Axillary carcinoma with apocrine differentiation: a case report

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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.

Introduction

Male breast cancer is a rare disease; however, male breast cancer derived from an accessory breast is an extremely rare entity. Moreover, apocrine sweat gland-derived adenocarcinoma is also extremely rare. Herein, we report a case of axillary carcinoma with apocrine differentiation in an elderly male patient, for which a differential diagnosis between axillary breast cancer and apocrine gland adenocarcinoma was needed.

Case presentation

An 87-year-old man was aware of an induration in his left axillary region for several years. Because the induration gradually increased to produce skin erosion, he visited Miyoshi Central Hospital.

A hard, subcutaneous tumor with an ill-demarcated border 3 cm in diameter was palpable in the left axillary skin. The tumor adhered to the skin, and an erosion was found in the center of the lesion. No tumor was felt bilaterally on the breast.

Computed tomography revealed multiple metastases to the lymph nodes in the left axillary and subclavian regions. Histopathological examination of a punch biopsy specimen showed invasive proliferation of tumor cells, which formed solid nests and strands. Tumor resection was performed under suspicion of accessory breast-derived carcinoma or cutaneous adnexal cancer. Considering his age and the presence of lymph node metastases, lymph node dissection was not performed.

Histopathological examination of the resected specimen revealed tumor cells that formed small solid nests and were proliferating at high density in the range of a diameter of 3.2 cm. No glandular structures were detected in the tumor. Partially, tumor cells with wide eosinophilic cytoplasm formed solid aggregations.

Tumor cells showed invasion into the epidermis, eccrine sweat glands, and subcutaneous fat tissue. Frequent lymphatic vessel infiltrations were recognized. The apocrine sweat gland was not observed in the whole specimen. Immunohistochemical examination revealed positive staining of the tumor cells for AE1/AE3, cytokeratin (CK) 7, androgen receptor (AR), in addition to gross cystic disease fluid protein 15 (GCDFP-15) in most tumor cells. In addition, p53 and Ki-67 were positive in 62% and 6% of the tumor cells, respectively. Meanwhile, the tumor tested negative for estrogen receptor (ER), progesterone receptor (PgR), and human epidermal growth factor receptor 2 (HER2). Smooth muscle actin (SMA)-positive tumor cells were not detected; however, SMA-positive fibers were observed in the tumor stroma. In the surrounding non-cancerous dermis, SMA-positive fibers were not found. In addition, tumor cells tested negative for CK 5/6, human melanoma black (HMB) 45, p63, vimentin, S100, cluster of differentiation (CD) 68, and CK 20.

From the histopathological findings, the patient was thought to harbor triple-negative invasive ductal carcinoma with apocrine differentiation derived from an accessory breast at the axilla. For residual cancer, chemoradiotherapy is considered (Figures 1 and 2).

Discussion

Differential diagnosis between apocrine adenocarcinoma (AAC) and apocrine-type breast cancer is the most important aspect in this case. In nosology, AAC refers to primary cutaneous apocrine sweat gland carcinoma, whereas apocrine carcinoma (AC) refers to the subtype with apocrine differentiation of breast cancer (Molina, WHO).

Male breast cancer comprises <1% of all breast cancers; [1,2] accessory breast cancer (ABC) composes 0.3% of all breast cancer cases

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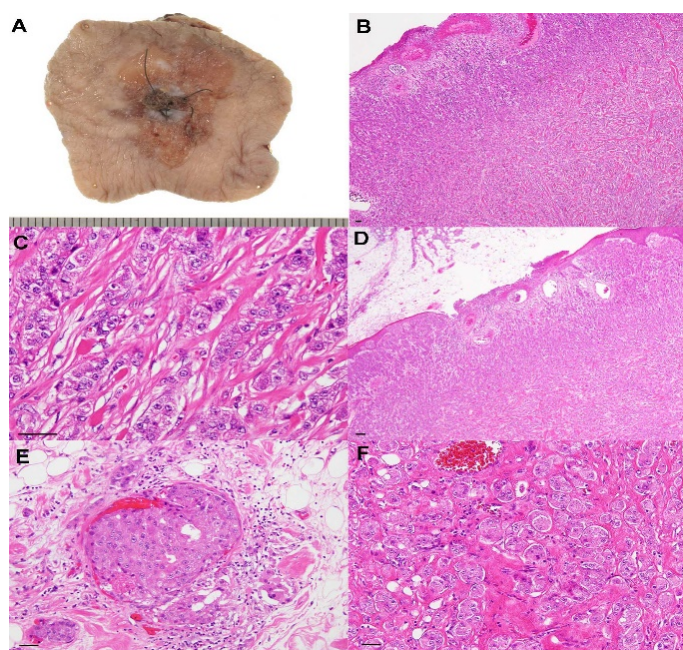
Figure 1. (A) Gross appearance of the excised axillary tumor. At the skin surface, a dip with erosion is observed. (B-F) Hematoxylin & eosin (HE)-stained photomicrogram. (B) The ill-demarcated tumor was located in the dermis and subcutaneous adipose tissue (4×). (C) The tumor comprised dense proliferation of solid nests (40×). (D) Tumor cells were invading the epidermis to form erosion (10×). (E) Venous and lymphatic-duct infiltration of the tumor was found (20×). (F) Tumor cells with wide, eosinophilic cytoplasm suggested apocrine differentiation (20×). Bar, 50 μm.
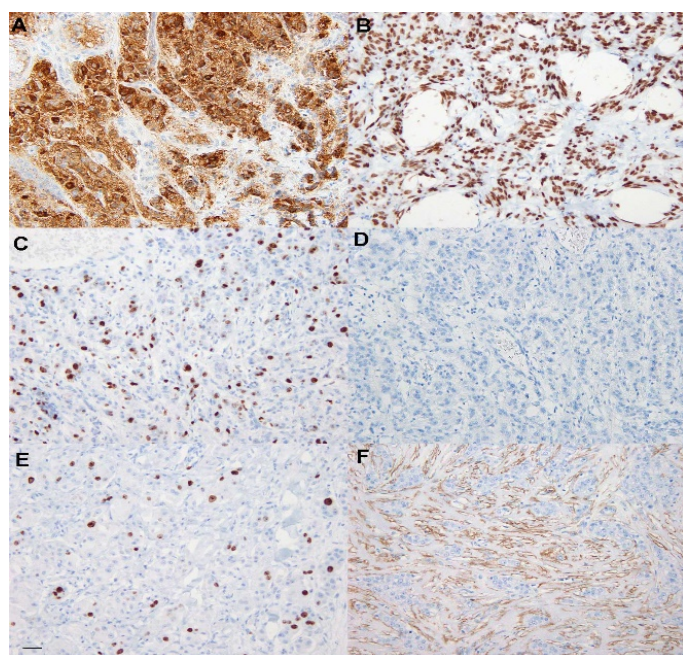
Figure 2. (A) Most of the tumor cells tested positive for gross cystic disease fluid protein-15 (GCDFP-15). (B) Most of the tumor cells tested positive for androgen receptor (AR). (C) Approximately 60% of the tumor cells tested positive for p53. (D) The tumor cells tested negative for estrogen receptor (ER). (E) Approximately 6% of the tumor cells tested positive for Ki-67. (F) Smooth muscle actin (SMA)-positive fibers were found in the tumor stroma, but not in non-cancer invaded dermis. Bar, 50 μm.

[3,4]. Most ABCs are derived from accessory breast tissue existing on the so-called milk line [5]; 70% of ABCs are located in the armpit [3,4]. ABCs in men are extremely rare. There are only several cases of male axillary breast cancer reported previously [6]. AAC is also rare,

the incidence of which is 0.0173 cases/100,000 persons per year in the whole body [7], and only 50 cases have been reported previously [8].

Male breast cancer is detected at advanced age in comparison with female breast cancer [2,9]. Many ABCs are found in women aged ≥ 40 years [10]. Moreover, AAC occurs in those with an average age of 67 years, and the sex ratio is equal [7]. The present case was also of an 87-year-old, elderly patient.

Family history of breast cancer, obesity, excessive alcohol consumption, and liver cirrhosis are the most common risks for male breast cancer [9]. Some male breast cancers occur in those who carry gene abnormalities, such as BRCA2 mutations and Klinefelter's syndrome [11]. In our case, the patient did not exhibit these risk factors.

The diagnosis of male breast cancer often occurs late, when the stage is advanced [2]. Lymph node metastases are detected at the time of diagnosis in 80% of cases, and 14% of these are T4 [9]. The diagnosis of ABC also tends to be delayed by more than an average of 40 months [10]. In contrast, AAC shows a highly malignant phenotype; lymph node metastases are present in 69% of cases [7]. 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.

While most histological types of breast malignancies are reported in ABC [12], 70–80% of ABCs are invasive ductal carcinoma (IDC) [10,13]. In male breast cancer, 80–90% of cases express hormone acceptors [2,9] and 10% of cases express HER2 [9]. Our case was triple-negative, but positive for AR.

The most important histopathological finding for the diagnosis of AAC is decapitation secretion in eosinophilic epithelial cells [14]. In the present case, glandular structures were not observed and decapitation secretion was not observed.

Based on immunohistochemical examination, AACs test positive for GCDFP-15 [15]. Regarding receptors, 36% of AACs are positive for AR, whereas <30% of these are positive for ER, PgR, and HER2 [16]. However, those with breast cancer also express GCDFP-15 at a high rate with 95% specificity and 74% sensitivity [17,18].

Furthermore, AR is positive in 60% of all cases of breast cancer and 13% of triple-negative breast cancers (TNBCs) [19]. In apocrine metaplasia and apocrine carcinoma, AR overexpression is associated with decreases in ER and PgR expression [20]. In addition, AR expression in ER-negative breast cancer relates to apocrine differentiation [21], and AR expression in TNBC suggests an apocrine cancer [22].

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 [24,25]. In this case, the tumor tested positive for p53 and was accompanied by SMA-positive stroma.

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 is 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].

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