Acta Dermatovenerol Croat 2007;15(3):148-151 CASE REPORT

Axillary Apocrine Carcinoma Associated with Apocrine Adenoma and Apocrine Gland Hyperplasia

Tatjana Bujas[1], Ivana Pavić[2], Tanja Leničeк[2], August Mijić[3], Božo Krušlin[2], Davor Tomas[2]

[1]Department of Pathology, Karlovac General Hospital, Karlovac; [2]Ljudevit Jurak Department of Pathology; [3]University Department of Surgery, Sestre milosrdnice University Hospital, Zagreb, Croatia

Corresponding author:
Davor Tomas, MD, PhD
Ljudevit Jurak Department of Pathology
Sestre milosrdnice University Hospital
Vinogradska cesta 29
HR-10000 Zagreb
Croatia
dtomas@kbsm.hr

Received: January 30, 2007
Accepted: July 10, 2007

SUMMARY Apocrine carcinomas represent a rare group of tumors with a potential for destructive local invasion, regional and distant metastases, and are equally common in both sexes. A case of a 79-year-old woman with axillary apocrine carcinoma associated with apocrine adenoma and apocrine gland hyperplasia is presented. To our knowledge, this is the first case diagnosed in a Caucasian and also the first case diagnosed in a female patient. Grossly, the tumor measured 3.2x1.5x1.2 cm and on cut section appeared granular, white to gray-tanned. Microscopically, the tumor was located in the dermis, poorly demarcated, focally necrotic with ulcerated overlying skin. It was predominantly composed of complex, closely packed tubuloglandular structures but in few areas papillary structures were also observed. The cells contained abundant eosinophilic, finely granular cytoplasm with pleomorphic nuclei and showed apocrine-like decapitation. The cytoplasm contained periodic acid Schiff diastase resistant granules. Mitoses were frequent and some were atypical. In one area, the tumor was lobular and composed of tubular structures lined with one layer of uniform cuboidal or columnar eosinophilic cells, indicating a pre-existing apocrine adenoma. Beneath the tumor, in the deep dermis and subcutaneous tissue, hyperplastic apocrine glands were also found. No additional therapy was used, and one year after the surgery the patient was alive and showed no signs of tumor spread. This and previously reported cases suggest that apocrine hyperplasia and apocrine adenoma may represent successive steps in the development of apocrine carcinoma.

KEY WORDS: apocrine carcinoma, apocrine adenoma, apocrine glands hyperplasia

INTRODUCTION

Apocrine carcinomas represent a rare group of tumors with a potential for destructive local invasion, regional and distant metastases. The disease is primarily diagnosed in the fifth to seventh decade of life, with similar incidence in men and women and without racial predilection (1-4). Apocrine carcinoma shows features of apocrine differentiation and most frequently arises in regions

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of high apocrine gland density, especially in the axilla. Rarely, it may also arise in the eyelids (originating from Moll's glands), upper outer aspect of the breast, perianal region and upper arm where apocrine glands are greatest in number (3,4).

The etiology of apocrine carcinoma is unknown. The fact that all patients were over 25 years suggests that full maturity of the apocrine glands is a prerequisite (2).

Herein, we present a case of a 79-year-old woman with axillary apocrine carcinoma associated with apocrine adenoma and apocrine gland hyperplasia.

CASE REPORT

A 79-year-old woman was admitted because of a painless tumor in her left axilla. The tumor had slowly enlarged during the past six months. Physical examination revealed a soft, pink, dome shaped tumor, about 3 cm in diameter, which adhered to the overlying skin and was centrally ulcerated. The cervical, supraclavicular and axillary lymph nodes were without signs of tumor spread. There were no palpable abnormalities of the left breast. Additional studies (ultrasonography and chest x-ray) revealed no primary breast tumor or metastatic disease.

The tumor was radically excised and submitted to pathology. Grossly, the tumor measured 3.2x1.5x1.2 cm and on cut section appeared granular, white to gray-tanned. Microscopically, the tumor was located in the dermis, poorly demarcated, focally necrotic and the overlying skin was ulcerated. It was predominantly composed of complex, closely packed tubuloglandular structures but in few areas papillary structures were also observed (Fig. 1A). The cells contained abundant eosinophilic, finely granular cytoplasm with pleomorphic nuclei and showed apocrine-like decapitation. The cytoplasm contained periodic acid Schiff diastase resistant granules. Mitoses were frequent (up to 15 mitoses *per* 10 high power fields) and some were atypical. In one area, the tumor was lobular and composed of tubular structures lined with one layer of uniform cuboidal or columnar eosinophilic cells, indicating a pre-existing apocrine adenoma (Fig. 1B). Beneath the tumor, in the deep dermis and subcutaneous tissue, hyperplastic apocrine glands were observed (Fig. 1C). Immunohistochemically, tumor cells were positive for cytokeratin and epithelial membrane antigen while carcinoembryonic antigen and S-100 protein were negative. In carcinomatous areas alpha smooth muscle actin was negative (Fig. 1D), while in adenomatous (Fig. 1E) and hyperplastic regions (Fig. 1F) positivity around tubules indicated the presence of myoepithelial cell layer. Adenocarcinomatous and adenomatous cells were negative for estrogen and progesterone receptors and HER2-neu. Ki67 and p53 positivity was 27.3% and 43.2% in adenocarcinoma, and 4.3% and 52.6% in adenoma, respectively.

No additional therapy was administered, and one year after the surgery the patient was alive and showed no signs of tumor spread.

DISCUSSION

Apocrine carcinomas are rare tumors which equally affect both sexes, but to our knowledge, this is the first case of axillary apocrine carcinoma associated with apocrine adenoma and apocrine glands hyperplasia diagnosed in a Caucasian and also the first case diagnosed in a female patient.

Apocrine carcinoma usually grows slowly and presents as painless, solitary or multiple, solid or cystic mass, ranging from 1 to over 8 cm in size (1,2). These lesions tend to vary in color from red to purple, and show ulceration of the overlying skin. There are no distinctive physical findings that would allow a clinician to suspect the diagnosis of apocrine carcinoma and most of them exist for less than one year before a correct diagnosis is made (3-5). Therefore, up to 50% of apocrine carcinomas have synchronous lymph node metastases at the time of diagnosis. Metastatic disease to the lung, skin, bone, brain, and kidney has been described and the disease is invariably fatal at this stage (3,4).

Histologically, apocrine carcinomas are nonencapsulated, infiltrative tumors located in the lower dermis and subcutaneous tissue, and consist of multiple ductal structures. Different growth patterns include papillary, tubular, cribriform, cord-like and solid. Tumor cells are eosinophilic with granular and sometimes vacuolated cytoplasm and contain periodic acid Schiff positive, diastase resistant granules (1). A key diagnostic criterion, decapitation secretion in the form of apical snouts, is usually recognizable but may be lacking in poorly differentiated tumors (2). Mitotic activity is variable, ranging from single mitotic figures in well differentiated tumors to up to 4 mitotic figures *per* high power field. Immunohistochemically, tumor cells usually express cytokeratin, epithelial membrane antigen and gross cystic disease fluid protein-15. Carcinoembryonic antigen is usually negative. Some cases demonstrate positivity for S100 protein (1-4).

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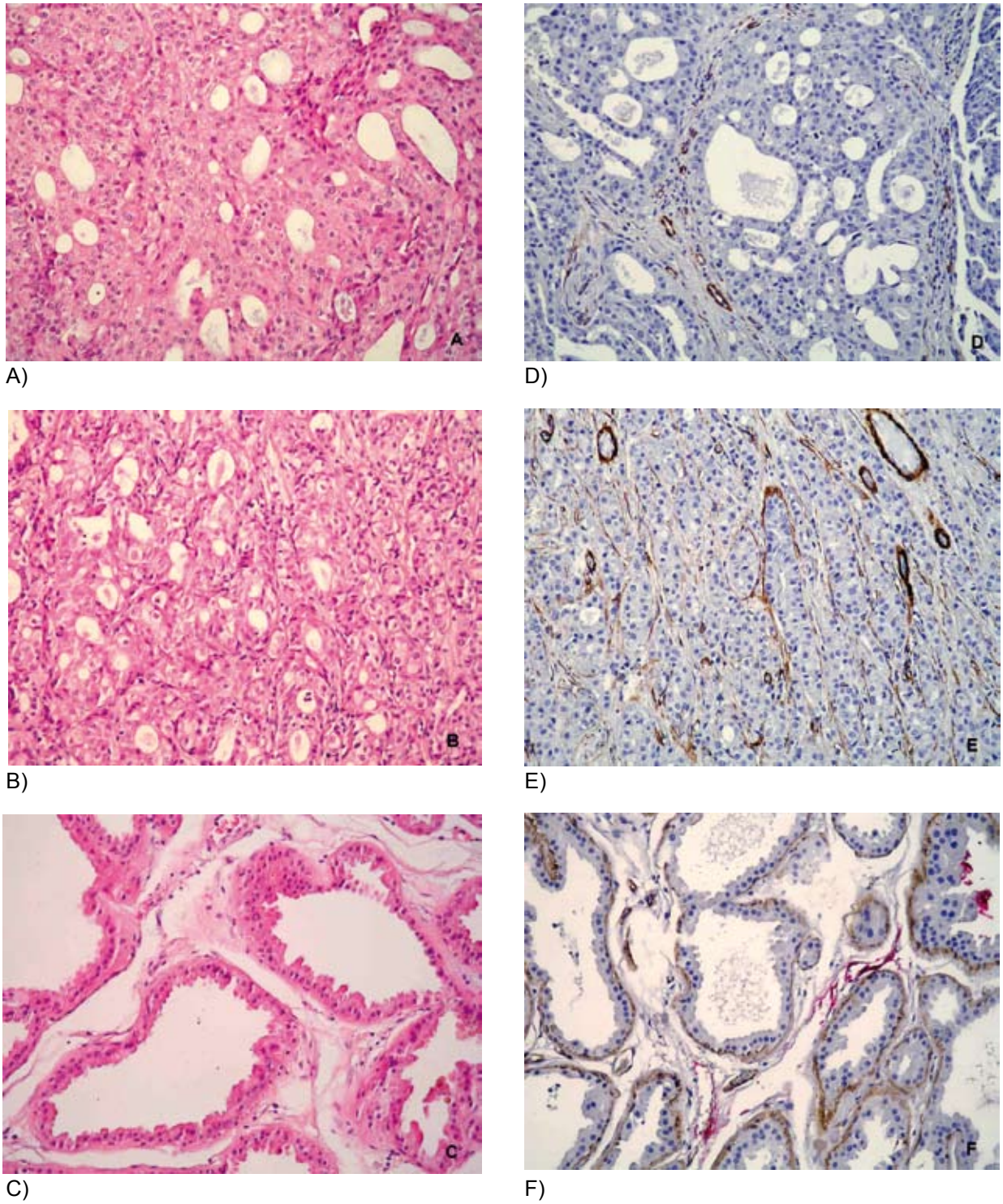

A) D)

B) E)

C) F)

Figure 1. (A) The tumor was predominantly composed of complex, closely packed tubulo-glandular structures. The cells contained abundant eosinophilic, finely granular cytoplasm with pleomorphic nuclei and showed apocrine-like decapitation (X200, HE); (B) in one area, the tumor was lobular and composed of tubular structures lined with one layer of uniform cuboidal or columnar eosinophilic cells, indicating a pre-existing apocrine adenoma (X200, HE); (C) beneath the tumor, in the deep dermis and subcutaneous tissue, hyperplastic apocrine glands were observed (X200, HE); (D) in carcinomatous areas alpha smooth muscle actin was negative (X200, α-SMA), while in adenomatous (E) (X200, α-SMA) and hyperplastic (F) regions (X200, α-SMA) positivity around tubules indicated the presence of myoepithelial cell layer.

The main differential diagnosis is apocrine adenoma, and histologic features that distinguish the two conditions are often subtle (1,2). Necrosis, infiltrative growth pattern, cellular pleomorphism and loss of myoepithelial cells, which is readily demonstrable with immunohistochemical staining for alpha smooth muscle actin or calponin, may provide a clue to malignancy (1-5).

In our case, the tumor was obviously malignant (pleomorphism, high mitotic rate, necrosis, infiltrative growth pattern, loss of myoepithelial cells) but in one area the tumor was lobular and composed of tubular structures lined with one layer of uniform eosinophilic cells, with preserved myoepithelial cells that were immunohistochemically positive for alpha smooth muscle actin. These findings indicate a pre-existing apocrine adenoma in apocrine carcnoma. In the deep dermis and subcutaneous tissue, hyperplastic apocrine glands were also found and the diagnosis of apocrine carcinoma with associated apocrine adenoma and apocrine gland hyperplasia was established.

Wide, local excision with complete removal of the tumor is the standard treatment for these lesions. Therapeutic lymph node dissection is indicated for confirmed lymph node metastases and may have a role in a setting of large or highly aggressive tumor. Apocrine carcinoma poorly responds to chemotherapy but adjuvant radiotherapy may have a role in a setting of advanced or disseminated disease (3,4).

Only five cases of coexistence of malignant and benign apocrine tumors in the axilla have been reported (5-9). All these patients were elderly Japanese men and some speculations, like in cases of triple extramammary Paget's disease (10), that androgens or some environmental factors might play a role in the pathogenesis of these tumors, have been proposed (5). In our case, the patient was a Caucasian and a female. This and previously reported cases (5-9) suggest that in certain cases apocrine hyperplasia and apocrine adenoma represent successive steps in the development of apocrine carcinoma.

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