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Surgical Biopsy Findings in Patients with Atypical Hyperplasia Diagnosed by Stereotaxic Core Needle Biopsy

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Purpose: To correlate the stereotaxic core needle biopsy results with those of surgical biopsy in patients with atypical lobular or ductal hyperplasia (atypical hyperplasia) diagnosed at stereotaxic core needle biopsy (SCNB).

Methods: We retrospectively reviewed the mammograms and pathology reports of 358 consecutive SCNBs performed in 323 patients. The results of SCNBs of 22 lesions reported as atypical hyperplasia were correlated with histologic findings at surgical biopsy.

Results: A histologic diagnosis of atypical hyperplasia at SCNB was found to be a poor predictor of the final surgical results. In the 19 patients with 22 lesions, surgical biopsy and SCNB results were in disagreement in 16, partial agreement in two, and complete agreement in only four lesions. Furthermore, five cases of atypical hyperplasia were shown to have invasive carcinoma on open biopsy, and five had ductal carcinoma in situ in the surgical biopsy, none of which was present on SCNB.

Conclusion: Given the frequent occurrence of malignancy in patients diagnosed with atypical hyperplasia by SCNB, it is recommended that all such patients undergo excisional biopsy.

Key Words: Stereotaxic breast biopsy—Atypical hyperplasia.

Stereotaxic large core needle biopsy (SCNB) is now widely accepted as a reliable method of providing a histologic diagnosis for mammographically detected suspicious and indeterminate breast lesions (1,2). Its role in the diagnosis and management of breast cancer is better established than in borderline conditions such as atypical ductal and lobular hyperplasia. The number of atypical hyperplasia cases reported in SCNB is relatively small, and there is little correlation with surgical or long-term mammographic follow-up. Results to date suggest that when surgical correlation is available, there is poor agreement between an SCNB diagnosis of atypical hyperplasia and surgery results (3–5).

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Women with atypical hyperplasia found in open breast biopsy carry a greater risk for subsequent development of breast cancer than does the general population, a risk that doubles for women with a family history of breast cancer (6–9). Atypical hyperplasia is not only a risk marker for future cancer development, but is also in fact found adjacent to 51% of breast carcinomas (10). Because of the uncertainties associated with a diagnosis of atypical hyperplasia and its association with malignant lesions, we decided to review our cases and compare the histologic results obtained from core biopsy with those obtained at surgical excision.

MATERIALS AND METHODS

We undertook a retrospective review of the radiographs and histologic specimens of 358 consecutive SCNBs performed in 323 patients between June 1992 and October 1994. All patients with a SCNB diagnosis of atypical hyperplasia were identified. The number of cores obtained by SCNB and the diagnosis per core were correlated with the surgical biopsy diagnosis. SCNB was performed on the Stereoguide

stereotaxic prone table (Lorad, Danbury, CT, USA) equipped with digital spot imaging and according to technique previously described by Parker et al. (1). Tissue samples were obtained with a 14-gauge Biopty-Cut needle (Bard Urological, Covington, GA, USA) and a long-throw (2.3-cm excursion) Biopty gun (Bard Urological). Depending on the size and appearance of the lesion and our degree of confidence in targeting, a range of five to 14 cores (mean = 6) were obtained per lesion. Further to evaluate the accuracy of targeting lesions with calcifications, radiographs of the individual cores were obtained after placing them on a Telfa pad to document the presence of calcifications. Additional samples were obtained if deemed necessary after reviewing the specimen radiograph. The specimens were subsequently placed in separate numbered containers of 10% neutral buffered formalin and submitted to pathologic examination. Histologic analysis was performed by the same pathologist at our institution, and the results were reported for each core separately.

The following criteria for ductal carcinoma in situ (DCIS) were used: proliferation of a single population of large abnormal cells with myoepithelial and apocrine cells not involved; possession of large, centrally placed, atypical nuclei; the regular location of cells and their nuclei; regular lumens in a solid, cribriform papillary, or micropapillary pattern; and in addition, necrosis may be present. The criteria for atypical ductal hyperplasia (ADH) are similar to those described by Page et al. (11–14): "ADH is diagnosed when some features of DCIS are present, but others are lacking." In addition, Tavassoli and Norris (15) added the stipulation that intraductal carcinoma occupied ducts with a cross-sectional diameter that, in aggregate, measured ≥2 mm. By their criteria, a proliferation with the appearance of intraductal carcinoma that was found in only a small duct that measured <2 mm in diameter would not qualify for the diagnosis of DCIS but would be considered ADH. Page et al. (13) also stipulated that more than one duct must be occupied by DCIS. These quantitative criteria may play a larger role in stereotaxic needle biopsies than they do in the larger specimens obtained by open biopsies. In this series, there was only a single case in which size alone was the discriminating factor between DCIS and ADH.

All mammograms were classified and scored before SCNB according to the American College of Radiology Bi-RADS (breast imaging reporting data system) in categories 1 to 5 as follows: 1, negative; 2, benign finding; 3, probably benign finding; 4, suspicious abnormality; 5, highly suggestive of malignancy (16). Only lesions classified ≥3 were considered for SCNB.

The pathology score was constructed, taking into account the specific type of benign diagnosis, as well as the adequacy of the tissue sample. The following pathology categories were created: category 1, benign specific diagnosis, including sclerosing adenosis, fibroadenoma; category 2, benign nonspecific, fibrocystic; category 3, borderline, atypical ductal hyperplasia, atypical lobular hyperplasia, and lobular carcinoma in situ; category 4, DCIS; category 5, infiltrating carcinoma.

Surgical biopsy was recommended for all lesions in pathology categories 3 to 5 and for those in category 2 (benign nonspecific lesions) with a mammographic score of 4 or 5. Surgical biopsy was also performed when SCNB failed to obtain a sufficient sample for lesions with calcifications when no calcifications were identified in the specimen radiograph and on core histology. Thus all lesions diagnosed as atypical hyperplasia by SCNB were recommended for surgical excision. The remaining benign lesions were followed up at 6- to 12-month intervals.

A diagnosis of atypical hyperplasia on SCNB was considered to be in complete disagreement with the surgical biopsy whenever the excised specimen contained a lesion other than ADH, or atypical lobular hyperplasia, or if, in addition to ADH and atypical lobular hyperplasia, the surgical specimen contained other histologic characteristics that changed patient care. This included cases in which a surgical diagnosis of DCIS or infiltrating ductal carcinoma or both were obtained. Partial agreement was recorded if in addition to atypical hyperplasia, other specific lesions not affecting patient management were present in the surgical specimen, such as sclerosing adenosis and radial scar. Agreement implied the presence of similar histologic characteristics at SCNB and surgical biopsy.

Of the total of 358 lesions, 270 (75.7%) were reported as benign, 62 (17%) were malignant, 25 (6%) cases were seen to have atypical hyperplasia, and 1 (0.3%) lesion had insufficient material for diagnosis. Radiographically, 161 (45%) were described as a mass with or without calcifications, 126 (35%) as calcifications alone, 60 (17%) as asymmetric densities, and 11 (3%) as architectural distortion with or without calcifications.

A diagnosis of atypical hyperplasia was made at SCNB in 25 lesions on 22 patients. Twenty lesions

TABLE 1. *Correlation between SCNB and surgical biopsy histology results*

SCNB	Total	Surgical biopsy				
		AH alone	AH + benign	Benign; no AH	AH + DCIS/LCIS	AH IC
AH alone	16	2	2	3	6[a]	3
AH + benign	3	0	1	1	1	0
AH + DCIS/LCIS	3	0	0	0	1	2
Total	22	2	3	4	8	5

AH, atypical hyperplasia; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; IC, invasive carcinoma; SCNB, stereotaxic core needle biopsy.
[a]Two LCIS.

were described as ADH, and five, as atypical lobular hyperplasia. Surgical correlation was available for 22 lesions in 19 patients, (18 ADH and four atypical lobular hyperplasia), which are the subjects of this study.

RESULTS

Of the 22 lesions with atypical hyperplasia, biopsies were performed of three because of the presence of a mass (16 due to calcifications, one because of a mass associated with calcifications, and two because of architectural distortion and calcifications). Thus 19 of 22 lesions were noted to have calcifications on the mammogram with calcifications confirmed in 18 at histologic analysis of the SCNB specimen.

Of the twenty-two lesions diagnosed as atypical hyperplasia on SCNB, 16 of them were reported as having atypical hyperplasia alone (Table 1). On follow-up excisional biopsy, only two were noted to have atypical hyperplasia alone; two had atypical hyperplasia in association with other benign pathologic conditions (sclerosing adenosis and radial scar); in three, open biopsy revealed benign pathologic characteristics with no atypical hyperplasia found; two lesions had diffuse lobular carcinoma in situ (lobular carcinoma in situ) with atypical hyperplasia; four lesions had DCIS in association with the atypical hyperplasia; and three had invasive carcinoma adjacent to the atypical hyperplasia, for a total of nine complete disagreements, five partial agreements, and two complete agreements. In the three patients reported as having atypical hyperplasia associated with other benign pathologic conditions on SCNB, one was found to be in complete agreement, one was found to have benign pathologic characteristics on open biopsy but no atypical hyperplasia, and one had DCIS in association with atypical hyperplasia (one disagreement, two agreements). None of the three had invasive carcinoma. At SCNB, three lesions were noted to have atypical hyperplasia in association with some elements of DCIS. At surgery, one of these lesions showed DCIS and atypical hyperplasia, and two were read as having invasive carcinoma (two disagreements, one agreement) (Tables 1 and 2).

Therefore, in the 22 SCNBs, there were eight agreements, two partial agreements, and 12 disagreements. At surgical excision, eight of the 22 lesions contained carcinoma in situ (six DCIS and two lobular carcinoma in situ), and another five were noted to have infiltrating carcinoma. In two of these infiltrating carcinomas, SCNB had obtained atypical hyperplasia with some elements of DCIS, and in three cases, it revealed atypical hyperplasia alone.

DISCUSSION

SCNB is rapidly gaining acceptance among referring physicians, radiologists, and patients as an alternative technique to obtain histologic samples of non-

TABLE 2. *Agreement between SCNB and surgical biopsy*

SCNB	Total	Complete agreement	Partial agreement	Complete disagreement
AH alone	16	3	2	9
AH + benign	3	2	0	1
AH + DCIS	3	1	0	2
Total	22	8	2	12

AH, atypical hyperplasia; DCIS, ductal carcinoma in situ; SCNB, stereotaxic core needle biopsy.

palpable breast lesions. Guidelines to standardize the technique have been adopted and are being followed in several recently reported studies, as well as in ongoing multiinstitutional trials (1–3). However, the lack of surgical correlation or sufficiently long follow-up of many borderline lesions has prevented the development of firm guidelines for care of patients with borderline lesions, such as atypical hyperplasia (2,17). The number of cases of atypical hyperplasia reported in SCNB series is relatively small, but a pattern of poor correlation between the SCNB results and those at surgical biopsy is emerging, prompting us to review our own experience (3–5).

Atypical hyperplasia is a borderline lesion with some but not all of the morphologic features of in situ carcinoma. The ability to diagnose this entity is highly dependent on sample size. The limited sample size of SCNBs makes it likely that this diagnosis will be made in cases of DCIS that are of low or intermediate grade.

Atypical hyperplasia has been identified as a risk factor for the subsequent development of invasive breast carcinoma (6–9). The risk appears magnified by the coexistence of sclerosing adenosis (15), microcalcifications (7), or a family history of breast cancer (8). It is still unclear whether atypical hyperplasia is a necessary precursor of breast cancer or simply a risk marker because invasive carcinoma may develop in either breast of a patient with atypical hyperplasia or in its absence. Only 30% of low-nuclear-grade DCIS progresses to invasive cancer.

The true incidence of atypical hyperplasia in biopsy specimens or in autopsy studies is difficult to assess because there has been a lack of standardization of the description and classification of benign proliferative breast lesions. Page et al. (11–14) have proposed a definition for atypical hyperplasia, but unfortunately, the criteria are not widely accepted or routinely adhered to. Several studies have documented significant interobserver variability among expert breast pathologists (18,19), even when agreed-on criteria are used (19). Similar difficulties in differentiating atypical hyperplasia from DCIS are reflected in a recent report of a multi institutional SCNB study, in which a category of "mammary intraepithelial neoplasia" was created to include low-grade DCIS, lobular carcinoma in situ, ADH, and atypical lobular hyperplasia as carrying similar connotations for purposes of histologic correlation and patient care (2).

The reported incidence of atypical hyperplasia also varies depending on the population being studied and the sampling technique used. Because the criteria for patient selection to undergo SCNB are similar to those for surgical biopsy, one should anticipate a comparable frequency of atypical hyperplasia in SCNB and surgical specimens. However, this has not been the case. Whereas the frequency of atypical hyperplasia in surgical biopsies performed for mammographic findings is 24%, atypical hyperplasia is present in 31% of biopsies of microcalcifications and in 40% of lesions with calcifications and adenosis (20). In comparison, the reported frequencies of atypical hyperplasia in recent SCNB series vary from 4% of all SCNBs (3) to 20% of SCNBs performed for microcalcifications (4).

In our own series, atypical hyperplasia was found in 6% of all SCNBs; in patients with microcalcifications, the incidence of atypical hyperplasia increased to 15%. The higher numbers of atypical hyperplasia obtained from surgical biopsies could be attributed to the larger volume of tissue sampled, and because the cores obtained by stereotaxic biopsy were not representative of the entire lesion.

Atypical hyperplasia is usually located within or in close proximity to other benign abnormalities, the closest correlation occurring with microcalcifications (21). However, in as many as one third of cases reported by Helvie et al. (21) and Stomper et al. (20), the atypical hyperplasia was found distant from the mammographic abnormality that prompted the excisional biopsy.

Our study showed very poor agreement between SCNB diagnosis of atypical hyperplasia and final surgical results. There were five lesions with invasive carcinomas and five with DCIS that were discovered only at surgical excision. For these 10 patients, the additional information obtained at surgery led to a change in management, usually an additional surgical procedure for wider excision or axillary lymph node dissection or both. Another patient with atypical hyperplasia diagnosed by SCNB was found to have diffuse lobular carcinoma in situ at surgical biopsy; she elected bilateral prophylactic mastectomy, although the recommended treatment of atypical hyperplasia and lobular carcinoma in situ is the same. Four other patients diagnosed as having atypical hyperplasia were found to have only benign calcifications at surgical excision. Whether the nidus of atypical hyperplasia was completely removed at SCNB or missed at surgery cannot be answered. Conceivably, these four patients may not have required surgery or may still have atypical hyperpla-

sia. Two other patients had atypical hyperplasia bordering on DCIS at SCNB; surgery revealed invasive carcinoma, requiring that the patients undergo an additional surgical procedure for axillary node dissection.

A similar poor correlation was noted by Jackman et al. (3); they found discordance of the results between SCNB and surgery in 11 of 16 cases with an SCNB diagnosis of atypical hyperplasia. Surgical excision discovered six patients with DCIS, three with infiltrating ductal carcinoma, and two cases without atypical hyperplasia. Liberman et al. (4) found eight and three infiltrating DCIS surgical specimens in 21 patients with atypical hyperplasia diagnosed by SCNB. Results from other series are difficult to evaluate because of differences in histologic criteria and incomplete surgical correlation.

A number of reasons may contribute to the poor correlation between SCNB and surgical biopsy in atypical hyperplasia. Interobserver variability among pathologists could lead to discrepancies in reporting atypical hyperplasia when the biopsies are interpreted at different institutions or by different pathologists (18,19); however, all biopsies in our study were interpreted by the same pathologist.

The number of cores obtained per lesion may not have been sufficient or representative enough of the mammographic abnormality. In the experience of Jackman et al. (3), the addition of core samples beyond the minimum five resulted in a decrease in the number of atypical hyperplasia lesions and in the disagreement found at surgical biopsy. A minimum of five cores was set as our guideline, and we obtained as many as 14 samples when a lesion was suspected or when calcifications were abundant.

Inaccuracy of targeting could be a factor; however, we corroborated accuracy by obtaining pre- and postfiring images and by obtaining specimen radiographs of the core samples in lesions with calcifications. All but one of the 19 cases of microcalcifications showed calcifications on histologic examination, and repeated samples were obtained in the case with missing calcifications. In addition, at surgical excision, the pathologist was able to recognize the needle track and organizing hematoma at the site of the SCNB in a number of cases. Thus it is unlikely that accuracy of targeting would account for the discrepancies.

The radial pattern of sampling could explain the disagreements in some of the lesions, particularly those with DCIS. By convention, the basic five samples were taken from the center of the lesion, and following a clock pattern, at 12, 3, 6, and 9 o'clock, thus favoring sampling of the periphery versus the core of the lesion. The observations by Stomper et al. (20) and Helvie et al. (21) indicate that at least one third of the atypical hyperplasias are somehow removed from the mammographic lesion that prompted the biopsy. More important, Lennington et al. (22) found that when atypical hyperplasia was associated with DCIS, the atypical hyperplasia was characteristically located in the periphery of the lesion, and the most severe atypia was adjacent to the centrally located DCIS. The authors recommended wide surgical excision in severe atypical hyperplasia to uncover a possible coexisting noncomedo DCIS.

SCNB is not an optimal technique for establishing a diagnosis of atypical hyperplasia, which is highly dependent on complete evaluation of several large sections of breast tissue with a surface area of 150 to 200 times that of a needle core.

CONCLUSION

When a diagnosis of atypical hyperplasia is made at SCNB, one should be aware that disagreement between stereotaxic core needle biopsy results and surgical biopsy results is likely. Although modifying the pattern of SCNB sampling and the number of cores obtained may decrease disagreements, ultimately all patients with atypical hyperplasia at SCNB should undergo wide-excision surgical biopsy and close mammographic surveillance thereafter because of the increased risk of present association and subsequent development of DCIS and invasive carcinoma.

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