiologic-pathologic concordance and without other high-risk lesions that require excision can be observed with clinical and imaging follow-up based on risk assessment and multidisciplinary input [1,4]. This is consistent with guidelines from the National Comprehensive Cancer Network (NCCN) [54]. Such lesions have very low upgrade rates (<3 percent) [15-17,55].

Surgical excision is recommended for any nonclassic LCIS (ie, pleomorphic LCIS, florid LCIS) diagnosed on CNB or any LCIS with radiologic-pathologic discordance.

After surgical excision — If classic LCIS is diagnosed on an excisional breast biopsy, no further surgery is required. Re-excision is not indicated when **classic** LCIS is present at the margin [35,56,57].

If pleomorphic or florid LCIS is identified on an excisional biopsy, evaluation of the surgical margins for the presence of these nonclassic variants of LCIS is required, and re-excision to negative margins is recommended. There are no data on the optimal width of negative margin or the benefit of radiation therapy for patients with pleomorphic or florid LCIS.

If an invasive carcinoma is detected, appropriate management should be initiated. (See "Overview of the treatment of newly diagnosed, invasive, non-metastatic breast cancer", section on 'Patient stratification'.)

LCIS is detected in association with an invasive carcinoma in approximately 5 percent of malignant breast specimens [58,59]. At least some data suggest that women with an invasive cancer and LCIS in the specimen may have a greater risk of disease recurrence than those without LCIS [58]. However, others have failed to document an increased risk of local recurrence after breast conservation in women with invasive breast cancer and associated LCIS (table 1). Thus, the presence of LCIS in association with an invasive cancer is not a contraindication to breast-conserving therapy, and there is no need to obtain negative margins around LCIS if the margins around the invasive component are negative. The only exception to this general rule is pleomorphic and florid LCIS.

Historically, women with LCIS were once treated with prophylactic bilateral mastectomy. Most experts now consider prophylactic bilateral mastectomy too drastic for the moderate level of risk associated with LCIS in the absence of other contributory risk factors (eg, family history of premenopausal breast cancer) [60,61]. While women with LCIS have a higher risk of developing invasive breast cancer compared with the general population, most will not develop invasive cancer. Because of the paucity of data on this topic and the enormous personal impact of bilateral mastectomy on an individual woman's life, the decision to pursue prophylactic surgery must be highly individualized [60].

Future breast cancer risk and its reduction — The relative risk of developing an invasive cancer in women with LCIS is approximately 7- to 11-fold higher than for women without

LCIS [1,34-37,43,62-65]. The absolute risk is approximately 1 percent per year and appears to be lifelong.

The best available risk estimates are derived from a population-based study of close to 20,000 women diagnosed with LCIS from the Surveillance, Epidemiology, and End Results (SEER) database between 1983 and 2014 in whom the cumulative incidences of subsequent breast malignancy were 11.3 percent (95% CI 10.7 to 11.9 percent) and 19.8 percent (95% CI 18.8 to 20.9 percent) at 10 and 20 years, respectively [66]. The cumulative incidence of a subsequent breast cancer diagnosis increased with increasing age, from 6.9 percent at 10 years in those under 40 to 13.9 percent in those over 70. At a median follow-up of 8.1 years (range 0 to 30.9 years), primary breast cancer was diagnosed in 9.4 percent of the cohort. The majority of the cancers were early stage, of low-to-intermediate histologic grade, and hormone receptor positive. Among the 1837 of them, 42, 20, 13.5, and 21 percent were invasive ductal cancer (IDC), invasive lobular cancer (ILC), mixed ductal and lobular cancer, and DCIS, respectively. IDC distributed equally across both breasts, whereas ILC was more likely to present in the ipsilateral breast (69.0 percent ILC versus 49.2 percent IDC). The 10- and 20-year breast cancer-specific survival for women with LCIS was excellent at 98.9 and 96.3 percent, respectively. On multivariable analysis, type of surgical treatment for LCIS had no effect on long-term survival.

Efforts to identify features of LCIS that are associated with a higher likelihood of developing invasive breast cancer have been unsuccessful [35,58]. In one report, women with both LCIS and a family history of breast cancer had a higher relative risk (RR) of invasive breast cancer than women with LCIS alone (RR 8.5 versus 5.7) [35]. In a reanalysis of these data, a positive family history increased the risk beyond that associated with LCIS alone only for women under the age of 40 at diagnosis of LCIS [67]. Others have found no association between family history and the risk of developing invasive cancer in women with LCIS [34]. A subset of LCIS, the so-called pleomorphic variant, appears to have an aggressive biologic profile, warranting a more aggressive therapeutic approach. (See 'Pleomorphic LCIS' above.)

Patients with LCIS, especially pleomorphic LCIS, should be offered active surveillance and options of chemoprevention [64]. (See 'Strategies of reducing breast cancer risk' below.)

FLAT EPITHELIAL ATYPIA

Flat epithelial atypia (FEA) is part of a group of lesions collectively referred to as columnar cell lesions. FEA has also been referred to as columnar cell change with atypia, columnar cell hyperplasia with atypia, or clinging carcinoma of the monomorphic type.

Diagnosis — FEA is typically diagnosed on core needle biopsies (CNBs) performed for microcalcifications found on screening mammograms [68-71]. FEA is present in <2 percent of

CNB specimens [72].

Histology — In an attempt to standardize the definition and description of these columnar cell lesions, the World Health Organization (WHO) introduced the term FEA, defining it as a "neoplastic alteration of the terminal duct lobular units (TDLUs) characterized by replacement of the native epithelial cells by one to several layers of a single epithelial cell type showing low-grade (monomorphic) cytologic atypia" [53].

Management

After core needle biopsy — Management of FEA identified on a CNB is evolving. While some authors recommend excision for FEA, observation of FEAs is a reasonable option for most patients if there are no other indications for excision [4].

Radiologic surveillance in radiologic-pathologic concordant cases and in the absence of residual mammographic calcifications has been advocated by some based upon retrospective reviews [73-77]. Based upon those studies, the risk of an upgrade to a concurrent malignancy in radiologic-pathologic concordant cases of pure FEA diagnosed on CNB ranges from 0 to 5 percent [77-81]. Incomplete removal of suspicious calcifications by CNB was the only factor associated with underdiagnosis [79]. In one meta-analysis, when >90 percent of the calcifications were removed, the upgrade rate was 0 percent [81]. In any case for which there is concern about sampling error, or mammographic-pathologic discordance (eg, a mammographic mass lesion), an excisional breast biopsy should be performed.

After surgical excision — When diagnosed by an excisional biopsy, no further therapy for FEA is necessary [82-84]. The presence of FEA at the margins of excision is not commented upon, and there is no evidence to suggest that a wider excision to obtain negative margins around FEA is necessary [85].

Future breast cancer risk and its reduction — The clinical significance of FEA is difficult to assess given the multiple names and definitions over the years. Several studies have shown that FEA is often seen in association with low-grade ductal carcinoma in situ (DCIS) or invasive cancer, specifically tubular or lobular carcinoma [68,73,86-93]. In addition, there are several cytologic and genetic similarities between FEA, DCIS, and tubular carcinoma [89,90,94,95]. These observations suggest that FEA represents a nonobligate precursor lesion to low-grade DCIS and tubular carcinoma [68,69,95,96].

Conversely, three studies identified almost 2000 patients with columnar cell lesions (including FEA) from among 6500 women, with an average follow-up of 17 years in the largest study [97-99]. Compared with nonproliferative disease, columnar cell lesions were associated with a mildly increased risk for breast cancer (relative risk 1.47, 95% CI 1.0-2.2), the magnitude of which was similar to that seen with proliferative disease without atypia

[97]. One study found columnar cell lesions not to convey any independent risk beyond that of the associated proliferative disease or atypical hyperplasia (AH) [99].

One study identified 25 patients among 9000 breast biopsies who had FEA on histology [94]. These patients had undergone diagnostic biopsy only, with no attempt at complete excision. One patient (4 percent) had recurrent or persistent FEA, while none developed breast cancer within an average follow-up of 19.2 years.

Among patients in the EORTC 10853 trial, which randomized women with DCIS to excision alone versus excision and radiation therapy, 59 patients were identified who would now be classified as having FEA. With a median follow-up of 5.4 years, none of these patients had a local recurrence or developed a subsequent invasive cancer [100-102].

Women diagnosed with pure FEA on excisional biopsy can be returned to routine surveillance with regular mammograms and breast examinations [80]. The risk of breast cancer associated with FEA is equivalent to that of benign proliferative disease without atypia [97,102]; there are no data to support the use of risk-reducing medications on the basis of FEA. (See "Overview of benign breast diseases", section on 'Proliferative lesions without atypia'.)

STRATEGIES OF REDUCING BREAST CANCER RISK

Women with atypical hyperplasia (AH) or lobular carcinoma in situ (LCIS) should be counseled regarding breast cancer risk reduction strategies. Ongoing surveillance with yearly mammography and twice-yearly breast examinations is appropriate [20,27,103-107]. Such women should stop taking oral contraceptives, avoid hormone replacement therapy, and make appropriate lifestyle and dietary changes. (See "Factors that modify breast cancer risk in women".)

Active surveillance — Breast cancer surveillance is performed for all women known to be at an increased risk of breast cancer (eg, positive family history of breast cancer, AH, or LCIS), as well as those at population risk.

Surveillance must last for the patient's lifetime, or until such time as the patient would not want to undertake treatment for breast cancer if one is found, because the increased risk of breast cancer persists indefinitely. We typically examine high-risk patients at six-month intervals and obtain annual diagnostic mammograms. Guidelines from the National Comprehensive Cancer Network (NCCN) suggest an interval history and physical examination every 6 to 12 months and annual screening mammography [54]. (See "Cancer risks and management of BRCA1/2 carriers without cancer", section on 'Cancer surveillance' and "Screening for breast cancer: Strategies and recommendations".)

Role of breast MRI — Magnetic resonance imaging (MRI) of the breast is more sensitive than mammography in detecting invasive breast cancers in high-risk women, but it is less specific, especially for younger women. A large number of unnecessary biopsies will be generated while finding cancer in only a small group of patients [108]. Despite that, MRI can detect smaller cancers and more node-negative malignancies in high-risk women than other imaging modalities; however, there is no evidence for a reduction in mortality or improved disease-free survival from screening with MRI [109]. (See "MRI of the breast and emerging technologies", section on 'Screening high-risk women'.)

There are insufficient data to support annual screening with MRI for women who are of an average risk, or an intermediate risk, such as those with a biopsy revealing AH or LCIS. A prospective database that included 776 women with LCIS found that women screened with MRI in addition to mammography and clinical breast examinations (n = 455) had the same crude breast cancer detection rate of 13 percent at a median of 58 months of follow-up [110]. MRI was not associated with earlier stage of detection, smaller tumor size, or node negativity.

Consequently, guidelines from major groups, including the American Cancer Society (ACS) and the NCCN, only integrate breast MRI into their recommendations for breast cancer surveillance in high-risk women (ie, an estimated lifetime risk of breast cancer greater than 20 to 25 percent, calculated using BRCAPRO or a similar model based on family history, rather than the Gail model) [54,111]. (See "Screening for breast cancer: Evidence for effectiveness and harms", section on 'Magnetic resonance imaging'.)

Chemoprevention — For patients diagnosed with atypical hyperplasia or LCIS, we suggest endocrine therapy as chemoprevention rather than observation [112]. The purpose is to prevent invasive breast cancer; chemoprevention has not been shown to confer a survival advantage to patients with high-risk lesions. The options for treatment include selective estrogen receptor modulators and aromatase inhibitors. The choice of agents and duration of therapy are discussed separately. (See "Selective estrogen receptor modulators and aromatase inhibitors for breast cancer prevention".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Evaluation of breast problems".)

SUMMARY AND RECOMMENDATIONS

- Benign lesions of the breast are generally categorized into three groups: nonproliferative, proliferative without atypia, and proliferative with atypia. Proliferative lesions with atypia include atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), and lobular carcinoma in situ (LCIS). These lesions are considered high-risk lesions because they are associated with an increase in the patient's future risk of developing breast cancer (approximately fourfold for ADH and ALH and eightfold for LCIS). Flat epithelial atypia (FEA) is less well characterized in terms of a patient's future risk of developing breast cancer (table 2). (See 'Introduction' above.)

- We suggest surgical excision for ADH diagnosed on core needle biopsy (CNB) rather than observation (**Grade 2C**). The upgrade rates are between 10 and 20 percent. (See 'Atypical ductal hyperplasia' above.)

- ALH with radiologic-pathologic concordance, and without other high-risk lesions that require excision, can be observed with clinical and imaging follow-up based on risk assessment and multidisciplinary input. Upgrade rates are <3 percent in this setting. Any case with radiologic-pathology discordance requires surgical excision. (See 'Atypical lobular hyperplasia' above.)

- Classic LCIS with radiologic-pathologic concordance and without other high-risk lesions that require excision can be observed with clinical and imaging follow-up based on risk assessment and multidisciplinary input. Upgrade rates are <5 percent in this setting. (See 'Lobular carcinoma in situ' above.)

- We suggest surgical excision for nonclassic LCIS (eg, pleomorphic LCIS, florid LCIS [LCIS with necrosis]) or LCIS with radiologic-pathologic discordance diagnosed on CNB, rather than observation (**Grade 2C**). Nonclassic LCIS should be excised to negative margins. (See 'Lobular carcinoma in situ' above.)

- Pure FEA diagnosed on CNB with radiologic-pathologic concordance and without residual microcalcifications of concern may be managed with clinical and imaging follow-up. Any radiologic-pathologic discordance requires surgical excision. (See 'Flat epithelial atypia' above.)

- Patients diagnosed with atypical hyperplasia or LCIS are at increased risk of developing breast cancer compared with the general population, and risk reduction strategies should be discussed with all patients:

    - Lifelong active breast cancer surveillance is required for patients with atypical hyperplasia or LCIS. We perform clinical breast evaluations every six months and mammography annually. Although annual screening magnetic resonance imaging (MRI) cannot be justified by a high-risk breast lesion per se, screening breast MRI is appropriate for those with atypical hyperplasia or LCIS **and** a ≥20 to 25 percent

lifetime risk of developing breast cancer calculated using BRCAPRO or a similar model based on family history, rather than the Gail model. (See 'Active surveillance' above and "Screening for breast cancer: Strategies and recommendations" and "MRI of the breast and emerging technologies", section on 'Screening high-risk women'.)

- For patients diagnosed with atypical hyperplasia or LCIS, we suggest endocrine therapy as chemoprevention rather than observation (**Grade 2B**). The choice of agents and duration of therapy are discussed separately. (See 'Chemoprevention' above and "Selective estrogen receptor modulators and aromatase inhibitors for breast cancer prevention".)

- Patients diagnosed with FEA alone can be returned to routine surveillance with regular mammograms and breast examinations. The risk of breast cancer associated with FEA is equivalent to that of benign proliferative disease without atypia, which does not warrant chemoprevention.

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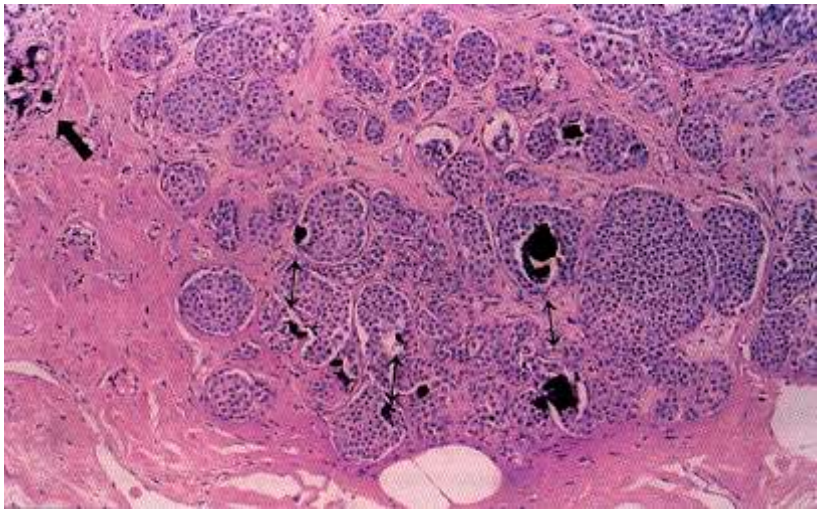
Topic 743 Version 34.0

GRAPHICS

Lobular carcinoma in situ of the breast



High-power photomicrograph of a hematoxylin and eosin-stained section of a breast biopsy specimen from a 43-year-old woman showing classic calcifications (double-headed arrows) in an area of lobular carcinoma in situ, and similar-appearing calcifications (single arrow) in an adjacent focus of adenosis.

From: Georgian-Smith D, Lawton TJ. Calcifications of lobular carcinoma in situ of the breast: Radiologic-pathologic correlation. AJR Am J Roentgenol 2001; 176:1255. Reprinted with permission from: the American Journal of Roentgenology.

Graphic 67947 Version 13.0

LCIS as a risk factor for local recurrence in women treated with breast-conserving therapy for early breast cancer

Study, year	Number of patients with LCIS within the specimen	Number of control patients	Median follow-up (months)	Risk of local failure, percent	
				+LCIS	–LCIS
Sasson AR; 2001	65	1209	76	5	3
				(5 years, NSS)	
				29	6
				(10 years, p = 0.003)	
Jolly S; 2006	56	551	104	14	7
				(10 years, p = 0.04)	
Moran M; 1998	51	1045	127	23	16
				(NSS)	
Abner AL; 2000	137	1062	161	13	12
				(NSS)	
Ben-David M; 2006	64	121*	45	1.7	1.6
				(NSS)	

LCIS: lobular carcinoma in situ; NSS: not statistically significant.

* Matched for histology, stage, age, and date of diagnosis.

Graphic 72607 Version 3.0

High-risk breast lesions and management

	Diagnosis	Management after core needle biopsy[1]	Upgrade rate with excision	Management of margins after excision	Relative risk for invasive cancer
Atypical ductal hyperplasia (ADH)	Found on biopsy performed for microcalcifications on screening mammogram	Surgical excision for most patients	10 to 20% [2]	No re-excision for margins	3.1 to 4.7[2]
Atypical lobular hyperplasia (ALH)	Incidental finding on biopsy performed for other reasons	Surgical excision for discordance or presence of other high-risk lesion Observation for other lesions	<3% for concordant, small-volume disease[2]	No re-excision for margins	3.1 to 5.9[2]
Lobular carcinoma in situ (LCIS)	Incidental finding on biopsy performed for other reasons	Surgical excision for non-classic features (pleomorphic, comedo necrosis, signet ring, or apocrine), or for discordance Observation for concordant classic LCIS	<5% for concordant, small-volume disease[2]	Re-excision to negative margins for pleomorphic LCIS No re-excision for margins for classic LCIS	6.9 to 11[2]
Flat epithelial atypia (FEA)	Found on biopsy performed for microcalcifications on screening mammogram	Surgical excision for discordance or FEA associated with residual microcalcification Observation for concordant pure FEA	0 to 3.2% for pure FEA[2]	No re-excision for margins	1.47[3]

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Contributor Disclosures

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