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Case Report

Pleomorphic adenoma of the breast: a report of two cases and a literature review

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Abstract: Pleomorphic adenoma of the breast (PAB) is an extremely rare tumor in the breast. Herein, we reported two Asian female patients diagnosed as PAB and reviewed the relevant literature briefly. The two cases were both diagnosed as fibroadenoma in breast ultrasonography before surgery. Case one is a 28-year-old woman presented with a seven year history of a slowly-growing painless mass in left breast, which was about 1.46×0.93 cm in size. Case two is a 47-year-old female who had a complaint of left breast mass three months ago, which was 2.31×1.37 cm in size. The two tumors both located under areola. The two patients both underwent lumpectomy. Microscopically, they were both comprised of mixture of epithelial cells and myoepithelial cells embedded in myxochondroid matrix background. Immunohistochemically, the two cases displayed positive cytokeratin 7 (CK7) for epithelial cells, positive smooth muscle actin (SMA) and S-100 for myoepithelial cells. PAS staining was positive in case two. According to the pathologic histology and immunohistochemical findings, the two cases were diagnosed as PAB. However, the pathogenesis of PAB has been unclear and further studies remain to be researched.

Keywords: Pleomorphic adenoma, fibroadenoma, breast

Introduction

Pleomorphic adenoma (PA) is a common tumor occurred in salivary glands. The occurrence of PA located in breast is extremely rare and PAB was mostly found in the mammary subareola [1] of postmenopausal female [2]. PA has a characteristic mixture of epithelial components and myoepithelial components embedded in myxochondroid matrix [3]. To our knowledge, only 77 cases of PAB [4-7] have been reported in the literature since the first reported case of PAB by French scholar Lecène in 1906 [8]. Indeed, the breast is a rare location of the PA and the rarity causes the confusion and difficulty in pathological diagnosis among other breast neoplasms, such as mucinous carcinoma [9] and metaplastic carcinoma [10]. Herein, we reported two cases of PAB and reviewed relevant literature briefly in order to avoid misdiagnosis in this rare location.

Case report

Case 1

A 28-year-old woman presented with a seven year history of a slowly growing painless mass in her left breast. Breast examination showed a palpable well-moved 1.5×1.0 cm mass with clear circumference at 4 o'clock direction, 1.0 cm from the nipple. Both sides of the breast were symmetrical; both nipples were aligned. No redness and swelling of the mammary skin and no temperature change. No abnormal in right breast and both axillary lymph nodes. Breast ultrasonography showed a hypoechoic mass located under left mammary areola at 4 o'clock direction, about 1.46×0.93 cm in size, with regular border and clear boundary. Color Doppler flow imaging (CDFI) demonstrated blood flow surrounded the mass. The breast ultrasound suggested the mass had the possi-

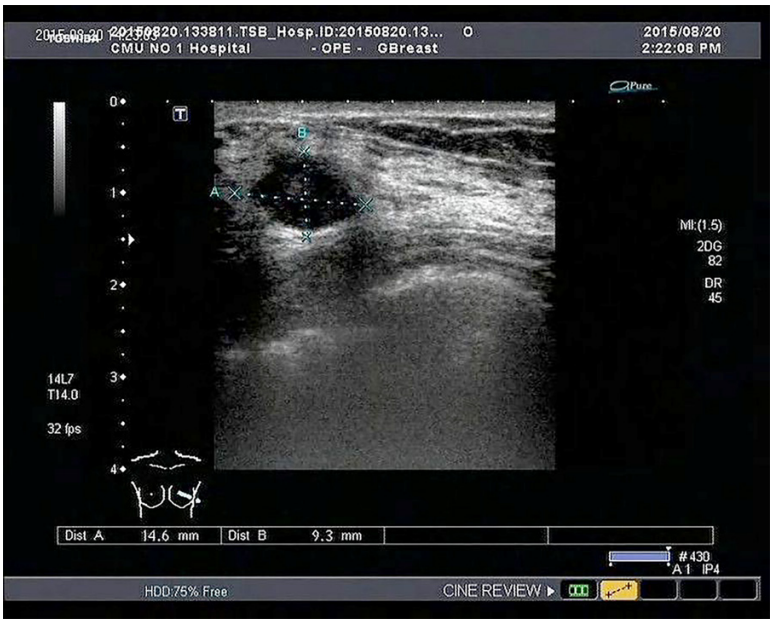

Figure 1. Breast ultrasonography of case 1 showed a left breast hypoechoic mass about 1.46×0.93 cm in size, with regular border and clear boundary.

bility of fibroadenoma of the left breast (BI-RADS 4A) (**Figure 1**). Then the patient underwent lumpectomy for left mammary mass. In gross examination, the lesion was a well-capsular mass, measuring 1.5×1.0 cm in diameter, showing silver-white at cut surface with toughness texture. Microscopically, the tumor was comprised of epithelial cells and myoepithelial cells embedded in myxochondroid matrix, with complete capsule and clear border (**Figure 2A-D**). Immunohistochemical (IHC) staining displayed the epithelial cells were positive for cytokeratin 7 (CK7) (**Figure 2E**), the myoepithelial cells were positive for smooth muscle actin (SMA) (**Figure 2F**), P63 (**Figure 2G**) and S-100 (**Figure 2H**). According to the histological patterns and IHC findings, the tumor was diagnosed as PAB.

Case 2

A 47-year-old female had a complaint of left breast mass three months ago. At beginning the lesion was in bean-size below the left nipple, and then it grew to peanut-size. Breast ultrasonography showed a hypoechoic mass in subareola location, measuring 2.31×1.37 cm. CDFI demonstrated no blood flow signal. The breast ultrasound suggested the mass had the possibility of fibroadenoma of the left breast. Then the patient underwent left breast local excision surgery at the local hospital. She was referred to our hospital for consultation in pathology and management. We reviewed the pathological slides of the patient and confirmed it to be PAB. Microscopically, the tumor was comprised of complex two components, containing epithelial cells and myoepithelial cells components (**Figure 3A**). Stroma structures showed chondromyxoid matrix, loose myxoid change, dispersed with scattered myoepithelial cells (**Figure 3B-D**). Immunohistochemically, the epithelial cells were positive for CK7 (**Figure 3E**), and the myoepithelial cells were positive for CD117 (**Figure 3F**) and S-100 (**Figure 3G**). Periodic Acid-Schiff (PAS) staining showed eosinophilic neutral mucopolysaccharides among myxochondroid matrix (**Figure 3H**).

Discussion

PA mainly occurs in the salivary gland, yet it also can be found in sella turcica [11], lacrimal gland [12], larynx [13], skin [14], vulva [15], lungs [16], and possibly in the kidney [17]. The breast is a modified sweat gland which shares similar embryological ectodermal layer with the salivary glands [3]. Hence, although breast is an extremely uncommon location, similar tumors and their pathological patterns can affect these locations.

According to the 77 cases of PAB have been reported in English literature, PAB most commonly occurs in women, however it can also occur in man and only four cases of PAB in men have been reported [18-21]. The age of the PAB patients ranges from 19 to 85 years old [5, 22]. The tumor size ranges from 0.6 to 20 cm in diameter, most were around 2 cm in diameter [3, 20]. PAB always presents with a solidary palpable mass in the subareola area. In our cases, the mass was considered as fibroadenoma of the breast through clinical and imaging examinations preoperatively. Some authors had reported the preoperative diagnosis was carci-

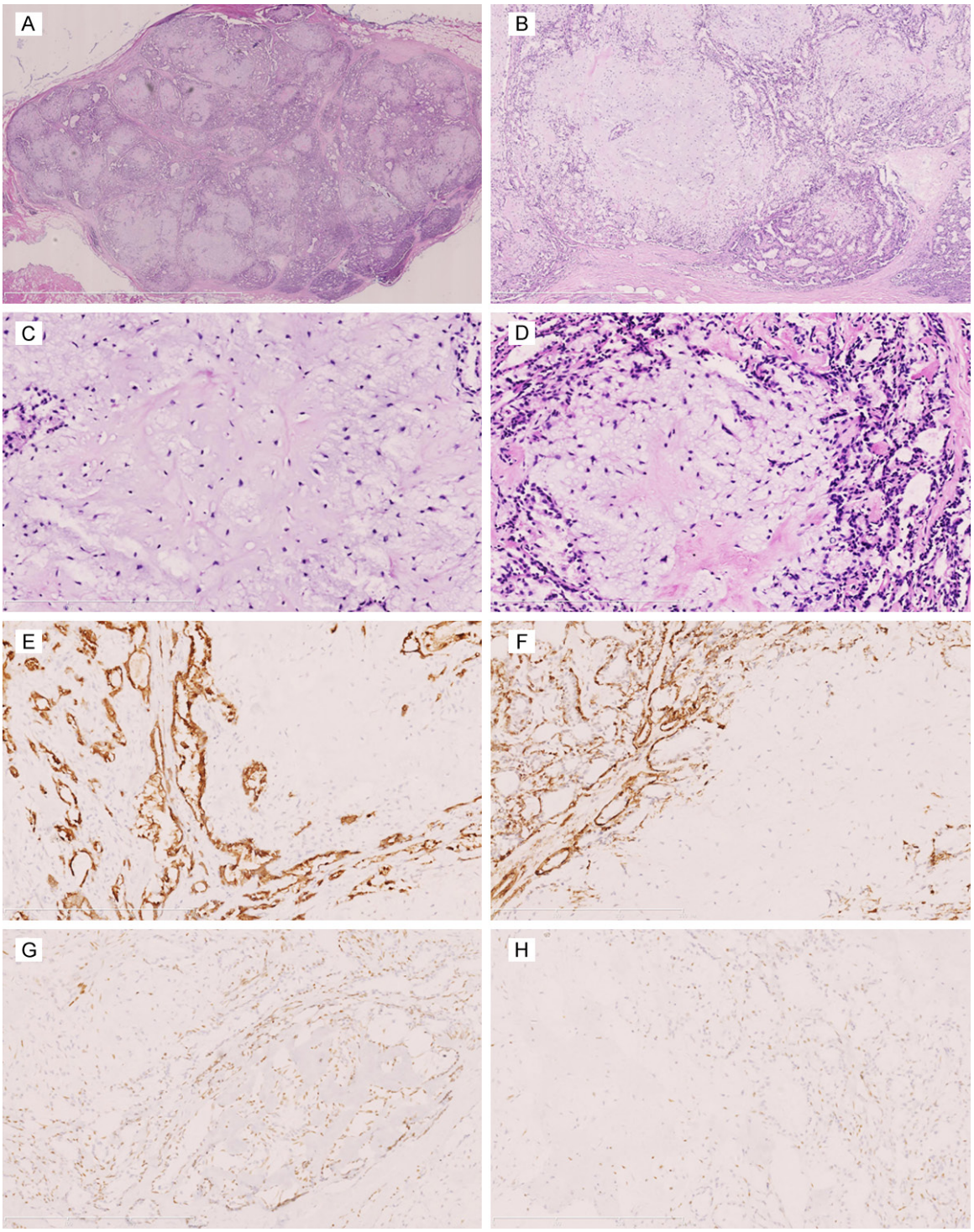

Figure 2. Pathological findings of PAB in case one. A-D: Hematoxylin and eosin (H&E) staining findings. E-H: Immunohistochemical staining findings. A. At low magnification, the tumor had complete capsule and clear border. 12.5×. B. The tumor had complex components and it was consisted of inner epithelial cells and outer myoepithelial cells. 50×. C. High magnification showed myxochondroid matrix. 200×. D. High magnification showed mucoid/myxoid and hyaline stroma. 200×. E. The epithelial cells were positive for CK7. 200×. F. The myoepithelial cells were positive for SMA. 200×. G. The myoepithelial cells were positive for P63. 200×. H. The myoepithelial cells and the chondroid matrix were positive for S-100. 200×.

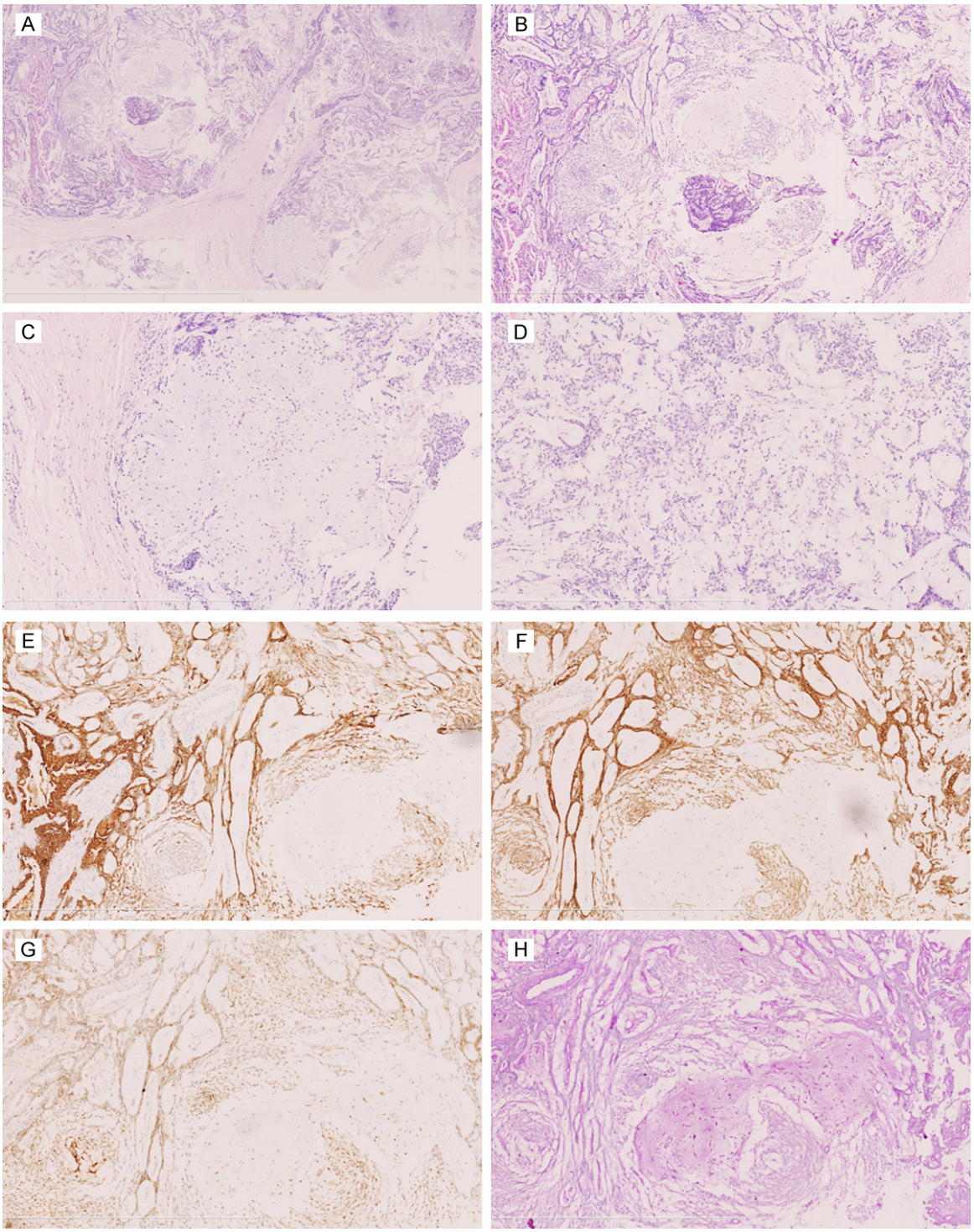

Figure 3. Pathological findings of PAB in case two. A-D: Hematoxylin and eosin (H&E) staining findings. E-G: Immunohistochemical staining findings. H. PAS staining. A. Low power view showed complex two components, containing epithelial cells and myoepithelial cells components. 25×. B. Low power view displayed myxoid and chondroid matrix. In peripheral, part ductal epithelium showed apocrine metaplasia. 50×. C. Medium power view showed chondroid matrix. 100×. D. Mesenchymal component showed loose myxoid change, dispersed with scattered myoepithelial cells.100×. E. The epithelial cells were positive for CK7. 100×. F. The myoepithelial cells were positive for CD117. 100×. G. The myoepithelial cells and the chondroid matrix were positive for S-100. 100×. H. PAS staining showed eosinophilic neutral mucopolysaccharides among myxochondroid matrix. 100×.

noma through both clinical and radiographic findings [9]. Diagnosis of PAB through preoperative clinical and imaging examinations is very challenging. Even through the preoperative biopsy, misdiagnosis can be found, such as mucinous carcinoma [9] and metaplastic carcinoma [10], due to limited tissue samples. The final diagnosis of PAB was made after operation and through the histopathological and IHC findings of paraffin sections and IHC stains.

Therapy of the PAB was surgical excision through reviewing the previous reports. The local excision of tumor margin with a narrow (2 to 5 mm) rim of normal breast tissue was recommended for PAB [20]. Though PA generally has indolent benign behavior, the local recurrence of PAB can also find in two cases [23, 24] and even one case recurred for the second time following surgery [24]. The local recurrence of PA in salivary glands had relationship with the extent of surgery, the pseudopodia outside the pseudopodia or fingerlike tumor extensions under microscopy [25], and multifocality of tumor [24]. Due to several multifocal PAB had been observed [22] and rare reports occurred malignant transformation of PAB [26], patients diagnosed as PAB should be informed of the risk of recurrence and John BJ et. al suggested that the patients do yearly examinations and follow-up at least for five years [24].

Three cases of malignant PAB (i.e., carcinoma ex PAB) have been reported [27]; however, none had metastasized to axillary lymph nodes or distant sites. The histological features of malignant PAB were depended on tumor infiltrative growth patterns, marked cytological atypia, high mitotic rate, presence of atypia, necrosis and high Mib-1 index [27]. No clinical criteria for diagnosis of malignant PAB had been presented.

The tendency of most PAB located in juxta-areolar region suggested PAB might originate from the large mammary ducts in subareola area [28]. The histogenesis of PAB remains controversial, whether PAB derived from epithelial cells, or myoepithelial cells, or both of them remains unclear. Many reports suggested myoepithelial cell proliferation as a key factor in oncogenesis [29, 30]. The abundant myoepithelial cells in large mammary ducts around the areolar region might explain the frequent occurrence in this area. Nartia et al. postulated that PAB originated from multipotent ductal cells, which differentiated into the myoepithelial cells [1]. Further studies on histogenesis of PAB are needed.

PA of the salivary glands harbor chromosomal translocations, involving 8q12 (with the target gene PLAG1) [31], 12q15 (with the target gene HMGI-C) [32], and 6p21 (with the target gene HMGIY) [33]. In PAB, Sato et al. reported IHC-positive staining of HMGI-C and HMGIY and they suggested the tumor might show abnormal expression of HMGI-C and HMGIY proteins [34]. Some further studies on chromosomal rearrangements in PAB and exact mechanisms remain to be evaluated.

In conclusion, we reported two cases of PAB. Diagnosis of PAB through clinical examinations, imaging findings and preoperative biopsy was difficult and the tumor may be misdiagnosed as fibroadenoma or malignant breast tumor. Clinical doctors and pathologists should pay more attention to the diagnosis of PAB.

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Disclosure of conflict of interest

None.

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