CASE REPORT

Encapsulated papillary carcinoma, apocrine type, of the breast

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Abstract

The apocrine type of encapsulated papillary carcinoma (EPC-A), of the breast is a rare neoplasm and there are only eight cases reported to date. Herein, we report the ninth case. A 68-year-old Japanese woman presented with a left breast mass. The cytoplasm of the tumour cells showed positive immunostaining for GCDFP-15. Myoepithelial cells were absent within the papillary structures and at the periphery of the lesion. The clinical course of the patient was uneventful 11 months after surgery. We postulate that EPC-A belongs to the molecular apocrine type of breast carcinoma.

Keywords: encapsulated papillary carcinoma, breast, apocrine.

INTRODUCTION

The disease entity of encapsulated papillary carcinoma (EPC) of the breast, previously termed intracystic papillary carcinoma, has been integrated into the recent World Health Organization classification. The common type of EPC is a luminal breast cancer. There are only eight cases of the apocrine variant of EPC (EPC-A) reported to date. In this article we present the ninth case and discuss the clinical and pathological significance of this subtype.

CASE REPORT

A 68-year-old Japanese woman presented to the Department of Surgery, Kochi Red Cross Hospital complaining of a mass in the left breast. Fine needle aspiration cytology obtained from the left lump showed indeterminate findings. The subsequent mammotome biopsy showed a malignant neoplasm and left partial mastectomy with sentinel lymphadenectomy was performed. The specimen was fixed in 10% buffered formalin for 8 hours and processed in an automated histology processor (LEICA, ASP200S) according to standard laboratory protocol. Histological sections were cut from the paraffin-embedded tissue blocks and stained with hematoxylin and eosin. In addition, immunostains were performed using the Ventana Benchmark XT autostainer (Ventana Medical Systems, Tucson, AZ). The primary antibodies employed included GCDFP-15 (23A3, 1:40, Novocastra Laboratories, Ltd, Newcastle, UK), ER (1D5, 1:2, DAKO, Glostrup, Denmark), PgR (PgR636, prediluted, DAKO, Glostrup, Denmark), androgen receptor (AR27, 1:100, Novocatra Laboratories, Ltd, Newcastle, UK), alpha smooth muscle actin (A14, 1:800, DAKO, Glostrup, Denmark), cytokeratin 14 (LL002, 1:20, Novocastra Laboratories, Ltd, Newcastle, UK), p63 (4A4, 1:20, Lab Vision, CA, USA), CD10 (56C6, prediluted, Novocastra Laboratories, Ltd, Newcastle, UK), S-100 protein (polyclonal, 1:2400, DAKO, Glostrup, Denmark) and calponin (CALP, 1:100, DAKO, Glostrup, Denmark). HER2 gene status was determined by FISH analysis using the Vysis system performed in the BML Laboratory (Kawagoe City, Saitama, Japan).

This patient is uneventful 11 months after the operation without local recurrence or metastasis.

PATHOLOGICAL FINDINGS

Macroscopic findings

The partial mastectomy specimen showed a well-circumscribed, light brown tumour with a fibrous capsule and a central partly cystic region which measured 29x24x12mm (Figure 1).
Microscopic findings

The lesion consisted of cystic and solid parts (Figure 2A). The solid portion showed a papillary configuration. The papillary structures were lined by neoplastic cells with deeply eosinophilic cytoplasm characteristic of apocrine cells (Figure 2B & C). Focally, cribriform structures were also seen (Figure 2D). Apocrine neoplastic cells accounted for more than 90% of total tumour volume. Nuclear atypia was generally mild to moderate, but focal areas of severe atypia were noted featuring large nuclei containing prominent nucleoli (Figure 2E).

FIG. 1: Macroscopic findings. The tumour is a well-circumscribed nodule consisting of cystic and solid regions.

FIG. 2: Microscopic findings. (A) The tumour consists of solid and cystic portions. (B) The papillary growth with fibrovascular cores is seen. (C) The neoplastic cells have an apocrine morphology. (D) The cribriform pattern is also seen. (E) Area of high-grade atypia with nuclei containing prominent nucleoli.
Mitoses were present but not numerous. No atypical mitoses, areas of hemorrhage or necrosis were noted. No lymphovascular invasion was observed. No ductal carcinoma in-situ (DCIS) components were identified in the surrounding tissue. The sentinel lymph nodes were negative for carcinoma. The TNM classification was considered to be pT1isN0M0, Stage 0 because the present WHO classification treats EPC as ductal carcinoma in-situ.

**Immunohistochemical findings**

Immunostains for alpha smooth muscle actin, p63 (Figure 3A), cytokeratin 14 (Figure 3B), CD10, S-100 protein and calponin (Figure 3C) showed absence of myoepithelial cells within the papillary structures and at the periphery of the tumour. Myoepithelial cells were present in the normal breast tissue immediately adjacent to the tumour. The apocrine cells within the neoplasm were diffusely positive for GCDFP-15 (Figure 3D). Stains for ER and PR were negative and the adjacent normal breast ducts showed adequate internal control staining for these markers. The nuclei of tumour cells showed diffuse labeling for androgen receptor.

**FISH findings**

The FISH analysis demonstrated a normal copy number of HER2-neu gene (HER2 total signal number/chromosome 17 total signal number=131/114=1.15).

**DISCUSSION**

The differential diagnosis of encapsulated papillary carcinoma includes papilloma, papilloma with atypia/DCIS, papillary DCIS and solid papillary carcinoma.\(^5\) In such situations, pathologists should pay attention to the presence and distribution of myoepithelial cells. In papilloma, papilloma with atypia/DCIS and papillary DCIS, myoepithelial cells are present at the periphery of involved spaces, whereas EPC lacks myoepithelial cells at its periphery.\(^5,6\) Recently, a diminished number or

![FIG. 3: Immunohistochemical findings. (A) Immunostaining for p63. Myoepithelial cells are absent in the papillae and at the periphery of the tumour. In the normal adjacent breast tissue, p63-positive myoepithelial cells are present. (B) Immunostain for cytokeratin 14 showing absence of myoepithelial cells in the tumour. (C) Immunostain of calponin shows the absence of myoepithelial cells in the papillae and at the periphery of the tumour. (D) The cytoplasm of tumour cells shows positive labeling for GCDFP-15 confirming their apocrine nature.](image-url)
complete absence of myoepithelial cells has been reported in metaplastic and neoplastic apocrine lesions of the breast.7-9 ASMA, calponin or S-100 protein seems to be more sensitive than p63 or CD10 for the detection of myoepithelial cells in benign apocrine papillary lesions of the breast.9 In the present case, no myoepithelial cells were identified even using all these markers. The fact that myoepithelial cells diminish in benign apocrine lesions creates a diagnostic pitfall in the diagnosis of EPC-A. Regrettably, there are no definite diagnostic markers that enable one to distinguish between benign and malignant non-infiltrative apocrine lesions. Pathologists need to pay attention to the presence of a monotonous epithelial cell proliferation, architectural and cytological atypia, presence of mitoses and the tumour size.10,11 In the present case, the tumour demonstrated cribriform structures, bridges and a focal solid growth pattern. The apocrine cells were monotonous in some areas, but in other areas showed marked cytological atypia, and contained some mitoses. The size exceeded 2.5cm in maximum diameter. As a result, we considered this tumour to be a neoplasm rather than a hyperplastic or metaplastic lesion. Furthermore, this tumour has the area of significant cytologic atypia that exceeds benignity and suggests malignancy, as shown as Figure 2D. As the tumour predominantly consists of apocrine cells with papillary configuration and immunohistochemically lack myoepithelial cells at both inside and at the periphery of the tumour, we finally diagnosed this tumour as an EPC-A. Whether EPC is an in-situ or invasive carcinoma is controversial. The immunohistochemistry for type IV collagen is not helpful in the evaluation of invasion.12 The absence of myoepithelial cells at its periphery suggests that ECP is an invasive carcinoma with an expansive or “pushing” growth pattern. Such an architecture probably confers a less aggressive behaviour compared with carcinomas that have the usual irregularly infiltrative growth pattern. Nevertheless, when small (<2.0 cm) and low-grade, EPC pursues an indolent clinical course with adequate local therapy alone.5,6 However, clinicians should recognize that EPC rarely involves lymph nodes and can recur locally.12 Accordingly, clinical follow-up after surgery is required. It is important to note that none of the cases of ECP-A studied to date have recurred or metastasized.

To date, there are only eight reported cases of EPC-A in the literature available to us.3-4 The clinicopathological data of nine cases including the present case are summarized in Table 1. Although ECP-A appears to have an indolent clinical behaviour, it has a triple-negative immunophenotype in contrast to the ER/PR+ve luminal A profile of ECP of usual type.2-4 Accordingly, standard hormonal therapy has no role in the management of EPC-A. The potential use of anti-androgen therapy has not been studied and would not be recommended in view of the indolent behaviour of this variant of apocrine carcinoma.

Recently, claudin-low and molecular apocrine subtypes of triple-negative cancer have been described.13-15 The molecular apocrine signature is associated with expression of the androgen receptor (AR) pathway.13,14 The combination of AR and MEK or Cdc25A inhibitors may be a therapeutic option in molecular apocrine breast cancer.16,17 In order to elucidate the clinical and pathological differences between the apocrine and usual types of encapsulated

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TABLE 1: Summary of nine cases of encapsulated papillary carcinoma, apocrine type, of the breast

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr)</th>
<th>Association of DCIS or IC</th>
<th>Follow-up (month)</th>
<th>Present status</th>
<th>Reporter</th>
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</thead>
<tbody>
<tr>
<td>1</td>
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<td>36</td>
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<td>Seal et al.</td>
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<td>41</td>
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<td>AWOD</td>
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<tr>
<td>5</td>
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<td>3</td>
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</tr>
<tr>
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<td>Calderaro et al.</td>
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<tr>
<td>8</td>
<td>?</td>
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<td>ND</td>
<td>ND</td>
<td>Calderaro et al.</td>
</tr>
<tr>
<td>PC</td>
<td>68</td>
<td>-</td>
<td>11</td>
<td>AWOD</td>
<td>Kuroda et al.</td>
</tr>
</tbody>
</table>

PC, present case; DCIS, ductal carcinoma in situ; IC, invasive carcinoma; ND, not described; AWOD, alive without disease.
papillary carcinoma of the breast, study of a larger number of cases by standard and molecular techniques and with clinical follow-up data will be required.

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REFERENCES


