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Apocrine metaplasia: A case report with review of literatures

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Apocrine metaplasia is one of the lesions in the spectrum of fibrocystic changes of the breast. Pathologically, the cysts are lined by large polygonal cells that have abundant granular eosinophilic cytoplasm with small, round nuclei. This is virtually always a benign condition. However, apocrine metaplasia may give an imaging feature that mimics malignancy, probably due to its high-viscosity content. We report a case of this entity presented with clinically silent growing breast mass with malignant-appearing imaging feature that warranted biopsy. A brief review of the literature about apocrine metaplasia and fibrocystic change is also included.

Key words : *Apocrine metaplasia, Apocrine cyst, Fibrocystic change of the breast.*

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Apocrine metaplasia เป็นรอยโรคหนึ่งซึ่งอยู่ในกลุ่มของการเปลี่ยนแปลงที่ให้ลักษณะเป็นถุงน้ำของเต้านม โดยมีพยาธิสภาพซึ่งประกอบด้วยถุงน้ำที่มีผนังเป็นเซลล์ลักษณะเป็นรูปหลายเหลี่ยมและมี cytoplasm ซึ่งมี granule ที่ย้อมติดสี eosinophil อยู่เป็นจำนวนมาก รวมทั้งมี nucleus ขนาดเล็กและรูปร่างกลม รอยโรคนี้เป็นภาวะที่ไม่ร้ายแรง แต่สามารถให้ลักษณะภาพทางรังสีและอุลตราซาวด์เหมือนเนื้องอกชนิดร้ายแรงได้ รายงานนี้นำเสนอคนไข้ ซึ่งมีอาการแสดงนำด้วยก้อนที่เต้านม โดยมีลักษณะภาพทางรังสีและอุลตราซาวด์คล้ายเนื้องอกชนิดร้ายแรง และคนไข้ได้รับการตัดชิ้นเนื้อไปพิสูจน์ ผลทางพยาธิวิทยาของชิ้นเนื้อพบเป็น apocrine metaplasia การทบทวนวรรณกรรมที่เกี่ยวข้องกับเรื่อง apocrine metaplasia และการเปลี่ยนแปลงแบบเป็นถุงน้ำของเต้านมอย่างย่อมีในตอนท้ายของรายงานนี้

Nonproliferative lesion of fibrocystic changes of the breast is a common type of alteration, characterized pathologically by an increase in fibrous stroma, dilatation of ducts and cyst formation. Apocrine metaplasia is one of the lesions that can be seen in the spectrum of fibrocystic changes and can appear as a discrete mass on a mammography. This lesion is virtually benign but confusion with malignancy is possible because of the mammographic and sonographic appearance, particularly when the given clinical manifestation is suggestive of malignant lesion. Radiologists and pathologists should be familiar with the benign processes that can be manifest as discrete masses on mammography and biopsy since all the lumps must be distinguished from cancer. We report a case of how this entity presented a clinically silent growing breast mass with radiographic malignant potential lead to an excisional biopsy. However, the pathological report turned out to be apocrine metaplasia. The purpose of this paper is to show that a benign cystic lesion of apocrine metaplasia could have malignant imaging features.

Case Report

A 60-year-old female patient presented for an annual check up and screening mammography in November 1995. On physical examination, there was an ill-defined nodular area in the upper inner quadrant of the right breast. The first mammography and additional sonography were normal (Fig.1A, 2A). The follow-up mammograms 1-year later revealed a small soft tissue density nodule in the upper outer quadrant of the left breast, measured about 4 mm. in size. No mass or cyst was found on the sonography. She was

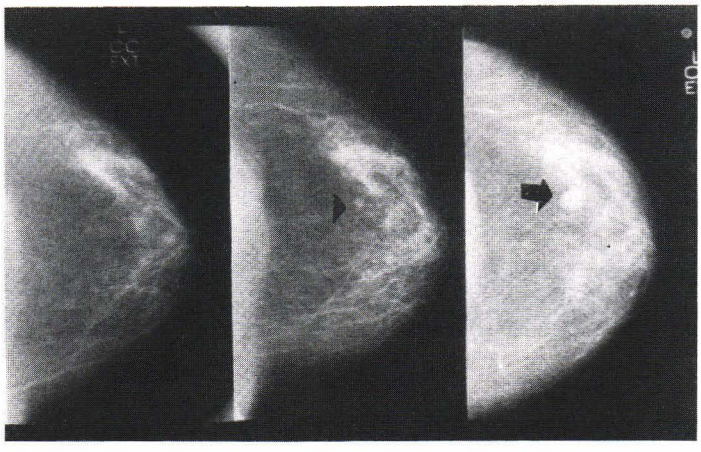


Figure 1. Left mammograms, craniocaudal views.

A. The first screening mammography on November 1995 reveals no definite mass.

B. The follow up study on July 1998 shows a small nodule at the outer quadrant. (arrowhead)

C. Enlargement of the soft tissue nodule in outer quadrant in 3 - year follow up study (January 1999), nearly double in size. (arrow).

then lost for follow up for 2 years. On July 1998, her mammograms showed a well-defined microlobulated nodule, 8 mm. in size, in left upper outer quadrant (Fig.1B,2B). This nodule had doubled in size since 1996. On a 6-month follow-up study on January 1999, there was mild increase in size of this nodule (Fig.1C,2C). Supplementary ultrasonography showed a microlobulated hypoechoic mass, that measured about 9.8 x 6.4 mm. in size that indicating a solid mass (Fig.3). According to the American College of Radiology Breast Imaging Reporting and Data System (ACR BIRADS), this mass was categorized as indeterminate or a probably malignant mass.[1] She was then clinically diagnosed with a nonpalpable left breast mass for which low-grade malignancy was not excluded. She was admitted for excisional biopsy under stereotactic needle localization (Fig.4). At surgery, a lobulated cyst was found with very sticky content.

Microscopically, the section from the breast mass showed several dilated mammary ducts surrounded by fibrotic breast stroma. One large cyst is lined by apocrine epithelium (Fig.5). Neither significant hyperplasia nor malignancy is seen. The surrounding breast tissue also revealed fibrocystic change. One small duct disclosed a moderate degree of epithelial hyperplasia. The pathological diagnosis was fibrocystic change with a moderate degree of focal ductal epithelial hyperplasia.

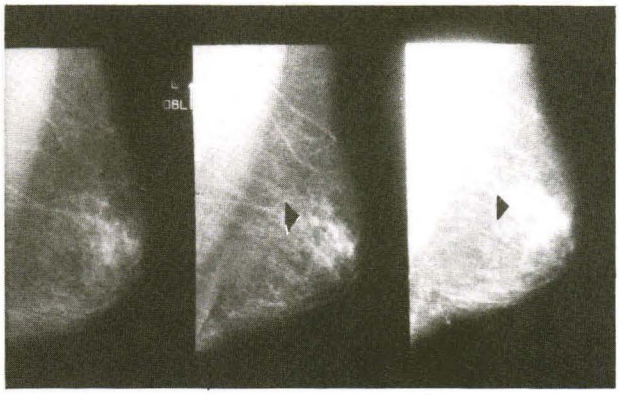


Figure 2. Left mammograms, mediolateral oblique views, correlate with the studies on figure 1 from A to C. Note the enlargement of the nodule in upper portion of the left breast. (arrowheads).

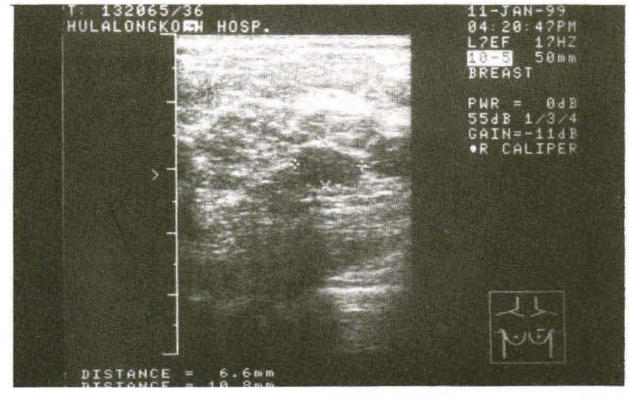


Figure 3. Corresponding ultrasonogram of the soft tissue nodule reveals a hypoechoic mass with microlobulated border. (+, X)

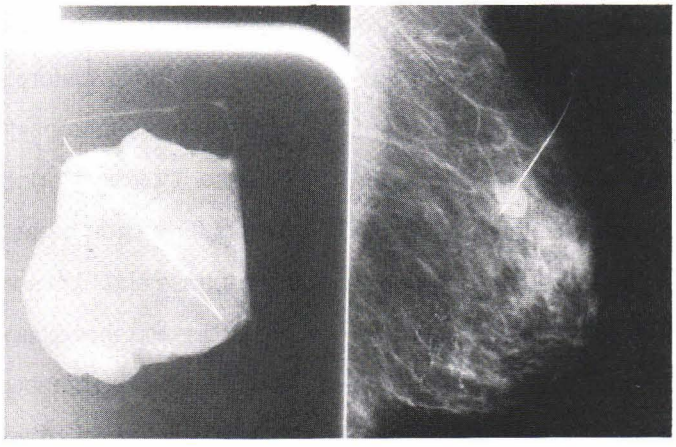
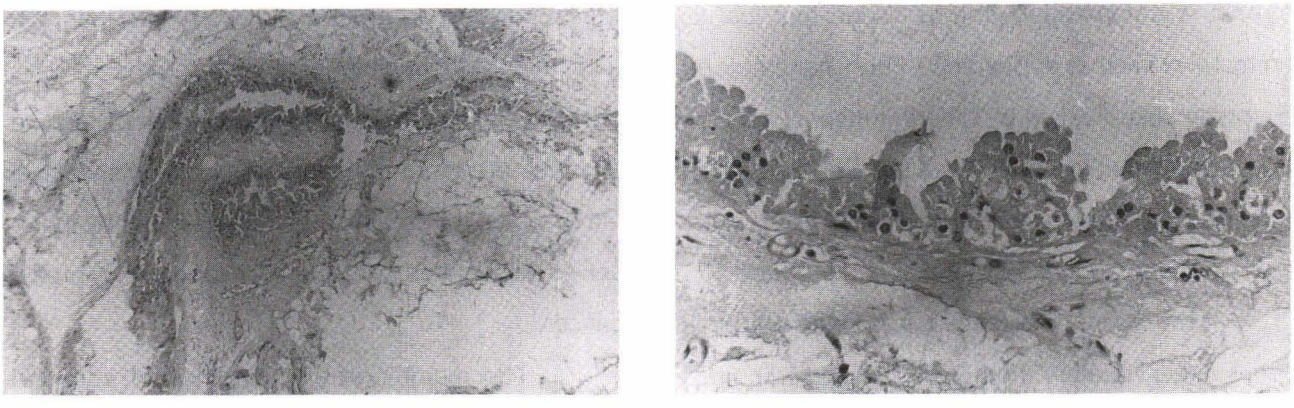


Figure 4. Needle localization was done under stereotactic technique. The hook of the needle is placing at the small round mass in left upper outer quadrant. The specimen radiograph shows the mass in excised breast tissue.



A B

Figure 5. A. The collapsed unilocular cyst is demonstrated. Note this delicate fibrous cyst wall and the loose surrounding fatty tissue. (H & E, original magnification X 40).
B. The lining of apocrine epithelium with secretory globules. (H & E, original magnification X 400).

Discussion

Fibrocystic changes of the breast are applied to a wide-range of changes that are the result of an exaggeration and distortion of the cyclic breast changes that occur normally in the menstrual cycle. There is tendency of this change to arise in reproductive age but may persist after the menopause. These changes can be further subdivided by their

histologic appearance into nonproliferative and proliferative patterns and are more common in the nonproliferative types, being found at the autopsy in 60 – 80 %. This has made the fibrocystic change, the most common cause of breast lumps. There is continuing controversy about the association of some variant with breast carcinoma. Histologically, the nonproliferative change is characterized by an increase in fibrous stroma association with dilatation of ducts and formation of cysts of various sizes, which can vary from smaller than 1 cm. to 5 cm. in diameter. Frequently, cysts are lined by large polygonal cells that have abundant granular eosinophilic cytoplasm, with small, round, deeply chromatic nuclei, so-called apocrine metaplasia. Microcalcifications can also be detected on the mammography from the calcified secretory products within the cysts. The surrounding stroma is compressed fibrous tissue that lost its normal myxomatous appearance. Further attempts for cyst type classification by different means, such as from the biochemical analysis of the breast cyst fluid was noted, and increased pepsinogen C levels in the fluid within the apocrine cyst has been reported.[2]

The reported incidence of apocrine metaplasia varies in the literature, from 3.8% histologic findings from core biopsy to 69 % in the nonpalpable breast lesions that had ultrasound-guided excisional biopsy.[3,4] The incidence increases with age but occurrence is most common in the fourth and fifth decades of life (range 37 - 95 years, mean age 57 years in Warner JK series of 17 patients).[5] In 1996, Pacchioni D et al. reported a case of gynecomastia in a male under spironolactone treatment and fine needle aspiration demonstrated the cystic lesion with apocrine change in the epithelial cells.[6] Despite this report, apocrine metaplasia in the male breast is considered to be a rare manifestation due to the absence of glandular structure in the male mammary gland.

A family history of breast cancer is also one of the factors increasing the risk of benign breast disease, including apocrine metaplasia. Other risk factors for benign breast disease are low parity, late menopause and high socio-economic status. Benign breast disease shows large variation in the subsequent risk of developing breast cancer. It is generally known that the history of breast cancer in the family has little effect on the risk of cancer in women with non-proliferative lesion and that cysts alone did not substantially elevate the risk. In 1985, Dupont WD et al. studied 10366 breast biopsies in 3303 women with the mean follow up period to 17 years. He concluded that, women with both cysts and a family history of breast cancer had a risk 2.7 times higher than that for women without either of these risk factors.[7] This could be explained assuming that the nonproliferative changes are more prevalent among women with a family history of breast cancer, but are not by themselves associated with the development of breast cancer.

The mammographic findings of apocrine metaplasia commonly are microlobulated mass correspond to the lobulated margins of a dilated terminal duct lobular unit with ectatic acini. The larger the microcyst formation, the more macrolobulated the mass. The masses usually show equal to low density compared to the parenchyma due to cystic content. The sonographic findings typically reveal a lobulated mass consisting of a cluster of small anechoic foci with septations and partial posterior acoustic enhancement. If a solid component was also

identified within the cystic lesion, this finding should warrant the need of biopsy and tissue diagnosis as apocrine metaplasia may occur in conjunction with other solid lesions. Cysts with normal epithelium cannot usually be distinguished from those with apocrine metaplastic change in the absence of histopathologic evaluation. On follow up study, the lesions may show to either be resolved or decreased in size in 6-12 months follow up examination.[5] A decrease in size or resolution of the mass is occasionally observed during core needle biopsy if a cyst is sampled, probably due to the cyst being punctured and had drained during the biopsy.[8]

In our reported case, the breast mass of this patient showed an interval increase in size during the 3-year period from normal study to a nearly 1 cm.-size mass. The mammographic finding of microlobulated mass, which doubled in size in the 1-year period, and a lobulated hypoechoic mass suggestive of solid nature by ultrasonography, raised the possibility of malignancy and led the patient to the excisional biopsy. In our experience, the microlobulated border with well-defined margin is not uncommonly seen in benign lesions, probably due to lobulated borders of group of small cysts in this case. According to the literature review, we found that an increase in size of the apocrine cyst could be due to fusion of the dilated acini over time, making the cyst enlarged. Besides,the thick contents of the cyst found during surgery gave the ultrasonographic feature of solid lesion. Basically, ultrasonography could help to differentiate cystic from solid lesions, but sometimes the cystic lesion may have a content that provides solid echotexture. As in our case, ultrasonography showing a hypoechoic area allowed the diagnosis of solid mass.

In summary, apocrine metaplasia is a benign epithelial alteration occurring in the lobular portion of the terminal ductal lobular unit. The mammographic and ultrasonography findings may mimic the malignant process, especially when the clinical history, family history and interval enlargement during the follow-up study were recognized. These may lead the patient to the unnecessary biopsy of the benign lesion.

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