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CASE REPORT

Apocrine papillary lesion: comparison of pathological findings from 22 years previously and the present

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Abstract
Apocrine papillary lesion (APL) is difficult to diagnose as benign or malignant. We experienced an APL remaining in the body for 22 years. We present a case of a 71-year-old woman who had undergone excisional biopsy 22 years previously at the first hospital that she visited. 1 year previously, she had undergone fine-needle aspiration cytology at a second hospital, and the lesion was diagnosed as potentially malignant. She underwent core-needle biopsy at a third hospital, but whether the lesion was benign or malignant could not be definitively diagnosed. We performed right mastectomy and sentinel lymph-node biopsy, because her tumor was suspected to be malignant based on imaging means, and malignancy could not be ruled out on either biopsy or cytology. The histopathological diagnosis was tiny foci of apocrine proliferative lesion with massive hemorrhagic necrosis and no tumor metastasis in two sentinel lymph nodes. Retrospectively, we compared all of the patient's previous specimens with the present ones, and applied the recent pathological diagnostic criteria. Although the biopsy specimen excised 22 years ago suggested an encapsulated apocrine papillary carcinoma or a papilloma with apocrine ductal carcinoma in situ, neither infiltration nor metastasis has occurred. Furthermore, neither the pathological findings nor the clinical behavior has changed over time.

Keywords Apocrine papillary lesion · Papilloma with DCIS · Encapsulated apocrine papillary carcinoma

Introduction

Apocrine papillary lesion (APL) is clinicopathologically difficult to diagnose as benign or malignant. We present a case of a 71-year-old woman with APL who had had the lesion for 22 years and visited our hospital complaining of a painful tumor. Right mastectomy and sentinel lymph-node biopsy were performed. We compared the present resected surgical specimens with those from the excision biopsy conducted 22 years previously and those from the CNB acquired 1 year previously using recently developed diagnostic criteria. In this report, we discuss the malignant potential of APL and present a literature review.

Case report

A 71-year-old postmenopausal woman visited our hospital with a painful large tumor in her right breast. A portion of the tumor had been excised 22 years previously at the first hospital she visited, but the rest of the tumor remained in her breast and she did not receive any pathology results. 1 year ago, fine-needle aspiration cytology (FNAC) was performed on the remnant lesion at a second hospital, and the results suggested malignancy. She underwent core-needle biopsy (CNB) at a third hospital and the results were inconclusive. When she visited our hospital, she insisted that the tumor was painful and growing larger. During a physical examination, palpation revealed a tumor with a large range of mobility (~4 cm) in the center of the right breast. By comparing ultrasound findings of the tumor between the

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third hospital and our hospital, the proportion of the solid component decreased and the proportion of the cystic component increased. CNB was not performed in our hospital.

Mammography showed a dense tumor in the right breast 4.5 × 4.0 cm in size with a partially unclear boundary (Fig. 1a). Ultrasonography revealed an irregularly shaped solid and cystic tumor. Computed tomography (CT) and magnetic resonance imaging (MRI) revealed an unevenly lobulated tumor with an interior that was primarily cystic, suggesting degeneration or bleeding, as well as a capsule and partition-like structure that were irregular, uneven in shape and thickness, and non-homogeneously enhanced by contrast agents (Fig. 1b). Tumor infiltration into the dermis could not be ruled out. Some malignant tumor types with solid and cystic components, such as mucinous carcinoma, metaplastic squamous cell carcinoma, encapsulated carcinoma, intraductal or intracystic carcinoma, and malignant phyllodes tumor, were suspected preoperatively. Neither axillary lymph-node swelling nor distant metastasis was observed on any imaging study.

Based on imaging results and previous pathological findings, a malignant tumor with ductal spread was thought to be more likely than a benign tumor. We worried that lumpectomy or breast-conserving surgery would intensely deform the remaining breast, because the tumor was large and located in the center of the breast. After explaining this to the patient and receiving her approval, right mastectomy and sentinel lymph-node biopsy were performed.

A hemorrhagic nodular lesion 28 mm in size, which is smaller than the size expected preoperatively due to fluid loss during specimen preparation, was found in the center of the breast tissue (Fig. 2a). Histologically, the major part of the lesion was characterized by necrotic changes with marked bleeding and was surrounded by thick fibrosis with inflammatory cells (Fig. 2b). Although some tiny foci of APL without a myoepithelial cell layer were observed, they were too small to determine whether they were malignant of benign (Fig. 2c). In almost all the necrotic regions, papillary and tubular structures remained, suggesting that a papillary lesion had undergone necrosis. No findings of carcinoma in situ were observed in surrounding breast tissue. Lateral and deep stumps and two resected sentinel nodes were free from tumor cell invasion. She has survived with no relapse for 1 year after surgery without any adjuvant therapy.

Discussion

Benign breast papillary lesions are classified as intraductal or intracystic papilloma or papillomatosis, while malignant papillary lesions include papilloma with ductal carcinoma in situ (DCIS), papillary DCIS, encapsulated papillary carcinoma, solid papillary carcinoma, and invasive papillary carcinoma [1–3].

In the past, papilloma with DCIS was not recognized entity. However, recent accumulation of immunohistochemical knowledges have revealed that carcinoma cells in papilloma lack expression of high-molecular-weight cytokeratins and typically show strong, diffuse expression of estrogen receptor. In addition, myoepithelial cells were not present or very few in number in the atypical lesion [4, 5].

Although a few case reports of atypical APL have been published, no consensus regarding its malignant potential has been obtained. The myoepithelial cell layer may

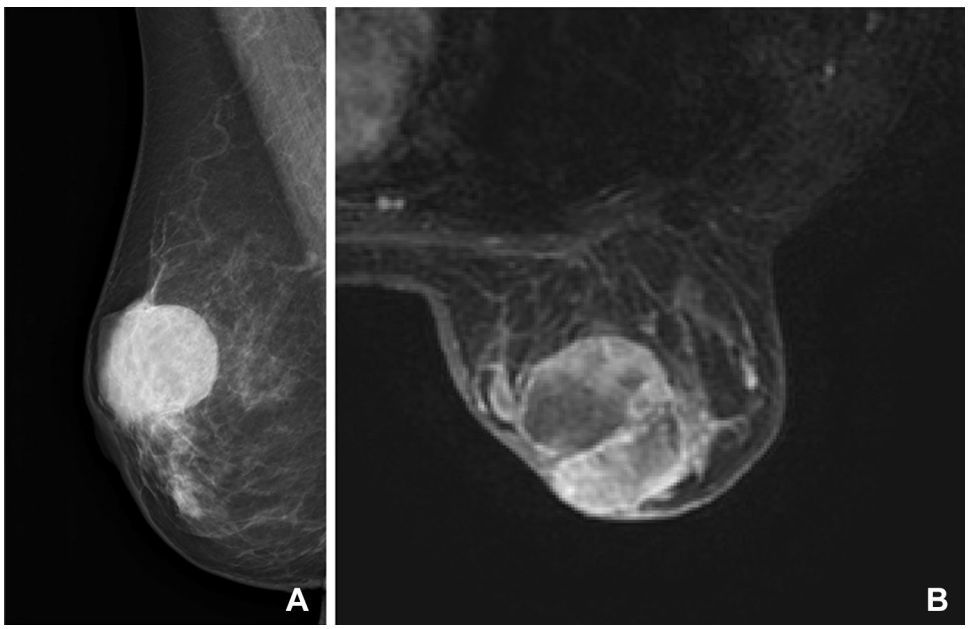

Fig. 1 Imaging findings. **a** Mammography showed a dense tumor 4.5 × 4.0 cm in size with a partial unclear boundary in the right breast. **b** Magnetic resonance imaging revealed an unevenly lobulated tumor with an interior that was primarily cystic, suggesting degeneration or bleeding and a capsule and partition-like structure that were irregular and uneven in shape and thickness and non-homogeneously enhanced by contrast agents

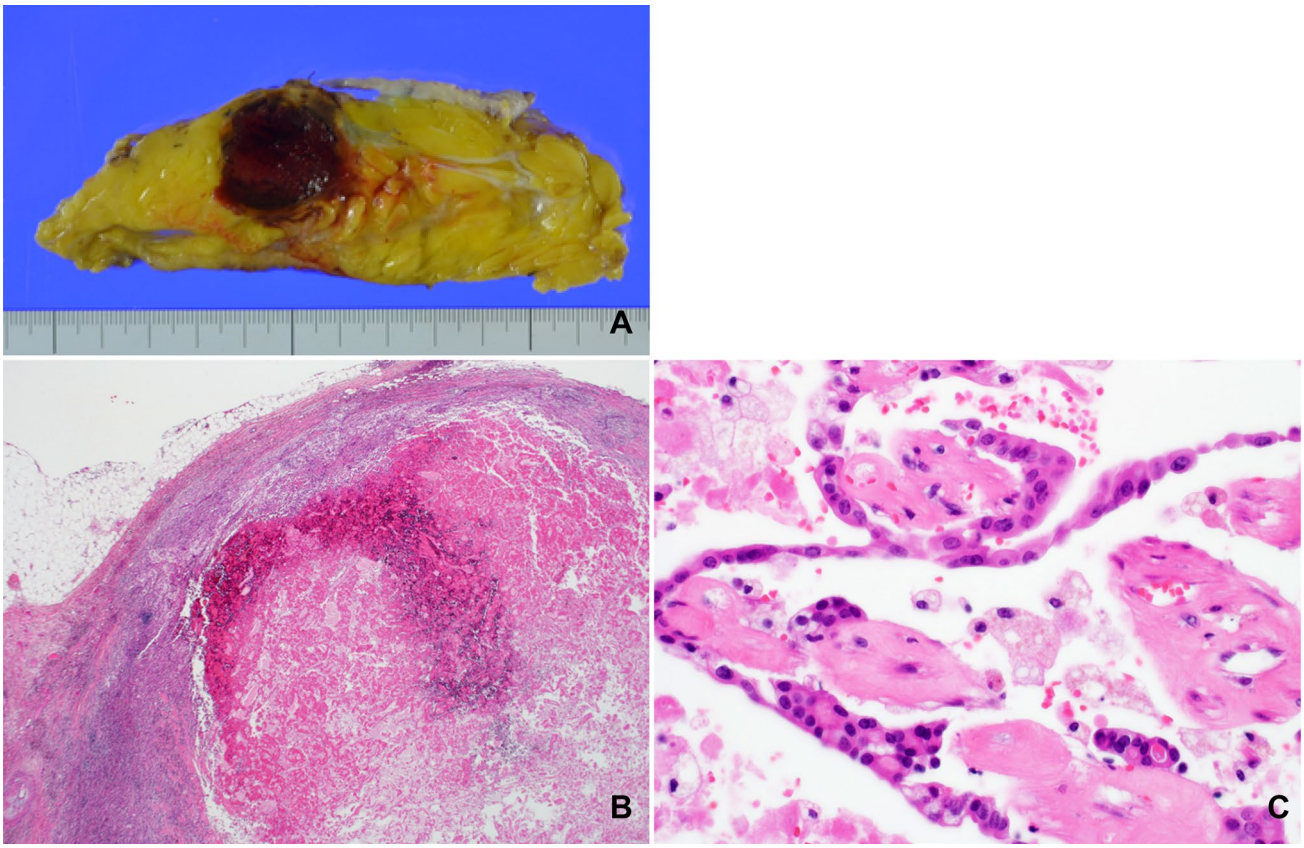

Fig. 2 Pathological examination: macroscopic and microscopic findings. **a** Hemorrhagic nodular lesion 28 mm in size, which is smaller than the size expected preoperatively due to fluid loss during specimen preparation, was found in the center of the breast tissue. **b** Major part of the lesion was characterized by necrotic changes with marked bleeding and was surrounded by thick fibrosis with inflammatory cells. **c** Some tiny foci of APL without a myoepithelial cell layer were observed

disappear even in obviously benign apocrine metaplasia; therefore, the presence or absence of a myoepithelial cell layer is not useful for differentiation between benign and malignant lesions [6–8]. In addition, benign apocrine lesions lack expression of high-molecular-weight cytokeratins and it is not useful in apocrine lesion diagnosis [9].

Seal et al. reported five cases of encapsulated apocrine papillary carcinoma of the breast. The follow-up periods for their cases ranged from 3 to 41 months. These investigators classified these cases as encapsulated apocrine papillary carcinoma according to the WHO classification of breast tumors. However, they also stressed that the malignant potential of these lesions has not yet been determined, and their lesions were probably better considered to be tumors of uncertain malignant potential for the purposes of clinical management [10].

We compared the present resected surgical specimens with those from the excision biopsy conducted 22 years previously and those from the CNB acquired 1 year previously. The 22-year-old specimen appeared to be an intracystic papillary tumor 5 × 4 cm in size. The majority of the tumor exhibited coagulative necrosis due to infarction, and there was a small amount of viable papillary architecture in the tumor. The papillary structures were covered by multilayered apocrine cells. Almost the entire papillary lesion was devoid of myoepithelial cells. A cribriform pattern was focally observed. The apocrine cells were monotonous, and their nuclei showed anisonucleosis and irregular arrangement with large nucleoli. A few mitotic figures were observed (1-2/50 HPF) (Fig. 3). Estrogen receptor was negative.

Moriya et al. reported that cases immunoreactive for Ki-67 and p53 were significantly more frequent in apocrine carcinoma than in benign apocrine lesions. They showed that positive cases for Ki-67 and p53 in apocrine DCIS were 88.9% and 100%, respectively, while those in benign apocrine lesions were 5.3% and 0%, respectively [11]. In resected specimens 22 years ago, Ki-67 was almost 0% and p53 was 22.44%. This result may be incorrect as it has been dyed again this time.

According to their criteria [11], most areas of this tumor might be diagnosed as apocrine carcinoma in situ.

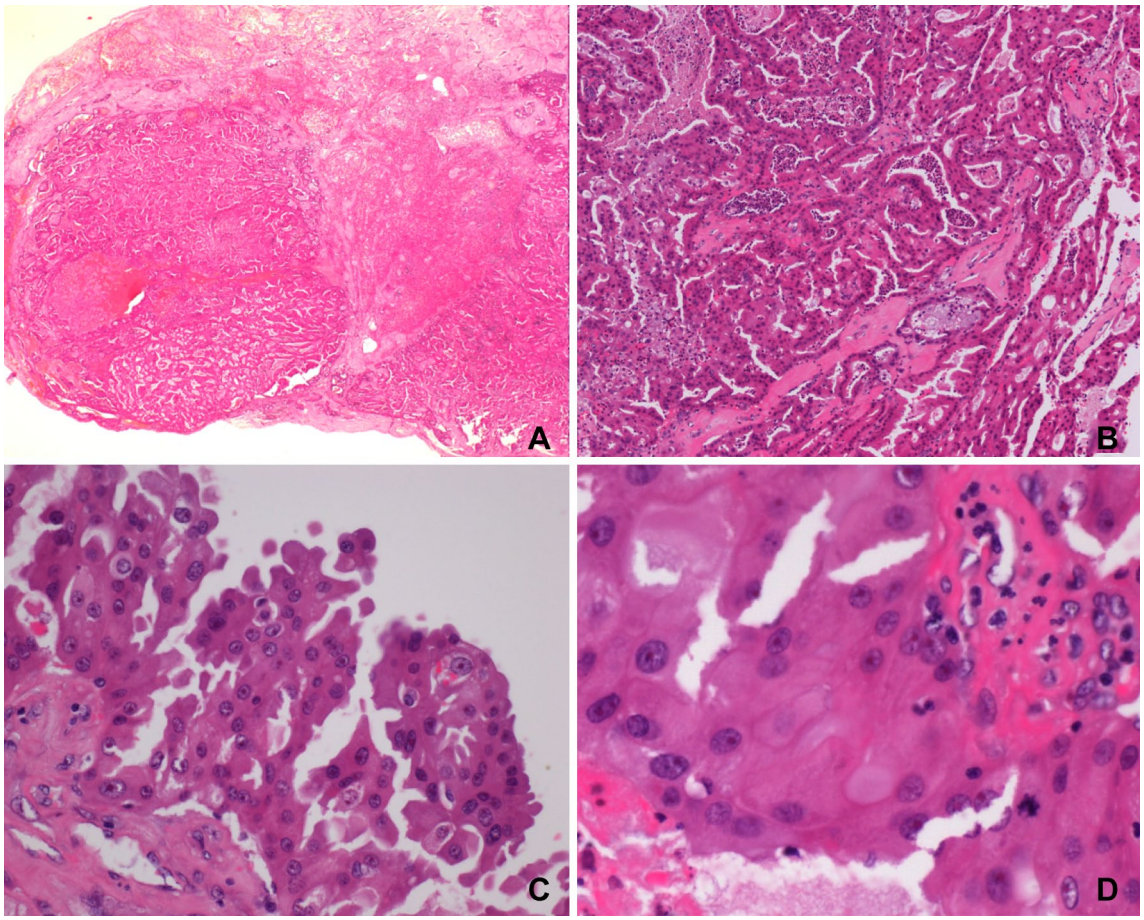

Fig. 3 Microscopic findings of the excision biopsy performed 22 years previously. **a** Majority of the tumor exhibited coagulative necrosis due to infarction and some apocrine cells were found. **b** Papillary lesion was devoid of myoepithelial cells. **c, d** Proliferating apocrine cells were monotonous, and their nuclei showed anisonucleosis and irregular arrangement with large nucleoli. A few mitotic figures were observed (1-2/50 HPF)

However, there are no broadly accepted criteria for distinguishing atypical apocrine proliferations from apocrine DCIS to date.

The CNB specimens acquired 1 year previously demonstrated characteristics of APL and resembled that of the excision biopsy taken 22 years previously. Monotonous apocrine cells appeared to be proliferating with papillary and/or tubular structures. The APL region was totally devoid of myoepithelial cells. Determination of whether the lesion was benign or malignancy was considered challenging based on the presence of a few fragments of pure APL in the CNB specimens (Fig. 4).

In the present case, most of the lesion was characterized by necrotic changes. Although some tiny APL foci lacking a myoepithelial cell layer were observed, they were too small to allow the determination of whether they were malignant or benign. In almost the entire necrotic portion, papillary and tubular structures remained, suggesting that a papillary lesion had undergone necrosis.

The APL lesion appeared to have almost no changes in histopathological appearance or clinical behaviors for 22 years, i.e., neither invasion to interstitial tissue nor nodal or distant metastasis occurred. A definitive diagnosis could not be made due to the massive necrosis; however, we think that the APL might be an encapsulated apocrine papillary carcinoma or papilloma with apocrine DCIS. Despite these limitations, our findings suggest that low-grade apocrine papillary carcinoma in situ may be an indolent lesion.

Conclusion

We compared the pathological findings from an APL in specimens acquired through excision biopsy 22 years previously, CNB 1 year previously, and the present surgical resection. The resulting pathological diagnosis is most likely encapsulated apocrine papillary carcinoma or papilloma with apocrine DCIS, although the pathological findings

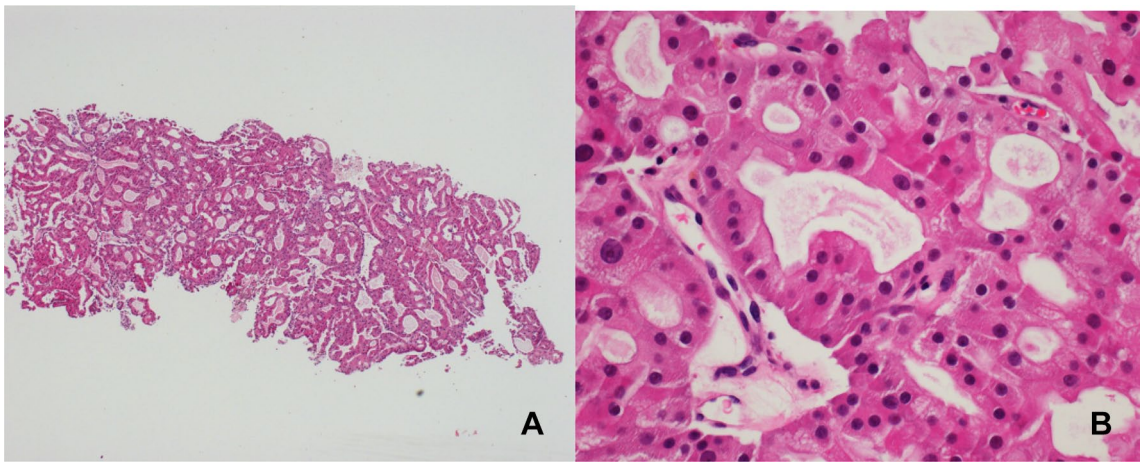

Fig. 4 Microscopic findings of the CNB performed 1 year previously. **a** APL resembled that of the excised biopsy acquired 22 years previously. **b** Atypical apocrine cells form papillary and/or tubular structures. The APL was totally devoid of myoepithelial cells

changed little over time, and no malignant changes have been observed, i.e., neither infiltration to interstitial tissue nor nodal or distant metastasis have occurred, explaining why this lesion has exhibited benign clinical behavior.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

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