Axillary carcinoma with apocrine differentiation: a case report

Rina Fujiwara-Tani 1, Junji Hashizume 2, Masayuki Ikeda 3, Kaori Hanaoka 3 and Hiroki Kuniyasu 1 *

1 Department of Molecular Pathology, Nara Medical University, 840 Shijo-cho, Kashihara, Japan
2 Department of Surgery, Miyoshi Central Hospital, 10531 Higashisakaya-cho, Miyoshi, Japan
3 Department of Pathology, Miyoshi Central Hospital, 10531 Higashisakaya-cho, Miyoshi, Japan

Abstract
An 87-year-old man presented with a 3.2-cm-sized tumor in the subcutis at the left axillary region with skin erosion and multiple lymph node metastases. Histologically, the excised tumor consisted of small solid nests of proliferation at high density. Partially, tumor cells with wide eosinophilic cytoplasm formed solid aggregations. The tumor resembled an invasive ductal carcinoma with apocrine differentiation derived from the axillary accessory breast based on the lack of decapitation secretion, abnormal accumulation of p53, and smooth muscle actin-positive stroma.

Correspondence to:
Hiroki Kuniyasu, Department of Molecular Pathology, Nara Medical University, 840 Shijo-cho, Kashihara, 634-8521, Japan, E-mail: coominh@zb4.so-net.ne.jp

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Apocrine differentiation is a rare type of breast cancer that is distinguished by its histological features, particularly the presence of glandular structures and decapitation secretion. This case report describes a patient with axillary carcinoma with apocrine differentiation, highlighting the diagnostic challenges and the importance of histopathological examination.

**Histopathological Findings**

- **Gross Appearance:** A dip on the skin surface with erosion was observed. The excised axillary tumor was located in the dermis and subcutaneous adipose tissue with ill-demarcated boundaries, suggesting a highly malignant phenotype. Lymph node metastases were present in 69% of cases.
- **Histological Features:** The tumor comprised dense proliferation of solid nests. Tumor cells with wide, eosinophilic cytoplasm suggested the presence of glandular structures. Venous and lymphatic-duct infiltration was observed, indicating a high risk of metastasis.
- **Immunohistochemistry:** The tumor tested positive for p53 and was accompanied by SMA-positive stroma. Ki-67 positivity was observed in approximately 60% of tumor cells, indicating high proliferation activity. Approximately 6% of tumor cells were positive for estrogen receptor (ER) and AR, whereas <30% of these were positive for ER, PgR, and HER2. GCDFP-15 expression was high in AAC, with decreases in ER and PgR expression. AR overexpression in TNBC suggests an apocrine cancer.
- **Imaging:** Hematoxylin & eosin (HE)-stained photomicrogram showed infiltrating duct cancer with apocrine characteristics.

**Discussion**

While most histological types of breast malignancies are reported in ABC, AAC is rare, characterized by a highly malignant phenotype. Lymph node metastases are detected at the time of diagnosis in 80% of cases, and 14% of these are T4. The diagnosis of AAC also tends to be delayed by more than an average of 40 months. It is difficult to distinguish between AAC and AC, but definitive diagnostic factors for distinguishing between AAC and AC are not yet conclusive.

- **Risk Factors:** Male breast cancer is detected at advanced age in comparison with female breast cancer. AAC is decapitation secretion in eosinophilic epithelial cells. Based on immunohistochemical examination, AACs test positive for GCDFP-15. Regarding receptors, 36% of AACs are positive for AR, whereas <30% of these are positive for ER, PgR, and HER2. However, those with breast cancer also express GCDFP-15 at a high rate with 95% specificity and 74% sensitivity.

**Conclusion**

While AAC is rare, it is important to recognize its characteristics for accurate diagnosis and treatment. The presence of glandular structures and decapitation secretion is a key feature, and immunohistochemical examination is crucial for distinguishing AAC from other histological types of breast cancer.

**References**

1. Fujiwara-Tani R (2018) Axillary carcinoma with apocrine differentiation: a case report. Clin Diagn Pathol, 2018 doi: 10.15761/CDP.1000127
2. Male breast cancer is detected at advanced age in comparison with female breast cancer. Many ABCs are found in women aged ≥ 40 years. Moreover, AAC occurs in those with an average age of 67 years, and the sex ratio is equal. The present case was also of an 87-year-old, elderly patient.
3. Family history of breast cancer, obesity, excessive alcohol consumption, and liver cirrhosis are the most common risks for male breast cancer. Some male breast cancers occur in those who carry gene abnormalities, such as BRCA2 mutations and Klinefelter’s syndrome. In our case, the patient did not exhibit these risk factors.
4. The diagnosis of male breast cancer often occurs late, when the stage is advanced. Lymph node metastases are detected at the time of diagnosis in 80% of cases, and 14% of these are T4. The diagnosis of AAC also tends to be delayed by more than an average of 40 months. In contrast, AAC shows a highly malignant phenotype; lymph node metastases are present in 69% of cases. In the present case, the patient was diagnosed several years after he noticed a subcutaneous tumor, which caused dermal invasion and multiple lymph node metastases.
5. While most histological types of breast malignancies are reported in ABC, 70–80% of ABCs are invasive ductal carcinoma (IDC). In male breast cancer, 80–90% of cases express hormone acceptors and 10% of cases express HER2. Our case was triple-negative, but positive for AR.
6. The most important histopathological finding for the diagnosis of AAC is decapitation secretion in eosinophilic epithelial cells. In the present case, glandular structures were not observed and decapitation secretion was not observed.
7. Based on immunohistochemical examination, AACs test positive for GCDFP-15. Regarding receptors, 36% of AACs are positive for AR, whereas <30% of these are positive for ER, PgR, and HER2. However, those with breast cancer also express GCDFP-15 at a high rate with 95% specificity and 74% sensitivity.
8. Furthermore, AR is positive in 60% of all cases of breast cancer and 13% of triple-negative breast cancers (TNBCs). In apocrine metaplasia and apocrine carcinoma, AR overexpression is associated with decreases in ER and PgR expression. In addition, AR expression in ER-negative breast cancer relates to apocrine differentiation. AR expression in TNBC suggests an apocrine cancer.
9. From these, the expressions of GCDFP-15 and AR are not definitive diagnostic factors for distinguishing between AAC and AC. In contrast, 46% of the AC components in breast cancer are positive for p53 [23], the incidence of which is higher than the p53-positivity rate being 15% in AAC [16]. In addition, in breast cancer, SMA-positive stroma formation results from cancer-associated fibroblasts and SMA-positive stroma. In this case, the tumor tested positive for p53 and was accompanied by SMA-positive stroma.
10. As mentioned above, it is difficult to distinguish between AC and AAC based on patient backgrounds or clinical images. In addition, the characteristics of both greatly resemble each other upon examination of histopathology and immunohistochemistry. The present case was considered to be of an invasive ductal carcinoma with apocrine differentiation derived from the axillary accessory breast based on the lack of decapitation secretion, abnormal accumulation of p53, and SMA-positive stroma. However, tumor excision was performed in male.
ABC and AAC; the response to chemotherapy is not optimistic [7,10]. The overall survivals of ABC and AAC are 40.5 and 51.5 months, respectively [7,10].

References
1. Fentiman IS, Fourquet A, Hortobagyi GN (2006) Male breast cancer. Lancet 367: 595-604.
2. Gomez-Raposo C, Zambrana Tevar F, Sereno Moyano M, Lopez Gomez M, Casado E (2010) Male breast cancer. Cancer Treat Rev 36: 451-7. [Crossref]
3. Evans DM, Guyton DP (1995) Carcinoma of the axillary breast. J Surg Oncol 59: 190-195. [Crossref]
4. Wysokinska EM, Keeney G (2014) Breast cancer occurring in the chest wall: rare presentation of ectopic milk line breast cancer. J Clin Oncol 32: e35-36. [Crossref]
5. Harris JR, Lippman MR, Morrow M, Osborne CK (2014) Diseases of the breast. (5th Edn) Conshohocken: Wolters Kluwer Health Adis.
6. Schneider S, Sariego J (2009) Male breast cancer presenting as an axillary mass: a case report and literature review. South Med J 102: 736-737. [Crossref]
7. Hollowell KL, Agle SC, Zervos EE, Fitzgerald TL (2012) Cutaneous apocrine adenocarcinoma: defining epidemiology, outcomes, and optimal therapy for a rare neoplasm. J Surg Oncol 105: 415-419. [Crossref]
8. Seong MK, Kim EK, Han K, Seol H, Kim HA, et al. (2015) Primary apocrine sweat gland carcinomas of the axilla: a report of two cases and a review of the literature. World J Surg Oncol 13: 59. [Crossref]
9. Liukkonen S, Saarto T, Maenpaa H, Maenpaa R, Sjostrom-Mattson J (2010) Male breast cancer. A comprehensive historical literature review. J Surg Oncol 64: e11. [Crossref]
10. Liukkonen S, Saarto T, Maenpaa H, Sjostrom-Mattson J (2010) Male breast cancer. Arch Pathol Lab Med 134: e11. [Crossref]
11. Agrawal A, Ayantunde AA, Rampaul R, Robertson JF (2007) Male breast cancer: a review of clinical management. Breast Cancer Res Treat 103: 11-21.
12. Nihon-Yanagi Y, Ueda T, Kameda N, Okamura S (2011) A case of ectopic breast cancer with a literature review. Arch Pathol Lab Med 125: 1372-1374. [Crossref]
13. Shin SJ, Sheikh FS, Allenby PA, Rosen PP (2001) Invasive secretory (juvenile) carcinoma arising in ectopic breast tissue of the axilla. Arch Pathol Lab Med 125: 1372-1374. [Crossref]
14. Robson A, Lazar AJ, Ben Naji J, Hanby A, Grayson W, et al. (2008) Primary cutaneous apocrine carcinoma: a clinicopathologic analysis of 24 cases. Am J Surg Pathol 32: 682-690. [Crossref]
15. Paties C, Taccagni GL, Papotti M, Valente G, Zangrandi A, et al. (1993) Apocrine carcinoma of the skin. A clinicopathologic, immunocytochemical, and ultrastructural study. Cancer 71: 375-381. [Crossref]
16. LeLL LP, Dias-Santagata D, Pawlak AC, Cosper AK, Nguyen AT, et al. (2012) Apocrine-ecrine carcinomas: molecular and immunohistochemical analyses PLoS One 7: e47290.
17. Fiel MI, Cerami A, Burstein DE, Batheja N (1996) Value of GCDFP-15 (BRST-2) as a specific immunocytochemical marker for breast carcinoma in cytologic specimens. Acta Cytol 40: 637-41. [Crossref]
18. Wick MR, Lillemoe T, Copland GT, Swanson PE, Manivel JC, et al. (1989) Gross cystic disease fluid protein-15 as a marker for breast cancer: immunohistochemical analysis of 690 human neoplasms and comparison with alpha-lactalbumin. Hum Pathol 20: 281-287. [Crossref]
19. Rakha EA, El-Sayed ME, Green AR, Lee AH, Robertson JF, et al. (2007) Prognostic markers in triple-negative breast cancer. Cancer 109: 25-32. [Crossref]
20. Gatalica Z (1997) Immunohistochemical analysis of apocrine breast lesions. Consistent over-expression of androgen receptor accompanied by the loss of estrogen and progesterone receptors in apocrine metaplasia and apocrine carcinoma in situ. Pathol Res Pract 193: 753-758. [Crossref]
21. Niemeier LA, Dabbs DJ, Beriwal S, Striebel JM, Bhargava R (2010) Androgen receptor in breast cancer: expression in estrogen receptor-positive tumors and in estrogen receptor-negative tumors with apocrine differentiation. Mod Pathol 23: 205-212. [Crossref]
22. Tsurumi Y (2012) Apocrine carcinoma as triple-negative breast cancer: novel definition of apocrine-type carcinoma as estrogen/progesterone receptor-negative and androgen receptor-positive invasive ductal carcinoma. Jpn J Clin Oncol 42: 375-386. [Crossref]
23. Moriya T, Sakamoto K, Sasano H, Kawanaka M, Sonoo H, et al. (2000) Immunohistochemical analysis of Ki-67, p53, p21, and p27 in benign and malignant apocrine lesions of the breast: its correlation to histologic findings in 43 cases. Mod Pathol 13: 13-8. [Crossref]
24. Cimpean AM, Raica M, Narita D (2005) Diagnostic significance of the immunoexpression of CD34 and smooth muscle cell actin in benign and malignant tumors of the breast. Rom J Morphol Embryol 46: 123-129. [Crossref]
25. Kojima Y, Acar A, Eaton EN, Mellody KT, Scheel C, et al. (2010) Autocrine TGF-beta and stromal cell-derived factor-1 (SDF-1) signaling drives the evolution of tumor-promoting mammary stromal myofibroblasts. Proc Natl Acad Sci U S A 107: 20009-20014. [Crossref]