

Apocrine carcinoma of the face in a 62-year-old Asian man

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Abstract

Apocrine carcinoma (AC) is a rare tumor with heterogeneous presentation. The disease has a highly morbid course and little is known about it. We present an otherwise healthy, 62-year-old Asian male who originally presented with chronic swelling of his left eyelid associated with excessive tears and diminished vision was diagnosed with AC. AC is often challenging to diagnose, yet it is critical to do so as early diagnosis and treatment can maximize patient survival.

Introduction

Apocrine carcinoma, also known as apocrine-gland carcinoma and sweat-gland carcinoma comprises of a group of extremely rare, malignant tumor, which shows features of apocrine differentiation. Uncertainties have surrounded the etiology of apocrine adenocarcinoma. The disease is primarily diagnosed in the fifth to seventh decade of life, with similar incidence in men and women and without racial predilection. Apocrine-gland carcinoma is a rare subtype of sweat-gland carcinoma. The malignancy arises at the sites of apocrine glands, which have a relatively limited distribution in the body and are found in the axillae, the medial aspect of upper arm, areola, lateral aspects of the breasts, ear canals, eyelids, and anogenital region.

Patients usually present with a slow-growing, purple or red skin mass, which can be either firm or cystic in consistency. Morphologically, the tumor is an adenocarcinoma with varying degrees of differentiation composed of cells with eosinophilic cytoplasm.^{1,3-5} Characteristic histopathologic findings include decapitation secretion, a feature considered pathognomonic for apocrine differentiation, Periodic-acid-Schiff-positive material in the cells or lumen, and immunoreactivity with gross cystic disease fluid protein. Normal apocrine glands and apocrine-gland adenomas are often found alongside the tumor and are occa-

sionally infiltrated by carcinoma cells. Apocrine-gland carcinoma spreads via both lymphatic and vascular routes, with metastatic disease found in regional lymph nodes, lungs, liver, and bone. Approximately one-third of patients have regional lymph node involvement at diagnosis; the incidence is higher in patients with higher grade tumors.

The female breast can be conceived developmentally and morphologically as a modified apocrine gland and therefore breast carcinoma with apocrine features can be indistinguishable from cutaneous AC. Breast parenchymal malignancy is more common than skin adnexal carcinoma, and therefore in a woman with a history of breast carcinoma it is customary to consider such a skin neoplasm the result of secondary spread unless it is possible to prove otherwise.

The only curative therapy for localized apocrine-gland carcinoma involves wide local excision with regional lymph node dissection and consideration of postoperative radiotherapy in patients with moderately or poorly differentiated tumors. Early diagnosis is, therefore, critical, and all patients with enlarging masses of unknown etiology in areas of apocrine glands should have excisional biopsies.

Regional lymph nodes are involved in approximately 30-50% of cases. The clinical course is characterized by a high incidence of local recurrence^{2,6} (28% in one report), which is often managed by resection and radiation therapy. Few reports suggest that AC might be radio-sensitive. However, no standard guidelines exist regarding appropriate schedules and doses due to the rarity of the diagnosis. Metastatic disease to the lung, skin, bone, brain, and kidney has been described and the disease is invariably fatal at this stage.

Case Report

A 62-year-old Asian male presented to a satellite hospital with the complaint of excessive tears for more than five years and left eye swelling for two months. Initially, swelling was limited to the left eyelid but progressed rapidly to size of a tennis ball. The swelling was not painful, pruritic or erythematous. The patient denied fever, vision loss, weight loss, or night sweats. Orbital computed tomography (CT) scan demonstrated a localized left orbital mass with suspicion for a tumor. Subsequently, the patient underwent a punch biopsy of the lesion. The biopsy revealed poorly differentiated adenocarcinoma with polygonal tumor cells with large, hyper-chromatic nuclei, prominent nucleoli and abundant eosinophilic cytoplasm (Figures 1-2). Immunohistochemical stains for cytokeratin, EMA, S-100 and PAS were positive. The pathognomonic findings of the decapitation

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secretion (Figure 1) and immunoreactivity with gross cystic disease fluid protein (Figure 2) supported the diagnosis of apocrine adenocarcinoma of skin.

The patient was recommended surgical resection of the tumor but he declined.

He presented again after several months with progressively increasing facial deformity and inability to open his left eye. The physical examination revealed significant periorbital erythema with significant sero-sanguineous discharge from the skin lesion. The patient agreed to surgical resection at this time. Metastatic survey with a bone scan unfortunately revealed multiple areas of uptake throughout the left orbital area. CT head and neck demonstrated a solid mass lesion in the medial part of left lower eyelid and enlarged cervical lymph nodes (Figure 3). Subsequent lymph node biopsy confirmed the presence of metastatic disease.⁷ These results precluded a surgical option. Non-surgical treatment including chemotherapy and radiotherapy was discussed in detail with the patient and he eventually agreed to chemotherapy. The patient received cisplatin 50 mg/m², adriamycin 50 mg/m², and cyclophosphamide 500 mg/m². Clinically, the patient had marked reduction of his left eye lid swelling. Post-chemotherapy CT scan showed a decrease in the size of lymph nodes. Thereafter, he was followed for several months.

A follow-up bone scan and CT scan of the left orbit unfortunately showed worsening disease 2 years later. The patient clinically had progressive proptosis and worsening soft tissue thickening on the left side of his face. The patient was eventually referred to our service

for consideration of enrollment in an experimental clinical trial. The patient was treated on several phase I experimental protocols, but eventually had persistent thrombocytopenia which precluded him from pursuing any additional therapy. The patient's disease started to cross the midline of the face and AC developed in his right eyelid as well. The right eye lid became quickly and progressively swollen causing his right eye to shut. Unfortunately, the patient became incapacitated, as he was

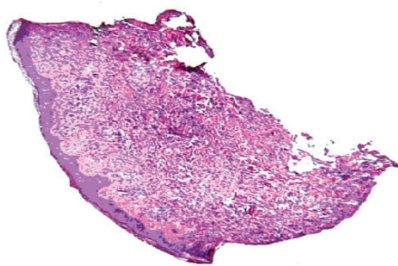


Figure 1. Skin with infiltrating tumor composed of complex glandular structures within dermis (hematoxylin and eosin staining).

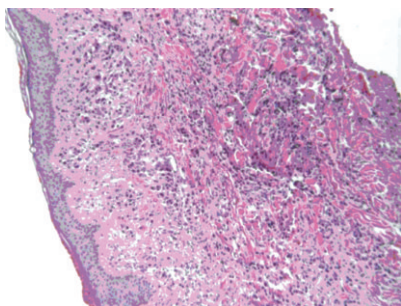


Figure 2. Large eosinophilic cells with prominent nucleoli lining glandular lumen.



Figure 3. Computed tomography scan showing infiltration of tumor.

not able to see out of both eyes; in essence the disease had rendered him blind. AC also was present on his lips and perioral area causing difficulty with eating and swallowing food and liquids. Six years after his initial diagnosis, the patient entered hospice for supportive and palliative care.

Discussion

The management of metastatic AC remains difficult. Case reports have described transient responses to various chemotherapy agents such as,^{1,6,8,9} vincristine, bleomycin, cyclophosphamide and doxorubicin. Bellman *et al.*⁸ described a patient with widely metastatic apocrine-gland carcinoma of the eyelid with an excellent response to systemic 5-Fluorouracil chemotherapy. Mezger J., *et al.*¹⁰ described two patients with sweat-gland carcinoma who responded to combination chemotherapy with doxorubicin, cyclophosphamide, vincristine, and bleomycin. In one of these patients, a complete remission of two years duration was achieved; the other patient had a partial remission of four months duration. Some authors recommend prophylactic node resection.^{5-6,8,11} The prognostic factors for sweat gland carcinoma are difficult to identify, again owing to the small number of reported cases. Clinical trials of therapy, although difficult to conduct in a disease of low prevalence, provide additional options for patients and physicians.

Conclusions

This case illustrates the detailed diagnostic evaluation and the need for high suspicion by the primary physicians to consider apocrine carcinoma of skin as a differential diagnosis for a skin lesion because of the high propensity of this tumor to locally metastasize and the lack of evidence-based clinical guidelines in literature for its management due to the rarity of the tumor. Patients should be highly encouraged to undergo surgical resection, as this often is the only modality of therapy with curative intent. Early diagnosis and aggressive follow-up are important to help improve patient survival.

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