

# A Case of Endocrine Mucin-Producing Sweat Gland Carcinoma Co-existing with Mucinous Carcinoma – A Case Report –

Sunhee Chang · Sang Hwa Shim  
Mee Joo · Hanseong Kim  
Yong Kyu Kim<sup>1</sup>

Departments of Pathology and <sup>1</sup>Plastic  
Surgery, Inje University Ilsan Paik  
Hospital, Goyang, Korea

Received : December 11, 2008  
Accepted : June 2, 2009

## Corresponding Author

Sunhee Chang, M.D.  
Department of Pathology, InJe University Ilsan Paik  
Hospital, 2240 Daewha-dong, Ilsanseo-gu, Goyang  
411-706, Korea  
Tel: 031-910-7138  
Fax: 031-910-7139  
E-mail: changsh@paik.ac.kr

An endocrine mucin-producing sweat gland carcinoma (EMPSGC) is a rare skin tumor that most commonly occurs on the eyelids of elderly women. This tumor is morphologically analogous to endocrine ductal carcinoma *in situ* and solid papillary carcinoma of the breast. We describe one case of a 51-year-old male with an EMPSGC co-existing with mucinous carcinoma of the eyelid. The tumor was composed of dilated ducts with a smooth border and was partially filled with a papillary proliferation. Tumor cells were uniform, small-to-medium in size, and oval-to-polygonal with light eosinophilic cytoplasm. Nuclei were bland with diffusely stippled chromatin and inconspicuous nucleoli. Tumor cells expressed chromogranin, synaptophysin, estrogen and progesterone receptors, cytokeratin 7, and epithelial membrane antigen.

**Key Words :** Sweat gland neoplasms; Adenocarcinoma, mucinous; Carcinoma, neuroendocrine

An endocrine mucin-producing sweat gland carcinoma (EMPSGC) is a rare, low-grade sweat gland carcinoma that is morphologically analogous to an endocrine ductal carcinoma *in situ* (E-DCIS)/solid papillary carcinoma of the breast.<sup>1</sup> An EMPSGC is characterized histologically by mucin production, low nuclear grade, and neuroendocrine differentiation. Twenty-three cases of EMPSGCs have been reported in the literature.<sup>1-9</sup> We describe one case of this under-recognized lesion.

## CASE REPORT

A 51-year-old male presented with a small flesh-colored nodule on the left lower eyelid, which had been growing slowly for 2 years. Incisional biopsy was performed. Gross examination found that the specimen was a pale, soft, ovoid nodule, measuring 0.8 cm in diameter. Histological examination of the specimen showed a well-defined tumor. The tumor was composed of a large pool of mucin, which was loculated by thin fibrous septa and contained

small, irregular floating epithelial islands (Fig. 1A). Tumor cells were organized into short cords or small nests within the epithelial islands; some of these had branching and cribriform patterns. Tumor cells were oval-to-cuboidal with a moderate amount of eosinophilic cytoplasm (Fig. 1B). Nuclei were centrally located with mild pleomorphism and diffusely stippled chromatin. These findings were consistent with mucinous carcinoma.

The patient underwent wide excision two months later. Gross examination showed that the specimen was ellipsoid, and measured 1 × 0.7 × 0.3 cm. Histological examination showed that the specimen was a dermal tumor with upward extension along the eccrine duct to the overlying epidermis (Fig. 2A). The tumor was composed of dilated ducts with a smooth border and was partially filled with a papillary proliferation. Tumor cells were uniform, small-to-medium in size, and oval-to-polygonal with light eosinophilic cytoplasm (Fig. 2B). Nuclei were bland with diffusely stippled chromatin and inconspicuous nucleoli. Some of the tumor cells lining the fibrovascular cores of the papillary projections were elongated. Extracellular mucin was observed

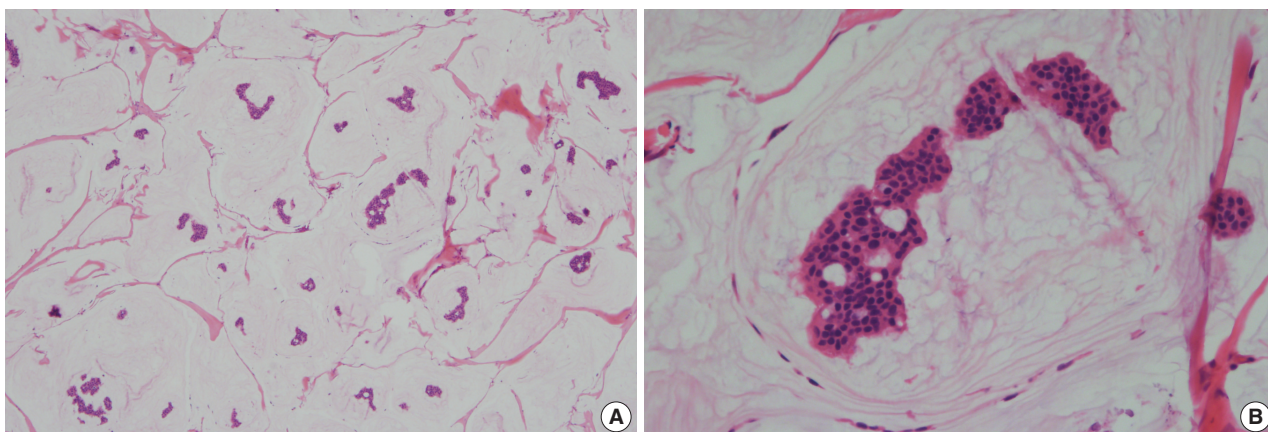


Fig. 1. (A) Epithelial islands float in mucoid material compartmentalized by delicate fibrous septa. Tumor cells are arranged in short cords or small nests, some of which had lumens. (B) Tumor cells are small-to-medium in size with oval-to-round nuclei and eosinophilic cytoplasm.

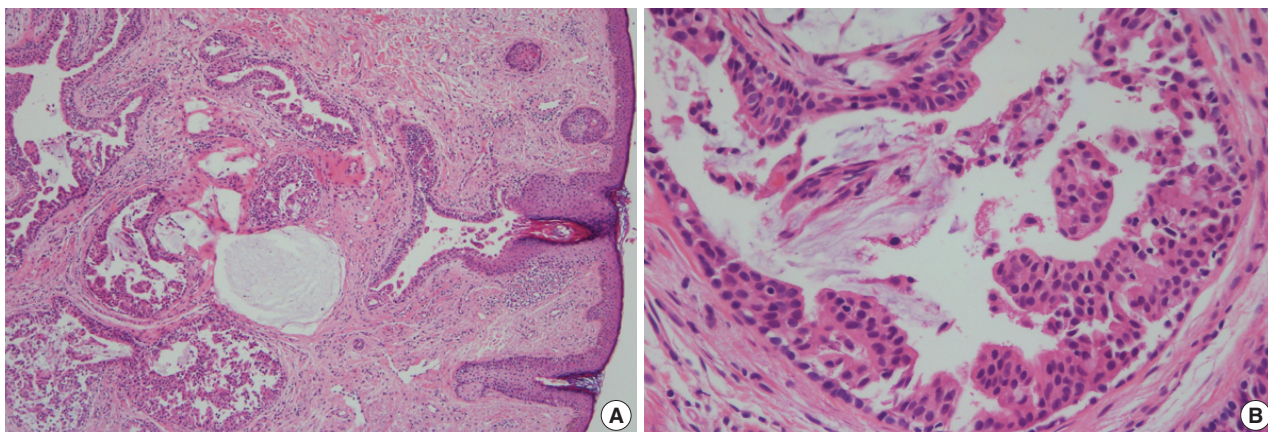


Fig. 2. (A) The tumor consists of dilated ducts with smooth border and partly filled with papillary proliferation. Some foci of extracellular mucin are present. (B) The dilated duct is lined by atypical epithelial cells and myoepithelial cells. The epithelial cells are uniform, small-to-medium in size, and oval-to-polygonal with eosinophilic cytoplasm. The nuclei are bland with diffusely stippled chromatin.

in the duct and adjacent dermis. Results from immunohistochemical stainings for chromogranin and synaptophysin showed a diffuse, positive reaction in an area of the EMPSGC and a focal positive reaction in an area of mucinous carcinoma (Fig. 3A, B). Both areas were positive for estrogen receptor, progesterone receptor, epithelial membrane antigen, and cytokeratin 7 (Fig. 3C, D). The myoepithelial cells were positive for p63.

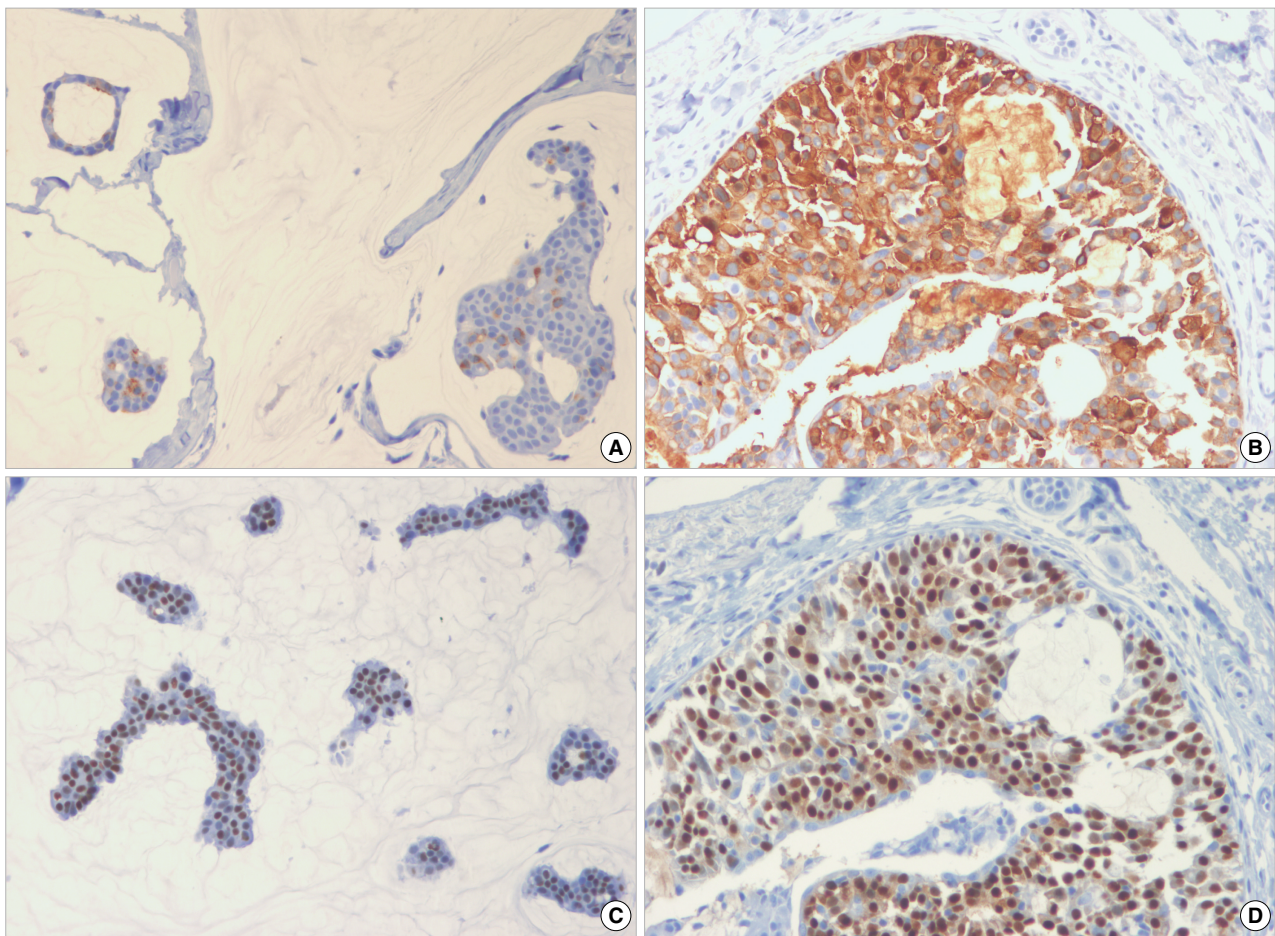
## DISCUSSION

An EMPSGC is a low-grade adnexal sweat gland carcinoma. The chief complaint was a slow-growing, skin-colored solid, sometimes cystic nodule.<sup>1</sup> An EMPSGC is found in adults' between the ages of 48 and 84 years, with a median age of 71 years. It is four times more common in females than in males. Approximate-

ly two-thirds of lesions occur on the eyelid,<sup>1,4-6,8</sup> however, it has also been observed on the cheek in proximity to the eyelid, scalp, labium major, and forehead.<sup>1-3,9</sup> The lesion described in the present case was observed on the eyelid of a 51-year-old male.

Histologically, an EMPSGC is characterized by solid, papillary, and cystic growth patterns, uniform medium-sized cells with neuroendocrine differentiation, intracellular and extracellular mucin, and a low nuclear grade.<sup>1,6</sup> Papillary architecture with hyalinized fibrovascular core can be identified. Small cysts, clefts, and variably developed, compressed, papillary structures may be observed even in predominantly solid nodules. Tumor cells are oval, polygonal, or, rarely, elongated or columnar with moderately abundant, fine, lightly eosinophilic cytoplasm. Rare cells contain mucin filled intracytoplasmic vacuoles and may resemble signet ring cells. Small pools of extracellular mucin can also be found in the clefts, however, mucin is never abundant.





**Fig. 3.** On immunohistochemical staining for chromogranin, the mucinous carcinoma shows focal positive reaction (A), while the endocrine mucin-producing sweat gland carcinoma (EMPSGC) shows a diffuse positive reaction (B). The mucinous carcinoma (C) and the EMPSGC (D) show a positive reaction for estrogen receptor.

Focal presence of moderate nuclear pleomorphism and hyperchromasia may be observed. Mitotic activity is low but always occurring.

Various markers of endocrine differentiation have been used by different groups.<sup>1-8</sup> However, there is no common marker across all cases. Neuroendocrine markers may be expressed focally; therefore, in a small specimen, lack of expression of neuroendocrine markers does not exclude a diagnosis of EMPSGC. Expression of chromogranin and synaptophysin was confirmed in the present case. Expression of estrogen and progesterone receptors was positive in all cases assessed.<sup>1,3-7</sup> Expression of estrogen and progesterone receptors was confirmed in the present case.

EMPSGC has been suggested as a precursor of cutaneous mucinous carcinoma. Morphologic and immunohistochemical resemblance of breast E-DCIS/solid papillary carcinoma to an EMPSGC has been well-described.<sup>6,10</sup> This variant of breast carcinoma frequently co-exists with mucinous carcinoma of the breast. A

subset of mucinous carcinoma in the breast shows the expression of neuroendocrine markers, argyrophilia with Grimelius staining, or the presence of neurosecretory-type granules on electron microscopy.<sup>3,7</sup> Zembowicz *et al.*<sup>1</sup> reported that 50% of EMPSGCs display an area of mucinous carcinoma. Co-existence of mucinous carcinoma with an EMPSGC led us to speculate on association between the two lesions. Cytologic features of both mucinous carcinomas and EMPSGCs are identical. As determined by positivity to neuroendocrine markers, endocrine differentiation is seen in both mucinous carcinomas and in EMPSGCs.<sup>5</sup> In the present case, the EMPSGC co-existed with a mucinous carcinoma. Both tumors showed similar cytologic features and expression of neuroendocrine markers (Fig. 3A, B). Thus, based on this common thread of spatial relationship, morphologic features, and immunophenotype, an EMPSGC is apparently a precursor of a cutaneous mucinous carcinoma.

An EMPSGC shares some clinical features with mucinous car-

cinoma of the skin. A mucinous carcinoma typically presents as a slow-growing, soft, sometimes cyst-like, and solitary mass. As with an EMPSGC, the periocular/eyelid region and cheek are its most common sites.<sup>3,11,12</sup> Also, like patients with EMPSGCs, patients with mucinous carcinomas are typically between 50 and 70 years of age; furthermore, mucinous carcinomas are more common in women. Mucinous carcinomas most often display indolent behavior.

Mucinous carcinomas can be easily recognized and distinguished from EMPSGCs by the presence of mucinous pools with floating tumor cells.

EMPSGCs can be distinguished from a hidradenoma by the absence of ductal differentiation, clear cellular change, squamoid differentiation, and epidermal attachment. Presence of mucin production and neuroendocrine nuclear appearance are helpful in differentiation of EMPSGCs from apocrine adenomas and apocrine hidradenocarcinomas.<sup>1</sup>

Follow-up data from previous series have supported the notion that even in cases associated with mucinous carcinomas, the prognosis for EMPSGCs is favorable. However, two cases have been reported on recurrence at 18 months and 3 years after complete excision.<sup>5,6</sup> Therefore, close clinical follow-up is critical for patients with EMPSGCs.

## REFERENCES

1. Zembowicz A, Garcia CF, Tannous ZS, Mihm MC, Koerner F, Pilch BZ. Endocrine mucin-producing sweat gland carcinoma: twelve new cases suggest that it is a precursor of some invasive mucinous carcinomas. *Am J Surg Pathol* 2005; 29: 1330-9.
2. Banerjee SS, Eyden BP. Neuroendocrine differentiation in eccrine carcinoma. *Histopathology* 1996; 29: 389-90.
3. Bellezza G, Sidoni A, Bucciarelli E. Primary mucinous carcinoma of the skin. *Am J Dermatopathol* 2000; 22: 166-70.
4. Bulliard C, Murali R, Maloof A, Adams S. Endocrine mucin-producing sweat gland carcinoma: report of a case and review of the literature. *J Cutan Pathol* 2006; 33: 812-6.
5. Emanuel PO, de Vinck D, Waldorf HA, Phelps RG. Recurrent endocrine mucin-producing sweat gland carcinoma. *Ann Diagn Pathol* 2007; 11: 448-52.
6. Flieder A, Koerner FC, Pilch BZ, Maluf HM. Endocrine mucin-producing sweat gland carcinoma: a cutaneous neoplasm analogous to solid papillary carcinoma of breast. *Am J Surg Pathol* 1997; 21: 1501-6.
7. Hanby AM, McKee P, Jeffery M, *et al.* Primary mucinous carcinomas of the skin express TFF1, TFF3, estrogen receptor, and progesterone receptors. *Am J Surg Pathol* 1998; 22: 1125-31.
8. Mehta S, Thiagalingam S, Zembowicz A, Hatton MP. Endocrine mucin-producing sweat gland carcinoma of the eyelid. *Ophthal Plast Reconstr Surg* 2008; 24: 164-5.
9. Rahilly MA, Beattie GJ, Lessells AM. Mucinous eccrine carcinoma of the vulva with neuroendocrine differentiation. *Histopathology* 1995; 27: 82-6.
10. Tsang WY, Chan JK. Endocrine ductal carcinoma in situ (E-DCIS) of the breast: a form of low-grade DCIS with distinctive clinicopathologic and biologic characteristics. *Am J Surg Pathol* 1996; 20: 921-43.
11. Snow SN, Reizner GT. Mucinous eccrine carcinoma of the eyelid. *Cancer* 1992; 70: 2099-104.
12. Kazakov DV, Suster S, LeBoit PE, *et al.* Mucinous carcinoma of the skin, primary, and secondary: a clinicopathologic study of 63 cases with emphasis on the morphologic spectrum of primary cutaneous forms: homologies with mucinous lesions in the breast. *Am J Surg Pathol* 2005; 29: 764-82.