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APOCRINE GLAND CARCINOMA OF AXILLA AND AN IPSILATERAL CONCURRENT BREAST CANCER

Lee JS\textsuperscript{1}, Kim YM\textsuperscript{2}
1. Department of Surgery, Haeundae paik hospital, College of Medicine, University of Inje, Busan, Korea
2. Department of Pathology, Haeundae paik hospital, College of Medicine, University of Inje, Busan, Korea

Correspondence: Dr. Jung Sun Lee. Department of Surgery, Haeundae paik hospital, College of Medicine, University of Inje, Busan, Korea
E-mail: gsjslee@gmail.com


ABSTRACT

When a palpable axillary mass in a young woman is referred to clinicians, the most likely causes are benign adnexal neoplasm, lymphadenitis, rare forms of metastatic breast cancer such as axillary presenting breast cancer, and other metastatic neoplasms. Apocrine carcinoma is a rare, malignant sweat gland neoplasm with apocrine differentiation. We report a case of a 35-year-old woman with a painless tumor in the right axilla concurrent with ductal carcinoma in situ in an ipsilateral breast.

Keywords: Axilla, breast neoplasm, apocrine carcinoma

INTRODUCTION

Apocrine gland carcinoma (AGC) in the axilla is a rare neoplastic disease. The most common locations for this tumor are the upper outer aspect of the breast, the axilla, and the upper arm, where apocrine glands are in the greatest abundance. AGC mimics axillary masses originating from ectopic breast tissue and metastatic breast cancer, particularly in women at ages in which these conditions are most prevalent. There are no distinctive physical findings that allow a clinician to suspect the diagnosis of AGC. Characteristically, these neoplasms are slow growing and present as a single or multilobular solid or cystic mass with red to purple overlying skin discoloration. They may develop at the site of other benign forms of apocrine disease. Because of their indolent nature, most AGCs have synchronous lymph node metastases when first detected. Treatment for AGC is by surgical excision with or without lymph node dissection. Adjuvant radiotherapy and intensive chemotherapeutic regimens may have a role in advanced or disseminated disease. We report a case of an indolent growing unilateral axillary mass concurrent with ductal carcinoma in situ in an ipsilateral breast.
CASE STUDY

A 35-year-old female presented to hospital with a right painless axillary mass that had developed six months earlier. She had undergone excisional biopsy at the right lower inner quadrant for a breast lesion two years ago, which revealed intraductal papilloma with a clear resection margin. She was not followed further after this initial excisional biopsy. Physical exam revealed a healthy, young female with a 2 cm x 1.5 cm x 5 cm mass in the right axilla without limitation of movement in the right shoulder. The mass was mobile and the skin overlying the mass was not changed. No ipsilateral axillary, cervical, or supraclavicular adenopathy was present, nor was contralateral axillary adenopathy. On mammography, dense breast parenchyma was observed, and breast ultrasonography showed a 2 cm hypoechoic mass in the right axilla area with a round shape and distinct margin (Figure 1). Excisional biopsy was done instead of core biopsy because of the very thin accessory breast tissue. Histological examination showed a well differentiated apocrine carcinoma of the axilla with a clear resection margin. Immunohistochemical staining revealed a positive reaction to cytokeratin 7 (CK7) and carcinoembryonic antigen (CEA), and a negative reaction to cytokeratin 20 (CK20). Periodic acid-Schiff (PAS), cytokeratin 5/6 (CK5/6), and gross cystic disease fluid protein (GCDFP) were focally positive. Estrogen receptor was weakly positive and Her-2/neu was negative by immunohistochemical staining (Figure 2). We decided a reoperation after evaluations excluding other origins, including metastatic breast cancer in ectopic breasts and other metastatic carcinomas.

Preoperative laboratory studies, an electrocardiogram, a chest radiograph, and FDG (Fluorodeoxyglucose) – PET/CT (Positron - emission tomography)/ computerized tomography) were unremarkable. Biochemical parameters and tumor markers (CEA; cancer antigen, CA 15-3) were within normal ranges. We evaluated breast magnetic resonance imaging before operation and observed a segmental, heterogeneous non-mass-like enhancement in the ipsilateral lower inner quadrant of the breast (Figure 3A). By second-look ultrasonography, we identified a 2.4 cm-sized indistinct hypoechoic lesion at the right lower inner quadrant of the breast (Figure 3B). Concurrent malignant breast disease could not be excluded, and the patient underwent radioguided breast resection in our institution for non-palpable breast lesions with skin wide excision and axillary lymph node dissection at the ipsilateral axilla. The final pathological report of the breast lesion was ductal carcinoma in situ with papillary type with apocrine change, and metastasis was not found in the 15 dissected lymph nodes (Figure 4). The patient underwent radiation therapy at the breast and axilla, together with tamoxifen adjuvant hormonal therapy for three years, and she has been well without local recurrence or metastasis.
Figure 1. Mammography and ultrasonography showed (A) dense breast parenchyma without axillary mass and (B) a 2.5 cm, well-defined isodense lesion with a round shape in the right axilla.
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Figure 2. Gross view of the right axillary mass (A: X40, Hematoxylin- Eosin stain). The tumor cells in the center exhibit papillary adenocarcinoma with varying degrees of differentiation, contain abundant eosinophilic cytoplasm, and show apocrine-like decapitation (B: X100, C: X200, Hematoxylin-Eosin stain). CEA (D) and CK7 (E) were both positive; GCDFP (F), PAS (G), and ER(H) were focally positive; and Her-2/neu (I) was negative.

Figure 3. Breast MRI (A) and second-look ultrasonography (B) showed a non-mass-like enhancement at fat subtraction image (thick arrow) at the right lower inner quadrant of the breast and an ill-defined hypoechoic lesion (thin arrow) consistent with the MRI finding.
DISCUSSION

AGC is a unique subtype of sweat gland carcinoma that is believed to originate from either normal or modified apocrine glands. Normal apocrine glands are distributed throughout the body but occur most commonly in the axilla, medial aspect of the upper arm, and lateral breast. One hundred cases of AGC have been reported in the literature, with the main site being the axillary area. Most authors have reported a long time interval between the initial identification of a mass and the subsequent diagnosis and initiation of treatment for AGC. In the case reported here, the patient first noted a right axillary mass six months before her most recent operative resection. In general, patients with AGC are usually more than 50 years of age, with a mean age of 57.9 years (range, 25–91 years) in the largest reported series. AGC shows a slight male preponderance (5:4, male: female), with no clearly defined racial or ethnic predilection. It presents as an isolated, asymptomatic, and slow growing lesion that may be firm or cystic. Clinically, there are no characteristic findings to suggest that a particular nodule or cyst may be AGC. In fact, an axillary mass is much more likely to be due to other neoplasms such as metastatic breast carcinoma, metastatic disease from other sites, melanoma, lymphoma, and benign apocrine disease. In the case reported here, the most likely initial clinical diagnoses were axillary presentation of breast cancer in ectopic breast tissue or benign skin neoplasm of the axilla.

Histologically, normal apocrine cells are easily identified by large lumens, prominence of secretory granules, occasional areas of decapitation, and multiple rows of myoepithelial cells longitudinally oriented below cuboidal or secretory cells. In addition,
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Apocrine cells possess oval nuclei, occasional clefts, moderately clumped chromatin, and a large central nucleolus. Mucin is produced within the lumens of normal apocrine cells and appears as PAS-positive and diastase-resistant coarse granules within the cytoplasm. In contrast, AGC cells are much larger than normal apocrine cells, may contain iron-positive granules within the cytoplasm, and exhibit poor glandular formation with varying degrees of differentiation within the same tumor. Histologic glandular patterns include papillary, complex glandular, anastomosing tubular, solid cellular sheets, and cord-like infiltration with desmoplasia. In addition to distinguishing AGC from other benign and malignant forms of sweat gland neoplasm, primary axillary AGC must be distinguished from metastatic breast cancer, carcinoma arising in ectopic breast tissue, and extramammary Paget’s disease. Unique features that would favor the diagnosis of AGC include the presence of mature apocrine glands high in the dermis, a transitional zone between normal and neoplastic glands, and the presence of intracytoplasmic iron granules. The most reliable histologic criteria for identifying apocrine skin carcinoma appear to be decapitation secretion, PAS-positive and diastase-resistant coarse granules within the cytoplasm, and immunoreactivity with GCDFP 15. Apocrine carcinoma cells expressed common epithelial antigens (cytokeratins, CEA, and epithelial membranous antigen), tumor-associated antigens (CEA and B72.3), and histiocytic-secretive antigens (Leu-M1, lysozyme, LN5, alpha-1-antitrypsin, and alpha-1-antichymotrypsin). The histologic diagnostic difficulties associated with unusual axillary apocrine carcinoma of the skin have previously been reported. GCDFP-15, a putative marker of apocrine differentiation, was found diffusely in AGC.

Sweat gland carcinoma primarily spreads through the lymphatic system; however, hematogenous spread has also been reported. Many patients relapse at the regional lymph node that drains the primary tumor within five years of diagnosis, although the annual local recurrence rate is 28%. The incidence of lymphatic spread correlates with the histologic grade of the tumor and the prognosis. Lungs and bones are the most frequent sites for metastasis. Chemotherapy and radiotherapy have been reported to be ineffective for the treatment of AGC, although formal clinical data are not available. The majority of information comes from case reports. Wide excision is critical. More than half of the reported patients with apocrine carcinoma had lymph node metastases at the time of diagnosis. Therapeutic lymph node dissection is indicated for confirmed lymph node metastases and may have a role in the setting of a large or highly aggressive tumor with narrow surgical margins, while prophylactic regional lymph node biopsy and dissection is still debatable, despite evidence of lymphatic spread. Considering their clinical behavior, it is important to distinguish AGC from both metastatic adenocarcinoma (mainly of the breast) and benign apocrine tumors. A clinical history of a long-standing mass, superficial location, and histologic detection of adjacent sweat glands favors a primary cutaneous origin. Likewise, specific immunohistochemical findings, such as PAS-positive, diastase-resistant material in the cells or lumina, and positive staining for GCDFP-15 support the diagnosis of AGC. This is the first reported case of apocrine carcinoma of axilla concurrent with breast ductal carcinoma in situ, and it emphasizes the importance of differentiating the origin of an axillary mass, especially with apocrine features in ductal carcinoma in situ.
COMPETING INTERESTS

The author declares that there is no competing interest.

REFERENCES