

Endocrine Mucin-Producing Sweat Gland Carcinoma

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Practice Points

- Endocrine mucin-producing sweat gland carcinoma is a rare, low-grade, cutaneous neoplasm commonly presenting on the eyelids of older individuals.
- Complete excision and close follow-up is recommended given a possible association with invasive mucinous carcinoma.

Endocrine mucin-producing sweat gland carcinoma (EMPSGC) is a rare, low-grade, cutaneous neoplasm that may be associated with invasive mucinous carcinoma. Tumors typically present as slow-growing, flesh-colored, nonspecific papules or nodules that favor the eyelids in older individuals. Histologic examination usually reveals basaloid nodules composed of cells with eosinophilic cytoplasm, with focal mucin production and occasional glandular structures. Definitive diagnosis requires immunohistochemical staining. Endocrine mucin-producing sweat gland carcinomas have been noted to stain positively with neuroendocrine markers such as synaptophysin and chromogranins as well as cytokeratin 7, cytokeratin CAM 5.2, epithelial membrane antigen, estrogen receptor, and progesterone receptor. Complete excision with close follow-up is important given EMPSGC's association with invasive mucinous carcinoma. Mohs micrographic surgery is an appropriate choice for treatment. We report 2 cases of EMPSGC presenting on the eyelids in a 72-year-old woman and a 74-year-old man.

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Endocrine mucin-producing sweat gland carcinoma (EMPSGC) is a rare, low-grade, cutaneous neoplasm with neuroendocrine differentiation that primarily is thought to occur on the eyelids in elderly individuals. We report 2 cases of EMPSGC presenting on the eyelids in a 72-year-old woman and a 74-year-old man.

Case Reports

Patient 1—A 72-year-old woman presented to her ophthalmologist with an asymptomatic, 4-mm, pink papule on the right lower eyelid (Figure 1). The patient reported the lesion had been present for several months and had not shown any recent dramatic changes. The lesion was biopsied to rule out basal cell carcinoma. After a diagnosis of EMPSGC was made, the patient was referred to our unit and the lesion was definitively treated with Mohs micrographic surgery.



Figure 1. A small, smooth, pink papule on the right lower eyelid with nonspecific features.

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Patient 2—A 74-year-old man presented to his ophthalmologist with a smooth, pink, umbilicated, 5-mm papule of several months' duration on the left lower eyelid. The patient reported no associated pain or pruritis. No drainage had been noted. The lesion was biopsied to rule out keratoacanthoma versus molluscum contagiosum; the pathology was read within the dermatopathology department. After a diagnosis of EMPSGC was made, the lesion was treated via full-thickness block excision by an oculoplastic surgeon.

Histopathologic Findings for Both Patients—Histologic examination of biopsies from both patients revealed multinodular tumors consisting of intradermal collections of basaloid cells with eosinophilic cytoplasm (Figures 2A and 2B). Patient 2 also showed extension from the epidermis, mucinous retraction clefts, and hyaline (Figure 2C). There was focal mucin production as well as occasional glandular structures (Figures 2 and 3). Immunohistochemical stains were performed on both samples. Cytokeratin 7, CAM 5.2, synaptophysin, estrogen receptor, and progesterone receptor all were positive in both patients; epithelial membrane antigen was weakly positive.

Comment

Endocrine mucin-producing sweat gland carcinoma is a rare, low-grade, cutaneous neoplasm with neuroendocrine differentiation. It may represent the endocrine variant of mucinous carcinoma of the skin¹ or may be a precursor of invasive mucinous carcinoma given the coexistence of invasive or infiltrative components in many cases.²⁻⁵ It also is thought to be analogous to solid papillary carcinoma of the breast (endocrine ductal carcinoma in situ).^{3,5} This malignancy has been known to recur but has been successfully treated after recurrence.^{1,2} One report noted the presence of 4 EMPSGC lesions in the right orbit as a possible indicator of in-transit metastases, but all lesions were successfully treated via surgery without recurrence at 2 years' follow-up.⁴ Overall, the prognosis and course of EMPSGC are favorable.^{4,5}

Clinically, EMPSGC typically presents as a slow-growing, nonspecific, flesh-colored nodule or papule that can resemble a hidradenoma² or a cyst.⁵ Other cases reported in the literature suggest a predominance of lesions on the eyelids of older individuals, similar to our 2 patients.¹⁻⁶

Histologic examination of EMPSGC typically reveals lesions that are composed of medium-sized, bland, round to oval cells with central nuclei and moderately abundant eosinophilic cytoplasm. As the name implies, there is both intracellular and extracellular mucin production, resulting in a mucinous basophilic stroma and a variably bluish hue to some cells.^{3,5} Microcysts and pools of mucin can be seen.^{1,2,6} The

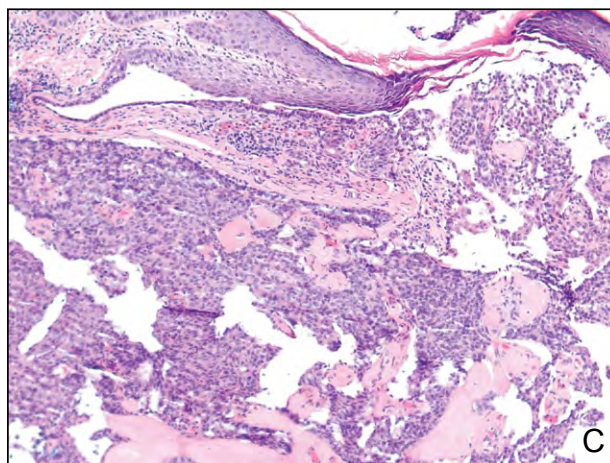
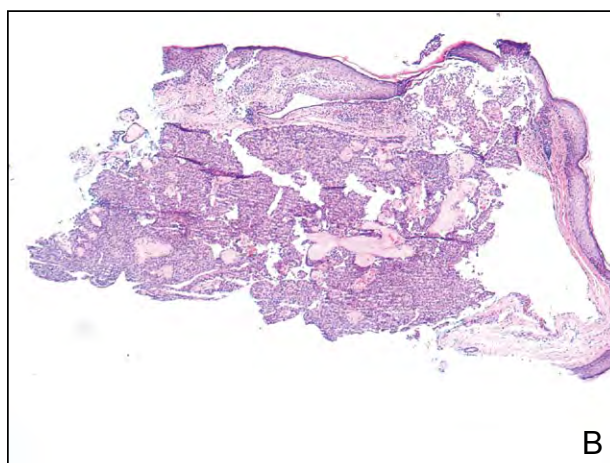
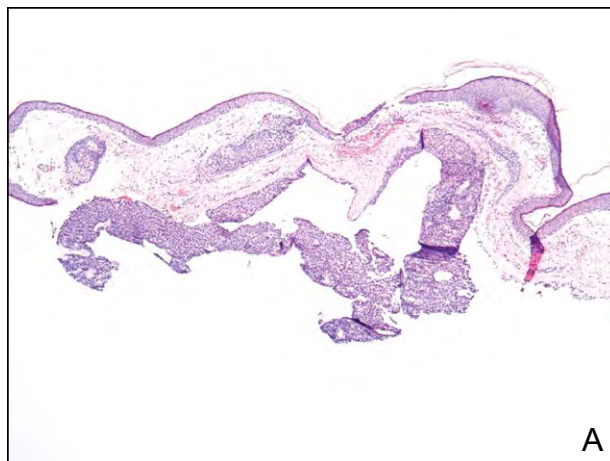


Figure 2. Basaloid intradermal nodules composed of cells with eosinophilic cytoplasm (A)(H&E, original magnification $\times 40$). Basaloid intradermal nodules extending from the epidermis were composed of cells with eosinophilic cytoplasm with focal mucin production, mucinous retraction clefts, and hyaline (B)(H&E, original magnification $\times 40$). Hyaline and glandular structures also were noted (C)(H&E, original magnification $\times 100$).

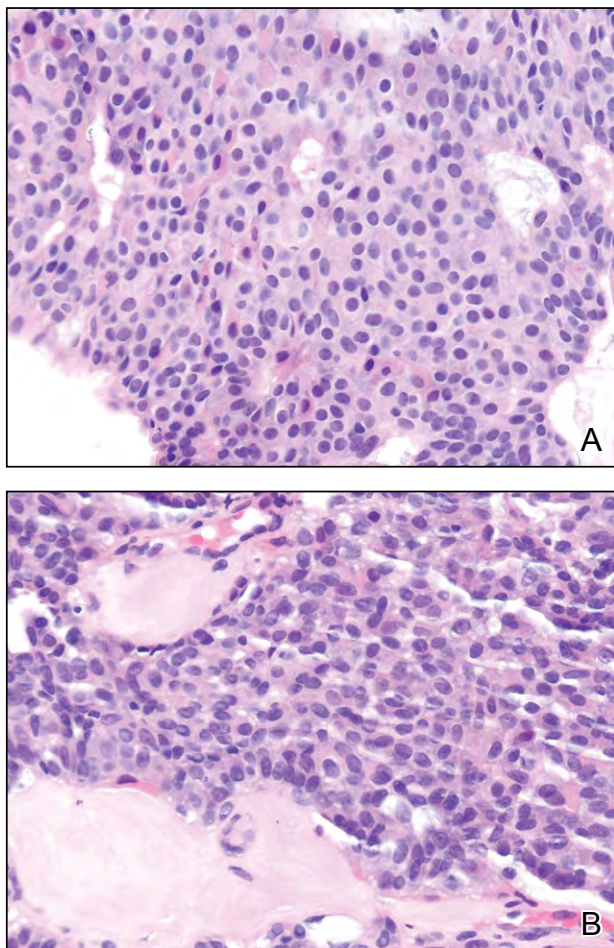


Figure 3. Cells with eosinophilic cytoplasm and focal mucin production (A)(H&E, original magnification $\times 400$). Cells with eosinophilic cytoplasm with focal mucin production and hyaline (B)(H&E, original magnification $\times 400$).

mitotic rate is low and atypia or necrosis are not present.^{2,5} The nuclei have diffusely stippled chromatin^{1,2,5} that has been described as having a salt-and-pepper appearance.⁵ Electron microscopy demonstrates dense core granules.^{1,3}

Cells usually are arranged in solid, cystic, or partially cystic nodules. There can be papillary and palisading arrangement around fibrovascular cores that occasionally are hyalinized.^{2,3,5} Pseudorosette formation,³ cribriform or pseudocribriform appearance,^{1,5} and ductal structures⁵ also have been described. Some reports have noted small areas of infiltration,^{2,3} while others have indicated the presence of islands of tumor cells floating in mucinous stroma resembling mucinous carcinomas.^{1,3,5} The histologic differential diagnosis includes basal cell carcinoma with apocrine differentiation, mixed mucinous cutaneous carcinoma,² hidradenoma, other apocrine neoplasms (eg, apocrine adenoma,

apocrine hidradenocarcinoma),⁵ and metastatic mucinous tumors (eg, breast, lung, ovarian, salivary gland).¹

Definitive diagnosis requires immunohistochemical staining.⁵ Although these tumors vary in their staining characteristics, they typically stain positively with neuroendocrine markers, such as chromogranins^{1-3,5,6} and synaptophysin.¹⁻⁵ Neuron-specific enolase,^{5,6} epithelial membrane antigen,⁵ estrogen and progesterone receptors,¹⁻⁵ and cytokeratins 7^{1,2,5} and CAM 5.2⁵ also commonly stain positive. Other positive stains reported in the literature include cytokeratin 20,¹ CD56,¹ CD57,⁵ and gross cystic disease fluid protein 15,¹ though cytokeratin 20 also has been reported as staining negative in several cases.^{2,5} Some cases also have stained negative for S-100⁵ and p63.² It should be noted that p63 staining can be positive in benign ductal areas but not in the nodules of the tumor, and the loss of p63 staining in areas of frank neoplasms have been taken as further evidence of the invasive potential of EMPSGC.⁵

Conclusion

Endocrine mucin-producing sweat gland carcinoma should be included in the differential diagnosis of basaloid tumors. It is important to rule out primary mucinous carcinomas. Although EMPSGC has not been known to metastasize, it can be locally aggressive and recur, and thus treatment via complete excision with wide margins or Mohs micrographic surgery is recommended.^{2,4,6} In addition, the potential association of EMPSGC with invasive mucinous carcinoma requires close clinical follow-up.

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