Case Report

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대한영상의학회지

Radiologic and Pathologic Findings of Atypical Ductal Hyperplasia in the Male Breast: Case Report and Literature Review

남성 유방에서의 비정형유관증식증의 영상 및 병리 소견에 대한 고찰: 증례 보고 및 문헌고찰

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In this case report, we present the radiologic and pathologic findings of atypical ductal hyperplasia (ADH) in the male breast. It is well known that a high-risk lesion such as ADH is a precursor of breast cancer in females. However, the clinical significance of these lesions in the male breast is still uncertain because male breasts mainly consist of ducts without lobule formation, unlike the female breast. To our knowledge, imaging findings of ADH in the male breast have not been reported previously, except for a few studies on the pathologic findings of these lesions. Through this paper, we would like to present the possible imaging features of this high-risk lesion in the male breast and review the related literature.

Index terms Breast Neoplasms; Clinical Decision-Making; Diagnostic Techniques and Procedures; Male; Precancerous Conditions

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INTRODUCTION

Atypical ductal hyperplasia (ADH) is a proliferative type of intra-ductal breast lesion that shares some characteristics with the low-grade ductal carcinoma in situ (DCIS) (1). High-risk lesions such as the flat epithelial atypia (FEA) and ADH have been identified as precursors of cancer in the female breast (1). However, the male breast mainly com-

prises of ducts without the lobule formation, in contrast to the female breast. Therefore, many clinicians have hypothesized that the pattern of carcinogenesis may differ between the male and female breasts (2). To date, there is no consensus in the literature regarding the existence of high risk lesions in the male breasts (3-5). Although a few studies have reported the pathologic findings of these high-risk lesions in the male breast (3-7), there were no reports in the literature regarding their imaging findings. In this report, we present the radiologic and pathologic findings of ADH in the male breast.

CASE REPORT

A 34-year-old man visited the breast outpatient clinic of our institution with a palpable subareolar mass in the left breast that had been detected 1 month earlier. A physical examination revealed a tender mass measuring approximately 2 cm in the left subareolar area. The patient had a history of kidney transplantation due to an end-stage renal disease 1 year earlier and was receiving tacrolimus as an immunosuppressant agent since then. He had a 3-year history of hypertension that was being medically treated with dilatrend. He had no history of any other medications. The physical examination revealed no other clinical symptoms or signs, and there was no history of chest wall trauma. Mammography (MMG) and breast ultrasonography (US) were performed for further evaluation.

MMG revealed flame-shaped areas of increased density in both the subareolar areas that extended into the posterior tissue with a peripheral tapering configuration. However, the left breast exhibited greater asymmetric density, and a dense nodule with an approximate size of 2.5 cm was noted. No calcifications or associated findings were observed in either breast (Fig. 1A).

US revealed an ill-defined hypoechoic area without an increase in the vascularity in the right subareolar area, which was suggestive of gynecomastia. The left breast contained a similarly hypoechoic subareolar area that was accompanied by an oval, partly indistinct isoechoic mass measuring 2.7 cm × 3.0 cm, at the 6 o'clock subareolar position. Color Doppler imaging revealed peripheral and intra-nodular branching vascularity. Associated architectural distortion or ductal changes were not visible within the mass (Fig. 1B). The lesion met the criteria for low suspicion for malignancy (4a) of Breast Imaging Reporting and Data system (BI-RADS) category due to its indistinct margins; therefore we recommended a core needle biopsy.

A US-guided core needle biopsy of the mass was performed using a 14-gauge needle. The biopsy was performed 5 times, and the mass was subsequently maintained (Fig. 1C).

Pathologic analysis of the biopsy revealed an FEA with an expression of the estrogen receptor (ER) and a loss of cytokeratin (CK) 5/6. Microscopic examination revealed terminal ductal lobular units (TDLUs) that had been replaced by several layers of epithelial cells that lacked polarity. A high-power field view showed several cellular tufts or mounds (Fig. 1D). Subsequently, the breast surgeon performed a local mass excision. The excised mass was finally confirmed as an ADH. The surgical specimen measured 3.5 cm × 2.2 cm and was composed primarily of a solid yellowish material. Microscopic examination revealed features of gynecomastia, with duct profiles scattered within a fibrous stroma. However, several ducts exhibited a rigid cribriform proliferation of uniform epithelial cells with bridges or micro-papillary

formation (Fig. 1E).

DISCUSSION

Male breast cancer is rare; accounting for approximately 1% of all breast cancers (8). These lesions resemble hormone receptor-positive postmenopausal female breast cancer but tend to be more aggressive on presentation (3). Although male and female breasts are identical at birth, during the peripubertal period the antagonistic effects of the androgens result in the differences in their appearance. Ultimately, fat contributes to the majority of the volume in the male breast, together with the involuted ducts and stroma (8). The male breast contains ducts, whereas the female breast contains TDLUs (3). The presence and role of the high risk lesions in the male breast remains unclear. Several conflicting results have been reported regarding these lesions in the male breast (3-5). Verschuur-Maes et al. (4) insisted that no con-

Fig. 1. A 34-year-old male with ADH.
A. Mammography reveals flame-shaped areas of increased density in both the subareolar areas. In the left breast, an obscured nodular density measuring approximately 2.5 cm was noted (arrows).
B. Ultrasonography shows a small amount of glandular tissue in the right subareolar area (upper images) with no increase in the vascularity on color Doppler imaging. In the left subareolar area (lower images), a partly indistinct hypoechoic mass measuring 2.7 cm × 3.0 cm is observed at the 6 o'clock position (arrowheads). Color Doppler imaging reveals an increased peripheral and intra-nodular vascularity associated with the mass.
C. No changes in the size and shape of the left breast mass are observed after the core needle biopsy.
ADH = atypical ductal hyperplasia, LCC = left craniocaudal view, LMLO = left mediolateral oblique view, RCC = right craniocaudal view, RMLO = right mediolateral oblique view

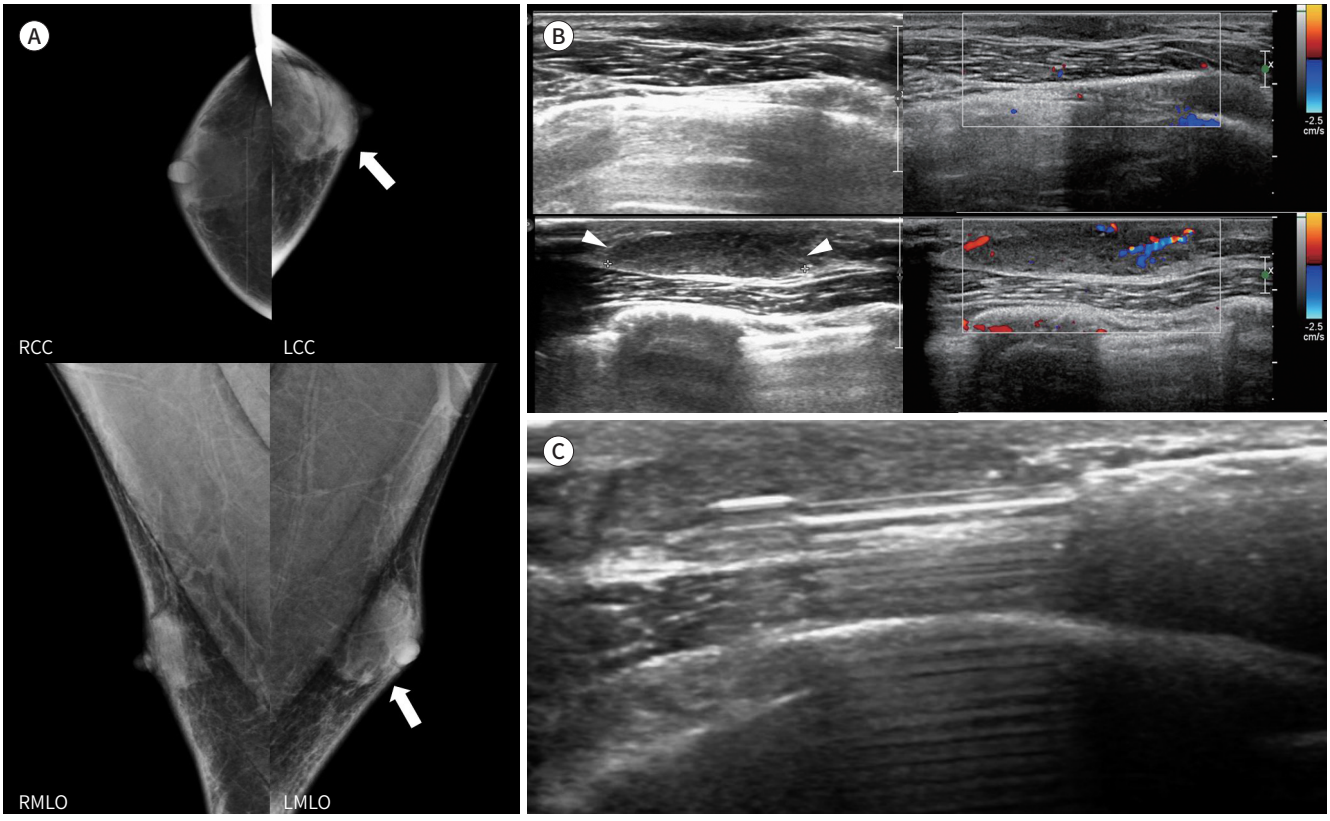
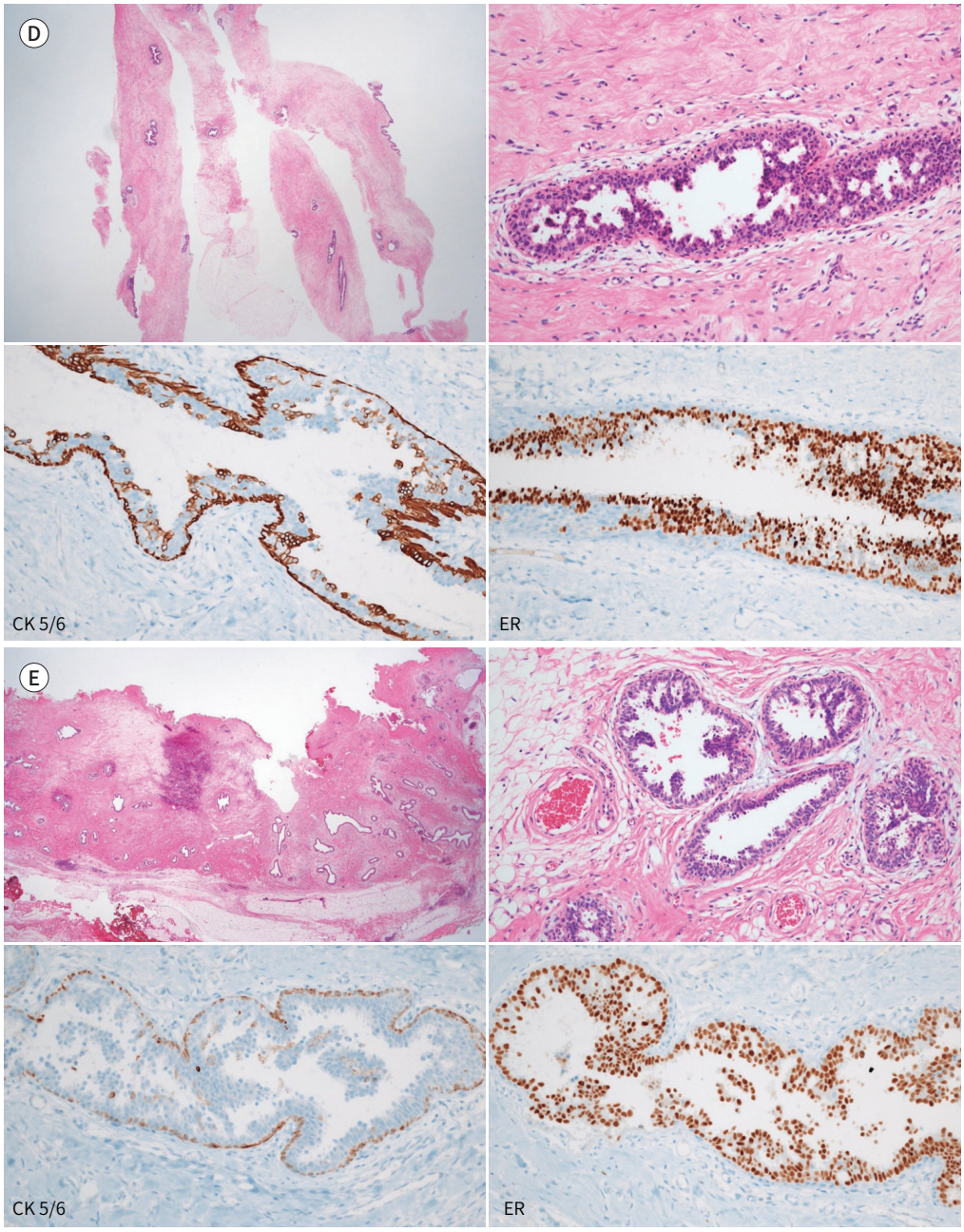


Fig. 1. A 34-year-old male with ADH.
D. Pathology of the biopsy specimen identified a flat epithelial hyperplasia. Microscopically, the involved duct exhibited replacement of the native epithelial cells of the TDLUs with several layers of columnar epithelial cells with monomorphic nuclei. Immunohistochemistry revealed a loss of CK 5/6 and expression of the ER. Magnification: × 12.5 (low-power field) and × 200 (high-power field). The upper images represent hematoxylin and eosin staining.
E. Pathology of the excisional specimen confirmed an ADH. Microscopically, the involved ducts contained proliferative monomorphic epithelial cells that had formed cribriform structures within the TDLUs. Immunohistochemistry revealed a loss of CK 5/6 and expression of ER. Magnification: × 12.5 (low-power field) and × 200 (high-power field). The upper images represent hematoxylin and eosin staining.
ADH = atypical ductal hyperplasia, CK = cytokeratin, ER = estrogen receptor, TDLUs = terminal ductal lobular units



vincing CCLs with enlarged TDLUs had been detected in the male breasts. Conversely, another study from the International Male Breast Cancer Program (3) reported a few cases involving the CCLs adjacent to the invasive breast cancer; these included dilated, twisted ducts with apical snouting which were morphologically similar to the adjacent invasive component. The study also reported similar genomic alterations in some patients with CCLs and an adjacent invasive component. The authors thus suggested the possibility of a causal relationship between the CCL and the adjacent invasive breast cancer, given the morphological and genetic overlap between these lesions. Notably, ADH of the male breast is rare, and only few cases have been reported (6, 7). In one case report, the authors described the pathologic findings of a bilateral ADH accompanied by gynecomastia in the male breast and mentioned the lack of conclusive guidelines regarding the further management of ADH in men (7).

In this report, we described the radiologic findings of ADH in a male breast for the first time. In the female breast, ADH is a well-known precursor of cancer, arising from the TDLU. Histologically, ADH usually shows intraluminal calcifications or secretions, and thus it appears as a microcalcification or a mass associated with microcalcifications on MMG (1). On US exam, the most common positive finding is an irregular, hypoechoic or complex echoic mass (1). However, as mentioned above, the male breast contains only dilated, twisted, and non-secretory ducts. These histopathologic characteristics may correlate with the radiologic findings in the present study. Our patient showed an eccentric, highly dense subareolar mass without microcalcification on MMG. On US, the lesion appeared as an irregular hypoechoic mass, with a complex echotexture and indistinct margins. Male breast cancers usually present as eccentric irregular masses with a relatively low incidence of associated microcalcification on MMG and US (8). Considering the current case, irregular and eccentric masses in the male breast should be further examined to rule out malignancy, although the existence of precursor lesions for male breast cancer remains controversial.

The patient in the present case was receiving tacrolimus. It is well known that many drugs can cause gynecomastia. Immunosuppressant agents such as cyclosporine A and tacrolimus effectively inhibit estradiol degradation, which would explain the increased levels of estradiol (9). Therefore, in this case, we propose that the use of tacrolimus combined with the presence of a chronic renal disease may have induced the gynecomastia. A previous study demonstrated that about 12.7% of the ADH cases were associated with gynecomastia (10), although the latter itself was not a risk factor for breast cancer, it was the most common benign lesion in the male breast. The reported cases of ADH in the male breast were rare, and some cases demonstrated ADH accompanied by gynecomastia including the current case. Further observations and case reports are required, as the relationship between gynecomastia and ADH remains uncertain.

We reported the surgical confirmation of ADH in a male breast with a palpable subareolar mass. The lesion showed pathologic findings similar to those of a female patient, even though the radiologic findings displayed a partly indistinct hypoechoic mass without microcalcification on US and MMG. Since ADH was considered as a high-risk lesion for the subsequent development of breast cancer in the female breast, the attitude of physicians with regard to the importance of treating these lesions. Although the clinical significance of ADH in the male breast is still uncertain, the radiologic and pathologic findings of a high-risk lesion

in the male breast can allow for a better understanding of this condition for clinical practice.

Author Contributions

Conceptualization, A.H.S.; data curation, H.S.M., K.M.K., K.H.S.; formal analysis, K.A., L.S.; investigation, K.A., A.H.S., L.S.; methodology, A.H.S.; supervision, A.H.S.; visualization, A.H.S., K.H.S.; writing—original draft, K.A.; and writing—review and editing, K.A., A.H.S.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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남성 유방에서의 비정형유관증식증의 영상 및 병리 소견에 대한 고찰: 증례 보고 및 문헌고찰

고아라[1] · 안혜신[1*] · 이승호[1] · 하수민[1,2] · 김민균[3] · 김희성[4]

이 증례 보고는, 남성 유방에서의 비정형유관증식증 소견에 대한 영상의학적, 병리학적 소견을 담고 있다. 비정형유관증식증은 고위험 병변에 속하며 유방암의 전구 병변으로 잘 알려져 있다. 하지만, 이런 병변이 남성 유방에서 어떠한 임상적 의미를 갖는지는 잘 알려져 있지 않다. 남성 유방은 여성 유방과 달리 유관이 소엽을 구성하지 않기 때문이다. 지금까지 이러한 전구 병변의 영상 소견과 병리학적 소견을 다룬 문헌은 극소수이다. 이 증례 보고를 통해, 우리는 남성 유방에서 유방암 전구 병변의 가능한 영상 및 병리 소견을 제시하고, 문헌고찰을 하고자 한다.

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