

Outcomes of ADH after Vacuum-Assisted Biopsy: Comparison Between Mass vs Microcalcifications

Myoung Kyoung Kim, Eun Young Ko, Eun Sook Ko, Boo-Kyung Han

Department of Radiology and Center for Imaging Science, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Background: The purpose of this study was to evaluate the outcomes of atypical ductal hyperplasia (ADH) on vacuum-assisted breast biopsy (VAB), and compare the results according to the lesion types; mass or microcalcifications.

Materials and Methods: A retrospective study was performed in 31 women (mean age, 45.7 ± 8.8 years) who underwent subsequent surgery for ADH diagnosed via VAB for imaging abnormalities observed on mammography and ultrasound. The imaging findings, histopathologic diagnosis of all VAB and surgical specimens, and association of malignancy with residual lesions were evaluated.

Results: Among 31 women (mean age: 45.7 ± 8.8 years) with histologically confirmed pure ADH, mammography revealed microcalcifications in 26 cases, while ultrasound detected masses in 5 cases. Subsequent surgical excision after VAB was conducted in 21 cases, resulting in 4 cases being upgraded to ductal carcinoma in situ (DCIS). Notably, all cases upgraded to DCIS exhibited residual microcalcifications on mammography after VAB. Conversely, lesions without residual microcalcifications remained as ADH. Masses detected on ultrasound in five cases were removed via VAB without evidence of residual lesion on images, and follow-up ultrasound over 2 years showed negative results.

Conclusion: In conclusion, follow up US is enough for ADH diagnosed after US-guided VAB removal for the mass without calcifications. ADH diagnosed after VAB for suspicious microcalcifications needs further surgical excision especially when there is residual calcification.

Index words: Atypical Ductal Hyperplasia (ADH), Vacuum-Assisted Breast Biopsy (VAB), Lesion Types: Mass, Microcalcifications

Correspondence to: Eun Young Ko, MD, PhD
Department of Radiology and Center for Imaging
Science Samsung Medical Center, Sungkyunkwan
University School of Medicine 81, Irwon-ro,
Gangnam-gu, Seoul 06351, Korea
Tel: 82-2-3410-6418, Fax: 82-2-3410-0084
e-mail: claudel@skku.edu

Introduction

Atypical ductal hyperplasia (ADH) is a premalignant breast lesion that defined as a ductal hyperplastic lesion with cellular atypia and

structural rigidity suggesting ductal carcinoma in situ (DCIS), involving only one duct profile or an area less than 2 mm in diameter (1). There seems to be a high incidence of discordance in diagnosis of ADH between surgical results and core needle biopsy (CNB). Therefore, the diagnosis of ADH after percutaneous needle biopsy is an indication for surgical excision to exclude the possibility of associated DCIS or invasive ductal carcinoma, so far (2,3).

Recent advancements in needle biopsy techniques, including the transition from 14- to 11-gauge needles and the incorporation of vacuum assistance, have facilitated the extraction of larger tissue samples. Historically, before the early 2000s, the standard practice following a diagnosis of ADH through micro-histology was surgical excision due to a high underestimation rate. However, the adoption of larger needles has significantly reduced underestimation rates, providing a basis for considering conservative management in selected cases (4-9). Despite this progress, there is an ongoing debate regarding the optimal approach for treating ADH lesions. The question arises whether all cases should undergo surgical intervention or if, in certain instances, follow-up after the removal of a radiographically identified lesion through vacuum-assisted biopsy (VAB) is a viable alternative (10,11).

The purpose of this study was to evaluate the outcomes of ADH after VAB in our institution and to compare the results based on the types of lesions observed in the images

Materials and Methods

We conducted a retrospective review of the pathological results from VAB cases conducted between February 2015 and December 2021, and selected the cases diagnosed with pure ADH as a result of VAB. We excluded the cases with mixed histology of ADH and other benign lesions, or the cases with focal ADH, or the cases with ADH

versus ductal carcinoma in situ (DCIS).

Patient age, lesion type on images, biopsy method (US-VAB, or stereotactic-VAB [S-VAB]), histological results, and subsequent surgical pathologic results were reviewed. All patients had both mammography and breast US before VAB. All mammograms were obtained with dedicated equipment (Senographe 2000D or 2000DS, GE Medical Systems, Milwaukee, WI, USA; Selenia Dimensions, Hologic Inc., Bedford, MA, USA). Standard cranio-caudal and mediolateral oblique views were routinely obtained, and additional magnification views were obtained as needed. Breast US examinations were performed using an IU22 machine with a 12-5 MHz linear array transducer (Philips Advanced Technology Laboratories, Bothell, WA, USA) or an Aixplorer machine with a 15-4 MHz linear array transducer (SuperSonic Imagine, Aix en Provence, France). Two radiologists who had 2 and 22 years of experience in breast imaging, retrospectively evaluated the mammography and US findings and categorized the lesion types as mammographic calcifications (without a distinct sonographic mass) and mass(es) on US, Breast Imaging Reporting and Data System (BI-RADS) final assessment category of the biopsied lesions from category 3 to 5, presence of residual lesion on follow-up mammography and US after VAB.

All image-guided biopsies were performed by one of 4 radiologists with 1-26 years of breast imaging experience. US-guided VAB was performed using an 8-11G probe (Mammotome, Devicor Endo-Surgery, Cincinnati, OH, USA; Suros, Hologic Inc. Bedford, MA, USA). S-VAB was performed for microcalcification with an 11G vacuum-assisted probe (Mammotome, Devicor Endo-Surgery, Cincinnati, OH, USA) using the stereotactic unit of a prone table (Lorad, Hologic Inc., Danbury, CT, USA).

We evaluated the results of subsequent surgical excision after VAB, and compared the clinical and radiological characteristics between the groups

with upgrade to carcinoma and the groups without upgrade. A univariable analysis was performed to compare the variables for predictors of pathologic upgrade, and variables with p-values less than 0.05 according to a univariable analysis were included in the multivariable analysis. A p-value less than 0.05 was regarded as statistically significant. The data analyses were conducted using the SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

There were 31 patients with histologic confirmation of pure ADH via VAB and the mean age was 45.7 ± 8.8 years. In 31 cases with histologic confirmed pure ADH, 26 cases were microcalcifications seen on mammography without definite mass on US, and 5 cases were masses seen on US. After VAB, 21 cases underwent surgical excision for the residual lesion or VAB site without residual lesion, and 10 cases underwent imaging follow up without subsequent surgery. In 21 cases with further surgical excision after VAB, four lesions (19%) were upgraded to DCIS. Table 1 summarized

Table 1. Comparison of Surgery group Results of Atypical Hyperplasia Diagnosed with VAB (n=21)

	Upgrade group (n=4) No. (%)	Non-upgrade group (n=17) No. (%)
Lesion type		
Calcifications	4 (100)	17 (100)
Mass	0	0
BI-RADS category		
3	0 (0.0)	2 (11.8)
4A	0 (0.0)	9 (53.0)
4B	2 (50.0)	3 (17.6)
4C	2 (50.0)	3 (17.6)
Presence of residual lesion		
Yes	4 (100.0)	13 (76.5)
No	0 (0.0)	4 (23.5)

BI-RADS, Breast Imaging Reporting and Data System; VAB, vacuum-assisted biopsy.

the comparison of surgery group with upgrade and non-upgrade to DCIS. In 10 cases without further surgery, follow up images for more than two years showed negative findings or no changes (Table 2).

All cases which were upgraded to DCIS after subsequent surgery showed lesion type of microcalcifications on mammography and all of them had residual microcalcifications after VAB (Fig. 1). BI-RADS category was 4B in 2 cases, and 4C in 2 cases. Among the 21 lesions with residual microcalcifications after VAB, 29% (2/7) BI-RADS 4B, 40% (2/5) BI-RADS 4C lesions were upgraded as DCIS after surgical excision. Among the 5 lesions without residual microcalcifications after VAB, all of them were remained ADH only (Fig. 2). Five cases of mass on US were all BI-RADS 3 lesions and removed using VAB without residual. Further excision was not performed, but follow-up US more than 2 years showed negative findings (Fig. 3).

In table 3, the univariable and multivariable analyses for the pathologic upgrade of atypical ductal hyperplasia to malignancy are presented. Except for extent of the lesion, there were no significant variables associated with upgrade of ADH.

Table 2. Comparison of Follow-up Group of Atypical Hyperplasia Diagnosed with VAB (n=10)

	Microcalcifications (n=5) No. (%)	Mass (n=5) No. (%)
BI-RADS category		
3	1 (20.0)	5 (100.0)
4A	2 (40.0)	0 (0.0)
4B	2 (40.0)	0 (0.0)
4C	0 (0.0)	0 (0.0)
Presence of residual lesion		
Yes	4 (80.0)	0 (0.0)
No	1 (20.0)	5 (23.5)

BI-RADS, Breast Imaging Reporting and Data System; VAB, vacuum-assisted biopsy.

Table 3. Univariable and Multivariable Analysis of Lesion for Pathologic Upgrade of Atypical Ductal Hyperplasia (n = 31)

Variable	Univariable		Multivariable	
	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
Age	1.04 (0.91-1.19)	0.58		
Extent (≥ 5 cm)	1.12 (1.01-1.24)	0.04	1.12 (1.01-1.24)	0.04
Lesion type				
calcifications	1			
mass	0.45 (0.00-5.40)	0.64		
BI-RADS		0.27		
3	1			
4A	0.74 (0.00-143.31)	0.27		
4B	7.73 (0.50-NA)	0.24		
4C	12.14 (0.74-NA)	0.11		
BI-RADS		0.40		
3	1			
4	3.92 (0.35-541.86)			
Biopsy type				
S-VAB	1			
US-VAB	1.25 (0.15-10.23)	0.84		
Presence of residual lesion				
No	1			
Yes	6.27 (0.58-862.07)	0.25		

BI-RADS, Breast Imaging Reporting and Data System; S-VAB, stereotactic vacuum-assisted biopsy, US-VAB, ultrasound guided vacuum-assisted biopsy.

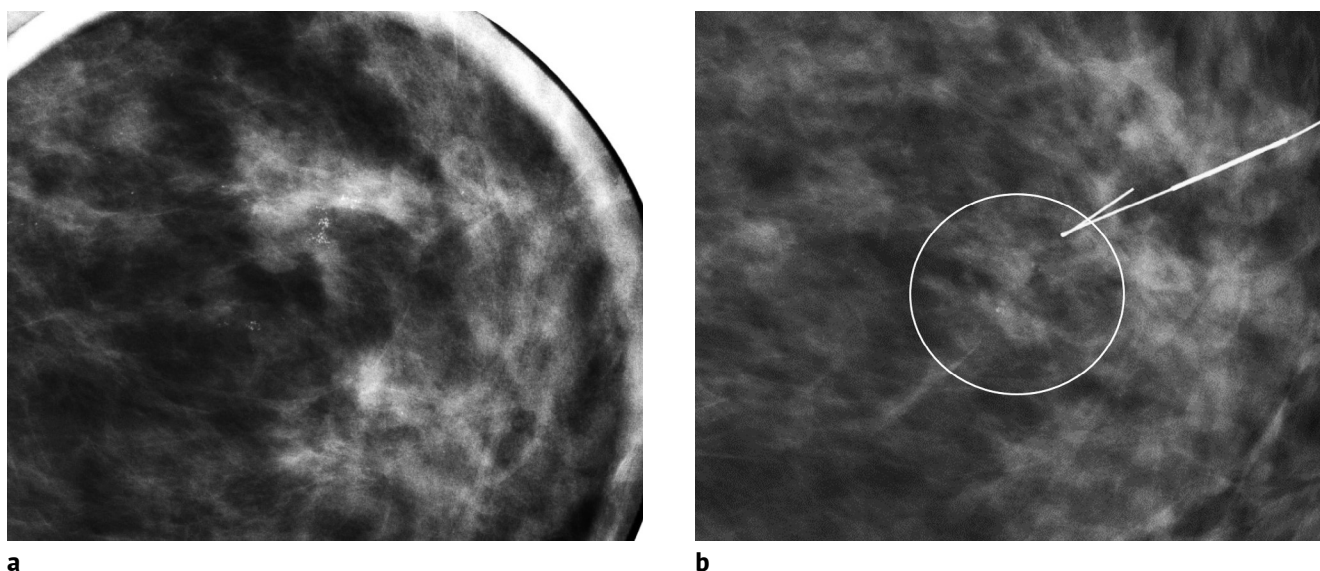


Fig. 1. A 51-year-old woman with ductal carcinoma in situ. (a) Magnification view of mediolateral mammography image shows grouped fine pleomorphic microcalcifications. This lesion was assessed as BI-RADS category 4B. Stereotactic-guided vacuum assisted biopsy with 11-gauge needle yielded diagnosis of atypical ductal hyperplasia. (b) Mediolateral mammography after 3 months shows residual microcalcifications (circle). Mammography-guided wire localization and excisional biopsy was performed. Final pathologic examination after surgical excision confirmed low grade ductal carcinoma in situ, micropapillary and flat type (4.5x3x1.6 cm).

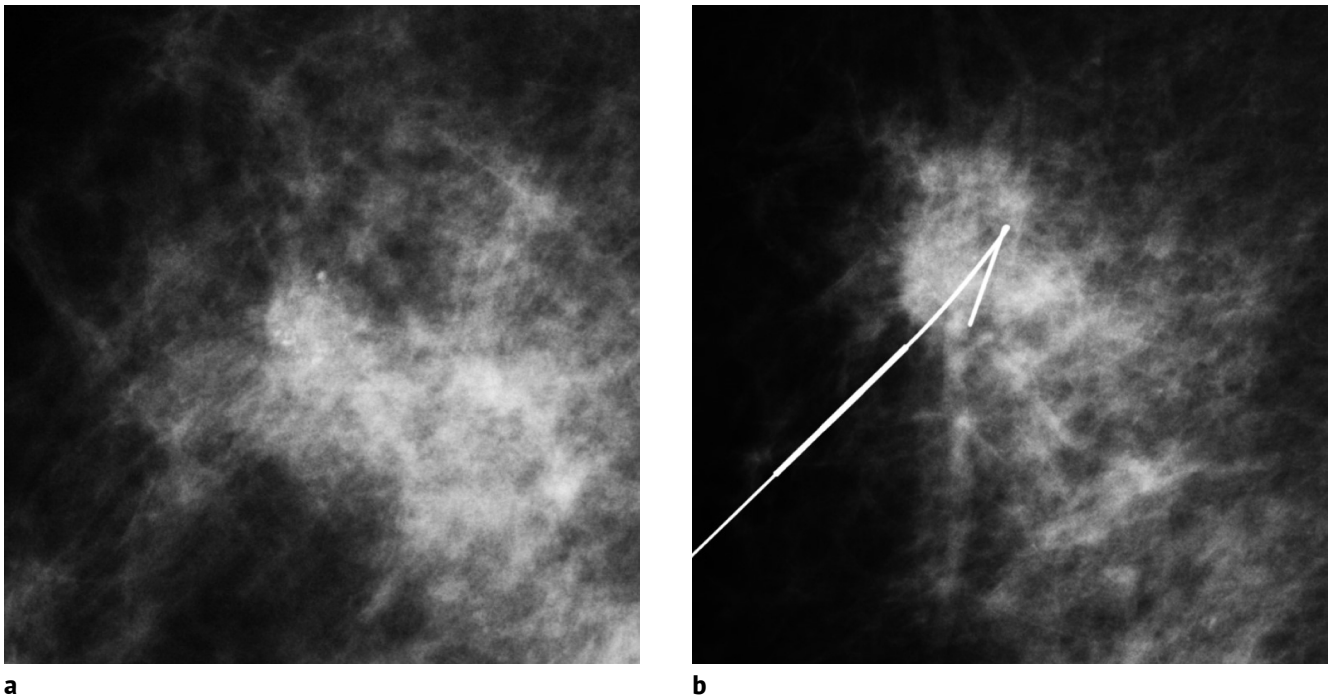


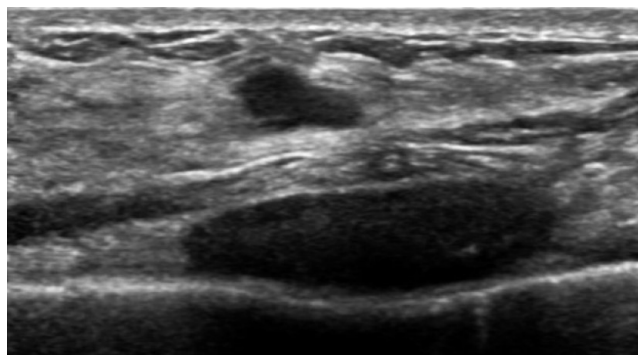
Fig. 2. A 58-year-old woman with atypical ductal hyperplasia. (a) Magnification view of mediolateral mammography image shows grouped amorphous microcalcifications. This lesion was assessed as BI-RADS category 4A. Stereotactic-guided vacuum assisted biopsy with 11-gauge needle yielded diagnosis of atypical ductal hyperplasia. (b) Mediolateral mammography after ultrasound-guided wire localization for the biopsy site shows no residual microcalcifications. Final pathologic examination after surgical excision confirmed as residual atypical ductal hyperplasia.

Discussion

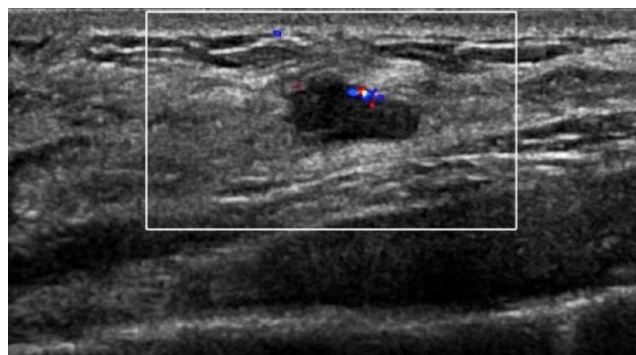
ADH has been reported in 2–11% of abnormal mammographic findings and is currently considered a high-risk lesion because invasive cancer or DCIS is discovered in approximately 19% of cases when additional tissue is removed (7). Therefore, after a diagnosis of ADH on stereotactic biopsy, surgical excision was recommended. Several studies indicate that removal of all calcifications result in lower underestimation rate of ADH with VAB (12,13). Also, Villa et al. (14) suggested that patients with a diagnosis of ADH after 11-gauge vacuum-assisted breast biopsy without residual microcalcifications which can duplicate an underestimation rate less than 2% could possibly be managed conservatively with 6 months mammographic follow-up and then with annual mammographic follow-up. However, there are still debates regarding the necessity of

further surgery after the diagnosis of ADH via percutaneous biopsy. Some studies suggest that patients with no residual calcifications on post-VAB mammograms require subsequent surgery because of the possibility of underestimation (8,15).

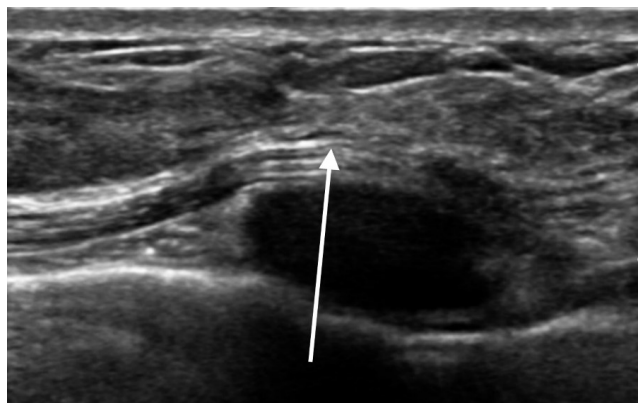
In our data, all four (19%, 4/21) upgraded cases showed lesion type of calcifications without definite mass and had residual microcalcifications after VAB. However, there were 13 non-upgraded cases (76.5%, 13/17) in subsequent surgery, that also had residual microcalcifications on the images. Also, all the mass-type lesions in US without microcalcifications that were removed via US-guided VAB had no evidence of residual mass and the follow up result was also negative or no change. All the BI-RADS 3 lesions did not show residual lesions regardless of their lesion type and did not upgrade to DCIS. However, the lesion type or presence of residual lesion were not statistically significant for pathologic



a



b



c

Fig. 3. A 26-year-old woman with atypical ductal hyperplasia. (a) Screening ultrasound image (US) shows a relatively circumscribed hypoechoic mass. (b) Doppler US shows slightly increased vascularity along the peripheral margin of the mass. This lesion was assessed as BI-RADS category 3. US-guided vacuum assisted biopsy (VAB) for the removal of the mass with 8-gauge needle yielded diagnosis of atypical ductal hyperplasia. After VAB, she followed up with US without further surgical excision. (c) Follow-up US after 26 months of VAB, there was no evidence of recurrent lesion at the VAB site (arrow).

upgrade of ADH. All upgrade cases (100%) had higher BI-RADS assessment category of 4B or 4C, whereas six (22.2%) of non-upgrade cases had BI-RADS category 4B or 4C. However, BI-RADS category also showed no statistical significance for pathologic upgrade of ADH. We consider that the negative statistical results were probably due to the small number of total case number and small number of positive cases in our study. We added Firth correction in the statistical analysis to overcome this problem, however, there were still difficulties in estimation. The only statistically significant parameter was the extent of the lesion. Using a 5 cm cut-off determined by Youden's index, we observed 1.12-fold increase in the likelihood of ADH upgrades.

Our study has several limitations. First, this is a retrospective study and ten ADH patients did not undergo additional surgery. Even though we had follow-up images for more than 2 years, ADH can

show very slow changes to reach overt malignancy. Second, as the samples were only from patients with pure ADH on VAB, the sample size is small. We selected "pure ADH" because we thought other benign lesions co-existing with ADH cannot represent the imaging findings of ADH. Another is that in our study, the cases predominantly exhibit lesions appearing as calcifications on mammography, with a limited number showing masses on ultrasound. This bias indicates a skewed distribution of lesion types towards calcifications. Studies with more cases with more balanced population are needed to derive more meaningful results. Although there are some problems, we conclude that follow up US is enough for ADH diagnosed after US-guided VAB for removal of mass without calcifications. ADH diagnosed after VAB for suspicious microcalcifications needs further surgical excision especially when the lesion is 5 cm or more and when there is residual calcification

after VAB.

References

1. Tavassoli FA, Norris HJ. A comparison of the results of long-term follow-up for atypical intraductal hyperplasia and intraductal hyperplasia of the breast. *Cancer* 1990;65:518-529.
2. Sewell CW. Pathology of high-risk breast lesions and ductal carcinoma in situ. *Radiol Clin North Am* 2004;42:821-830.
3. Berg WA. Image-guided breast biopsy and management of high-risk lesions. *Radiol Clin North Am* 2004;42:935-946.
4. Burak WE, Jr, Owens KE, Tighe MB, Kemp L, Dinges SA, Hitchcock CL, et al. Vacuum-assisted stereotactic breast biopsy: histologic underestimation of malignant lesions. *Arch Surg* 2000;135:700-703.
5. Cangiarella J, Waisman J, Symmans WF, Gross J, Cohen JM, Wu H, et al. Mammotome core biopsy for mammary microcalcification: analysis of 160 biopsies from 142 women with surgical and radiologic followup. *Cancer* 2001;91:173-177.
6. Darling ML, Smith DN, Lester SC, Kaelin C, Selland DL, Denison CM, et al. Atypical ductal hyperplasia and ductal carcinoma in situ as revealed by large-core needle breast biopsy: results of surgical excision. *AJR Am J Roentgenol* 2000;175:1341-1346.
7. Jackman RJ, Birdwell RL, Ikeda DM. Atypical ductal hyperplasia: can some lesions be defined as probably benign after stereotactic 11-gauge vacuum-assisted biopsy, eliminating the recommendation for surgical excision? *Radiology* 2002;224:548-554.
8. Winchester DJ, Bernstein JR, Jeske JM, Nicholson MH, Hahn EA, Goldschmidt RA, et al. Upstaging of atypical ductal hyperplasia after vacuum-assisted 11-gauge stereotactic core needle biopsy. *Arch Surg* 2003;138:619-622; discussion 622-623.
9. Zhao L, Freimanis R, Bergman S, Shen P, Perrier ND, Lesko N, et al. Biopsy needle technique and the accuracy of diagnosis of atypical ductal hyperplasia for mammographic abnormalities. *Am Surg* 2003;69:757-762; discussion 762.
10. Putti TC, Pinder SE, Elston CW, Lee AH, Ellis IO. Breast pathology practice: most common problems in a consultation service. *Histopathology* 2005;7:445-457.
11. Rageth CJ, O'Flynn EA, Comstock C, Kurtz C, Kubik R, Madjar H, et al. First International Consensus Conference on lesions of uncertain malignant potential in the breast (B3 lesions). *Breast Cancer Res Treat* 2016;159:203-213.
12. Liberman L, Smolkin JH, Dershaw DD, Morris EA, Abramson AF, Rosen PP. Calcification retrieval at stereotactic, 11-gauge, directional, vacuum-assisted breast biopsy. *Radiology* 1998;208:251-260.
13. Philpotts LE, Lee CH, Horvath LJ, Lange RC, Carter D, Tocino I. Underestimation of breast cancer with 11-gauge vacuum suction biopsy. *AJR Am J Roentgenol* 2000;175:1047-1050.
14. Villa A, Tagliafico A, Chiesa F, Chiaramondia M, Friedman D, Calabrese M. Atypical ductal hyperplasia diagnosed at 11-gauge vacuum-assisted breast biopsy performed on suspicious clustered microcalcifications: could patients without residual microcalcifications be managed conservatively? *AJR Am J Roentgenol* 2011;197:1012-1018.
15. Arora S, Moezzi M, Kim U, Menes TS. Is surgical excision necessary for atypical ductal hyperplasia diagnosed with 8 gauge stereotactic biopsy? *Breast J* 2009;15:673-674.

진공 보조 생검 후 비정형관상피증식증의 결과 비교: 종괴 대 석회화 병변

김명경 · 고은영 · 고은숙 · 한부경

성균관의대 삼성서울병원 영상의학과

배경: 저자들은 진공 보조 유방 생검(VAB)에서 비정형관상피증식증(ADH)으로 진단된 병변들에 대해 병변의 유형에 따른 결과를 비교하고자 하였다.

방법: 영상 소견 이상으로 내원하여 VAB를 통해 ADH로 진단된 31명의 여성(평균 연령: 45.7±8.8세)을 대상으로 영상 소견과 조직검사 결과, 수술 결과, 및 잔여 병변의 악성 여부를 비교하였다.

결과: ADH로 진단된 환자들은 유방촬영술에서 보이는 미세석회화 병변으로 발견된 경우가 26례, 초음파에서 보이는 종괴로 발견된 경우가 5례였다. VAB후 수술적 절제를 진행한 경우는 21례로 그 중 4례에서 관상피내암(DCIS)으로 진단이 상향되었다. 특히 DCIS로 상향 조정된 모든 사례들은 VAB 이후에 잔여 미세석회화 병변이 남아있는 경우였고, 반대로 잔여 석회화가 없거나 초음파에서 발견된 종괴를 모두 제거했던 5례는 추가적인 수술이나 2년 이상의 추적검사에서 잔여 ADH나 음성 결과를 보였다.

결론: 석회화가 없는 종괴에 대해 초음파 유도하 VAB로 종괴를 모두 제거하여 ADH로 진단된 경우에는 추적 초음파만으로 충분하다. 의심스러운 석회화 병변에 대해 VAB 후 ADH가 진단된 경우에는 특히 잔여 석회화가 남아있는 경우 추가적인 수술적 절제가 필요하다.

Index words: Atypical Ductal Hyperplasia (ADH); Vacuum-Assisted Breast Biopsy (VAB);
Lesion Types: Mass; Microcalcifications

Corresponding author: Eun Young Ko, M.D., Ph.D.