

# Sebaceous Carcinoma With Apocrine Differentiation

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## Abstract

Sebaceous carcinoma is a rare malignant cutaneous adnexal tumor arising most commonly in the eyelids. We are reporting such a case of sebaceous carcinoma showing apocrine differentiation occurring at an extraocular site with in-depth immunohistochemical and molecular studies and briefly reviewing the current approaches to such tumors.

## INTRODUCTION

Sebaceous carcinoma is a rare high grade malignant adnexal neoplasm arising from sebaceous glands. This mostly occurs on the eyelid, where it originates in the tarsal meibomian glands, rarely in the glands of Zeis of the eyelashes or the sebaceous glands of the caruncle. It is often associated with Muir-Torre Syndrome. The purpose of this is to report an extraocular sebaceous carcinoma with apocrine differentiation and to update the immunohistochemical and molecular approaches on this subject.

## CASE REPORT

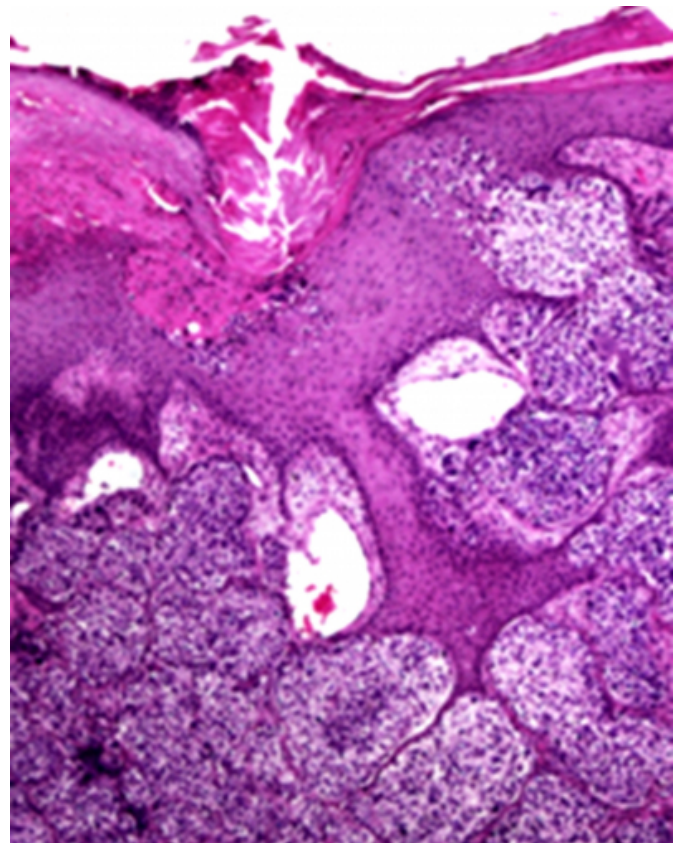
A 69-year-old man presented with a clinically suspected squamous cell carcinoma on the left parotid region of cheek. The patient underwent an excisional biopsy of the lesion followed by a wide-excision with partial parotidectomy.

Gross examination showed a 2.0 X1.5 cm, ulcerated, encrusted, dome-shaped lesion involving skin and subcutaneous tissue. Microscopically (Figs. 1 and 2), the infiltrating neoplasm with vaguely lobular configuration extended from the epidermis to the parotid gland. Many scattered small clusters and irregular tongues of the neoplastic were present in dermis and subcutaneous tissue extending into the parenchyma of the parotid gland. The Pagetoid spread in the epidermis and lymphovascular invasion were evident. The malignant cells had basaloid and clear cell populations, and showed moderate nuclear polymorphism with brisk mitotic activity and apoptosis. Most of nuclei were oval with discernable to prominent nucleoli and nuclear clearing. The cytoplasm was amphophilic to slightly eosinophilic to completely clear with vesicular to bubbly texture. Overt peripheral palisading or keratinization was not seen. There was suggestion of focal

apocrine differentiation.

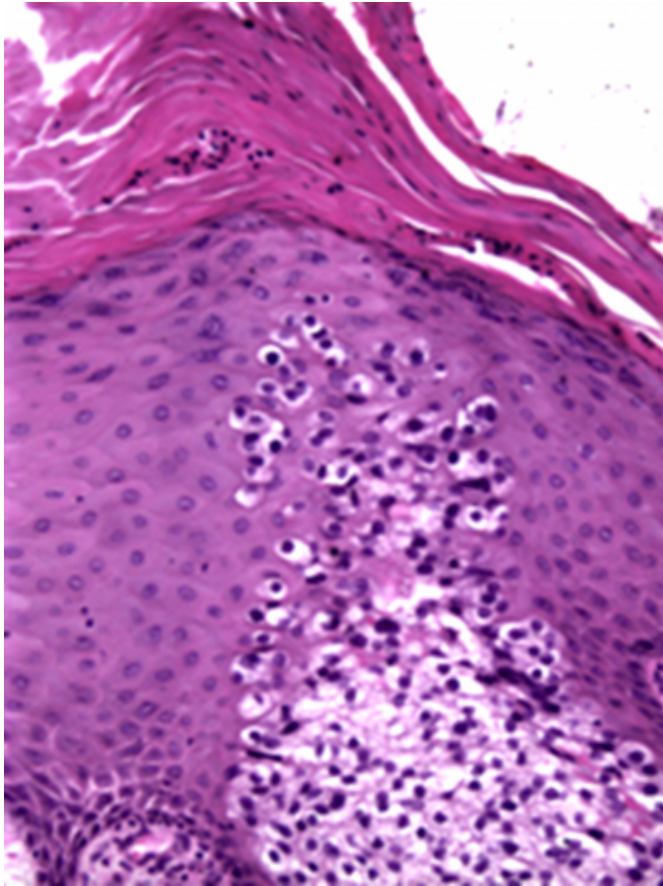
## Figure 1

Figure 1: Sebaceous carcinoma of skin.



### Figure 2

Figure 2: Sebaceous carcinoma showing intraepidermal spread.



The immunostains and RT-PCR were performed on formalin fixed and paraffin embedded specimen. The tumor cells were immunoreactive for EMA, BerEp-4, CK7, and, AE1/3 with variable positive stains of Androgen receptor, CK8/18, and Vimentin, but were negative for immunostains of S100, HMB45, CK20, TTF-1, RCC, and PSA. The neoplastic cells from the foci of apocrine differentiation were immunoreactive for GCDFP-15 and CK8/18. Immunostains for mismatch repair genes including hMLH1, hMSH2, hMSH6, PMSH2 and RT-PCR for microsatellite instability studies including MSI (T) and MSI(C) were negative suggesting the absence of Muir-Torre syndrome or hereditary non-polyposis colorectal cancer (HNPCC) or Lynch syndrome.

### DISCUSSION

The sebaceous carcinoma is a very rare malignant tumor primarily found in the area of the eyelid with approximately 25% occurring in the extraocular location. It occurs predominantly in female ( 2:1 of female versus male ratio) at an average age of 65 years. The tumor usually presents as a

slowly growing, firm, and painless mass. Its prognosis is much worse than those of most cutaneous malignancies except for malignant melanoma due to local recurrences and distant metastases.

Poorly differentiated sebaceous carcinoma is difficult to differentiate from other cutaneous malignancies histopathologically. Androgen receptor has been recently shown as a sensitive and reliable marker for sebaceous differentiation (1). Androgen receptor antibody (AR) with anti-breast carcinoma associated antigen-225 (CU18) and anti-CA15.3 antibody (CA15.3) (The latter two antibodies are currently unavailable commercially) are able to identify sebocytes and seboblasts (2). Sebaceous carcinoma with apocrine differentiation is even more rarely seen, but it is readily understandable because the malignancy originates from the embryonal folliculosebaceous-apocrine unit (3).

Sebaceous carcinoma is often associated with Muir-Torre syndrome and hereditary non-polyposis colorectal cancer (HNPCC) or Lynch syndrome. Muir-Torre syndrome is an autosomal dominant disorder with variable penetrance that consists of at least one sebaceous gland tumor (adenoma, epithelioma, or carcinoma) and a minimal one internal malignancy such as colorectal carcinoma, genitourinary neoplasm or breast carcinoma. In a subgroup of Muir-Torre syndrome patients, the patients have germline DNA mismatch-repair (MMR) defect(s) and microsatellite instability, which is identical to the DNA defect of hereditary non-polyposis colorectal cancer (HNPCC) or Lynch syndrome. Therefore, Muir-Torre syndrome has been postulated as a variant of HNPCC or Lynch syndrome.

Recently, Popnikolow (4) et al have demonstrated that approximately 80% sebaceous gland malignancies lost mismatch repair proteins (either hMLH-1 or hMSH-2) or microsatellite instability. Their data clearly show that the sebaceous gland lesions can often precede or occur concurrently with the visceral neoplasms and strongly imply the significance of detection of MMR and microsatellite instability for appropriate clinical management.

In our patient, we have confirmed the diagnosis of sebaceous carcinoma with histopathologic and immunohistochemical methods. Other immunohistochemical and molecular studies excluded DNA mismatch repair protein defects and microsatellite instability in our patient. A careful distinction of sebaceous carcinoma from other cutaneous neoplasms and a combination of immunohistochemical and molecular approaches may be utilized to rule out germline DNA

mismatch repair defects and microsatellite instability.

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