

# Secretory carcinoma of the skin: Case report and review of the literature



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**M**ammary analogue secretory carcinoma is a primary salivary gland tumor that was first described in 2010, with histologic, immunophenotypic, and genetic features reminiscent of secretory carcinoma of the breast.<sup>1</sup> Both tumors harbor the same defining *ETV6-NTRK3* fusion gene, resulting from the t(12;15) (p13;q25) translocation. Of interest to dermatopathologists, primary cutaneous tumors resembling secretory carcinoma of salivary gland and breast have been recently described in several case reports and a case series. Such cases likely arise from skin adnexa, given the absence of adjacent ectopic breast or salivary tissue, along with subsequent exclusion of extracutaneous involvement. Unlike their salivary gland and breast counterparts, secretory carcinoma originating from skin adnexa have demonstrated inconsistent positivity for the *ETV6* gene rearrangement.<sup>2-4</sup> We describe the first reported case of secretory carcinoma involving the cutaneous surface of the upper lip, harboring the classic genetic signature of its salivary gland and breast secretory carcinoma counterparts.

## CASE REPORT

A 79-year-old man who was a smoker presented to an outside dermatology clinic with a 4-mm pearly telangiectatic papule located on the right upper cutaneous lip. His medical history was notable for basal cell carcinoma and prostate cancer. The clinical impression was of basal cell carcinoma, and a shave biopsy specimen was obtained. The case was received by our institution for consultative opinion.

Microscopic examination revealed a circumscribed epithelial neoplasm within the superficial

dermis, adjacent to normal appearing adnexal structures and overlying unaffected epidermis. A connection to native skin adnexa was not present, nor was salivary gland tissue identified. Solid nests of tumor cells were arranged in a microcystic pattern with intraluminal colloid-like material. Tumor cells had eosinophilic vacuolated cytoplasm with low-grade cytologic atypia and small distinct nucleoli. Neither perineural invasion, lymphovascular invasion, nor necrosis were present. Atypical mitoses were not identified. The lesion extended to the deep biopsy margin (Fig 1).

By immunohistochemistry, neoplastic cells were strongly immunoreactive for mammaglobin and pancytokeratin stains, along with weak positivity for Sox10 and S100. Expression of p63, CD31, and Mart-1 was negative. The histologic and immunophenotypic findings were consistent with secretory carcinoma of skin. *ETV6* gene rearrangement was detected in 44% of nuclei by break-apart fluorescence in situ hybridization with normal cutoff of <12% for separation of the *ETV6* signal. Subsequently, the patient underwent an excision with local flap reconstruction with negative tumor margins. Clinical investigation revealed no evidence of extracutaneous disease.

## DISCUSSION

We report a case of secretory carcinoma in the lip, likely arising from skin adnexa, with *ETV6* gene rearrangement. To our knowledge, this case is the fourteenth description of secretory carcinoma of skin and the first reported occurrence on the cutaneous lip.

Microscopically, secretory carcinoma is a solitary, well-circumscribed, and unencapsulated tumor. The

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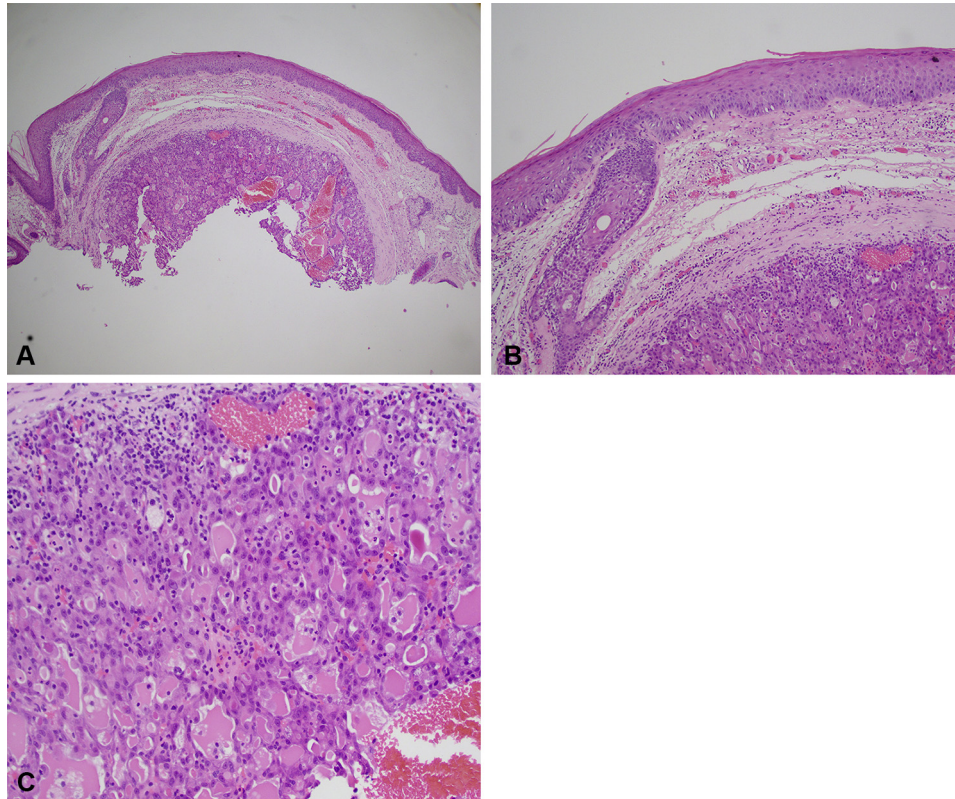
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**Fig 1.** Secretory carcinoma of the skin. **A**, Shave biopsy specimen of skin with a circumscribed epithelial neoplasm located within the dermis. **B**, Tumor adjacent to native skin adnexa. **C**, Solid tumor nests show low-grade cytologic atypia, microcystic pattern, and intraluminal colloid-like secretion. (Hematoxylin–eosin stain; original magnification: **A**,  $\times 40$ ; **B**,  $\times 100$ ; **C**,  $\times 200$ .)

tumor may have variable growth patterns, including combinations of solid, papillary, tubular, and cystic architecture. Neoplastic cells have vacuolated, eosinophilic cytoplasm with round to oval nuclei, vesicular to granular chromatin, and distinct nucleoli. The tumor has characteristic intraluminal secretions comprised of pink colloid-like material. Unless high-grade transformation occurs, secretory carcinoma has a low mitotic rate and lacks necrosis or marked cytologic atypia.<sup>5</sup> Aggressive features, including perineural invasion, lymphovascular invasion, brisk mitotic activity, and necrosis, have not been reported in primary cutaneous cases.

Secretory carcinoma has strong immunostaining for a variety of markers, including mammaglobin, S100, Sox10, CK7, MUC4, GATA-3, GCDFP-15, and STAT5A.<sup>6,7</sup> Mammaglobin, S100, and STAT5A are expressed in nearly all cutaneous secretory carcinomas.<sup>8</sup> However, these markers are not specific. For example, mammaglobin positivity has been reported in cases of sweat gland carcinoma.<sup>9</sup> S100 also stains myoepithelial cells of apocrine tumors.<sup>10</sup>

Secretory carcinoma of skin has been largely reported in the axilla, followed by involvement of

head and neck, flank, and forearm (Table D). Unexpectedly, several cases have not harbored *ETV6* rearrangement and had inconsistent immunophenotypic features with secretory carcinoma of salivary gland.<sup>3</sup> In our patient, tumor cells were found to have the classic *ETV6* rearrangement.

Secretory carcinoma is considered to be a low-grade malignancy. Patients commonly report slow growth of the tumor over a period of years. Cutaneous cases present as a painless nodule or mass. At initial presentation, cutaneous lesions have ranged from 0.4 to 6.0 cm with a mean of 1.4 cm ( $n = 13$ ). Similar to its salivary gland counterpart, cutaneous secretory carcinoma has nearly equal gender predilection and an average age of presentation at 45.3 years ( $n = 14$ ).

In limited available follow-up, tumor recurrence and metastases have not been observed in 8 cases with an average follow-up of 25 months. All cases have been treated with excision, except in 1 case where sentinel lymph node mapping was performed.<sup>4</sup>

Clinical evaluation is necessary to exclude the possibility of extracutaneous involvement. Importantly, high-grade salivary gland secretory

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