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Original article

Atypical ductal hyperplasia: Our experience in the management and long term clinical follow-up in 71 patients

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ABSTRACT

Introduction: Atypical ductal hyperplasia (ADH) is a high-risk benign lesion found in approximately 1–10% of breast biopsies and associated with a variable incidence of carcinoma after surgical excision. The main goal of our study is to present our experience in the management and long-term follow-up of 71 patients with ADH diagnosed on breast biopsy.

Materials and methods: Results of 3808 breast biopsy specimens from 1 January 2000 to 31 December 2005 were analyzed to identify all biopsies which resulted in a diagnosis of ADH.
The histopathological results of the 45 patients who underwent surgery were analyzed. Long-term follow-up for the remaining patients was carried out.

Results: 45 of 71 (63.4%) patients with histological diagnosis of ADH on breast biopsy underwent surgery. Definitive histological results revealed invasive carcinoma in 7 cases (15.6%), high grade Ductal Carcinoma in situ (DCIS) in 10 (22.2%) patients, Lobular Carcinoma in situ (LCIS) in 4 cases (8.9%) and benign findings in 24 cases (53.3%). 12 of 71 (16.9%) patients underwent only long term follow-up; one (8,3%) of these developed invasive breast carcinoma after 6 years.

Conclusion: Atypical ductal hyperplasia diagnosed on breast biopsy is associated with a relatively high incidence of invasive carcinoma and high grade ductal carcinoma in situ at the time of surgical excision. Certain radiological and cytological criteria can be used to help determine which patients should forgo surgery and be followed up with good results.
Long term follow-up is always crucial for patients who have not undergone surgery.

1. Introduction

Atypical ductal hyperplasia (ADH) is a high-risk benign lesion first described in 1941 by Foote et al. [1], that is found in approximately 1–10% of breast biopsies [2–4]. Many studies in literature show that ADH is associated with a variable incidence of invasive carcinoma and high grade ductal carcinoma in situ diagnosed histopathologically on surgical excision [5–8].

Atypical ductal hyperplasia (ADH) can be defined as a borderline group of lesions having some histological features of carcinoma in situ but not sufficient alteration in cell morphology to support an unequivocal diagnosis of carcinoma in situ [5,9]. Briefly ADH is an intraductal proliferation of monomorphic epithelial cells with histological and cytological features resembling those seen in low grade ductal carcinoma in situ. However, the atypical proliferation in ADH is either admixed with a second population of proliferative cells without atypia, or completely involves the terminal ductal lobular unit(s) to a limited extent.

No single qualitative feature reproducibly distinguishes ADH from low-grade DCIS, as both are part of the same morphologic spectrum and closely related at the molecular level. Lesion size provides a quantitative criterion to distinguish ADH from low-grade DCIS, and involvement of 2 separate ducts or size > 2 mm have been proposed as arbitrary cutoff points.

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Abbreviations

ADH	Atypical ductal hyperplasia
DCIS	Ductal Carcinoma in situ
LCIS	Lobular Carcinoma in situ
VABB	Vacuum Assisted Breast Biopsy
US	Ultrasound
MX	Mammography
SADH	Simple Atypical Ductal Hyperplasia
ACH	Atypical Columnar Hyperplasia
G	Gauge

Lesion extent, such as > 2 mm span and involvement of ≥ 2 separate basement membrane bound spaces (ie, ducts) are quantitative criteria proposed in the past for DCIS [10].

On the basis of microscopic appearance and grade of atypia two types of atypical hyperplasia are described: simple atypical ductal hyperplasia (SADH) and atypical columnar hyperplasia (ACH) the latter being characterized by a higher degree of atypia [6,11,12].

Both SADH and ACH represent a marker of increased risk for breast cancer and a possible precursor of malignancy. The management of patients with ADH is not well defined, in spite of the multiple works which demonstrate that ADH confers a relative risk for the development of breast cancer [3,5,13–16].

The aim of our study is to present our experience in the management and long-term follow-up (10 years) of 71 patients with ADH diagnosed on breast biopsy, while attempting to define the correct therapeutic management of patients with ADH: estimating the risk of women with atypia is crucial for risk-benefit analysis and decision making regarding risk-reduction strategies, especially when considering that current evidence on the management of these type of patients is scarce.

2. Materials and methods

Institutional review board approval was obtained and patient informed consent was waived.

Results of 3808 breast biopsy specimens from 1 January 2000 to 31 December 2005 were analyzed to identify all biopsies, which resulted in a diagnosis of ADH: the histopathological results of all cases were reviewed and comparison was made with histological results following surgical excision of the same lesions in patients who underwent surgery.

The mammograms based on which the 3808 biopsies were taken were performed either for screening purposes or in patients with a past history of breast cancer or who were at increased risk of developing breast cancer due to a strong family history.

All biopsies were performed under ultrasound (US) or stereotactic guidance. Biopsy specimens were sent in containers with formalin and subsequently embedded in paraffin.

ADH was identified in 71 cases of 3808 biopsies performed. 66/71 biopsies were performed under stereotactic guidance and 5/71 under ultrasound guidance.

Women with a diagnosis of ADH on biopsy underwent immediate excision if the lesion was classified as BI-RADS 4 or 5, in cases of patients with BRCA1 and/or BRCA2 mutation and in those with a family history or past history of breast cancer. Furthermore we suggested surgery in presence of amorphous, coarse, heterogenous calcifications and fine linear or branching calcifications that are associated with a higher risk of tumour development. The presence of residual disease after biopsy was also considered as conferring an increased risk for progression to tumour development [10]. In keeping with recent recommendations found in the literature, age was not considered a major risk factor for which patients should undergo surgery [17].

The presence of a high percentage of atypia, multiple foci of hyperplasia and flat lesion detected at cytology were suggested as risk factors by the pathologist. Evidence of microscopic calcification were always reported in the pathologist's report.

Long-term follow-up for 10 years was the choice for other patients. The follow-up consisted of 1 digital mammography and 1 breast ultrasound per year.

2.1. Stereotactic vacuum-assisted biopsy

Stereotactic vacuum-assisted breast biopsy (VABB) was performed using a prone biopsy table and 11 gauge (G) biopsy device. All VABB procedures were performed under local anesthesia. Craniocaudal and mediolateral mammograms were taken before targeting the lesion. Following appropriate prone positioning, the scout view and stereotactic paired images were used for accurate needle placement using the x-y-z coordinates determined by the machine. If the calculations showed that the procedure was possible, a local anesthetic (2% prilocaine hydrochloride with no adrenaline) was administered and the needle was inserted into the breast. Further pre- and post-fire stereo images were obtained. Depending on the needle-lesion relation in these post fire images, the position of the lesion relative to the needle was determined, and unlike the conventional technique, tissue retrieval was predominantly performed from that location, followed by a complete 360° rotation if needed. In this way, the lesion was better targeted and less biopsy specimens were required. Specimen radiographs were acquired in all lesions. Our aim was total excision for lesions smaller than 1 cm. After the procedure, a radiopaque marker was placed if the lesion seen at mammography was completely or almost completely removed or if a large area was sampled and documentation of the precise site of biopsy was desired. Post-clip mammograms were then taken to ensure accurate clip deployment.

The median duration of the procedure was 27.5 min (range, 20–40 min). It became shorter as our experience increased, and our modified biopsy method allowed us to finish the procedure in a short period of time. The actual specimen retrieval time was around or under half a minute. The procedure was very well tolerated by almost all patients. Later, ice compression was locally applied, and patients were advised to apply intermittent ice compression during the rest of the day. Specimens that contained calcifications were determined from the specimen radiograph and those with and with-out calcifications were sent in two separate labeled formalin containers for pathologic examination.

2.2. Ultrasound guided biopsy

Core needle biopsies under ultrasound guidance were performed with an 8 G or 11G automated needle or a 14 G Tru Cut needle with a 22-mm throw. Four or five core specimens were obtained for each core biopsy.

3. Results

Of 3808 breast biopsies, 73 cases with a diagnosis of ADH were detected. 2 cases were excluded from this study due to the presence of ipsilateral carcinoma at the time of biopsy leaving a total of 71 ADH cases to be included in this study. Of these, 48 (67.6%) cases were represented by simple atypical ductal hyperplasia (SADH): 44 identified with stereotactic vacuum-assisted biopsy and 4 with