

Endocrine Mucin-Producing Sweat Gland Carcinoma and Primary Cutaneous Mucinous Carcinoma: A Case Series

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PRACTICE POINTS

- Endocrine mucin-producing sweat gland carcinoma and primary cutaneous mucinous carcinoma are rare low-grade neoplasms thought to arise from apocrine glands that are morphologically and immunohistochemically analogous to ductal carcinoma in situ and mucinous carcinoma of the breast, respectively.
- Management involves a metastatic workup and either wide local excision with margins greater than 5 mm or Mohs micrographic surgery in anatomically sensitive areas.

Endocrine mucin-producing sweat gland carcinoma (EMPSGC) and primary cutaneous mucinous carcinoma (PCMC) are rare low-grade neoplasms thought to arise from apocrine glands that share many histological features and are proposed to be on a single histopathologic continuum, with EMPSGC as the in situ form that may progress to the invasive PCMC. Management involves a metastatic workup and either wide local excision (WLE) with greater than 5 mm margins or Mohs micrographic surgery (MMS) in anatomically sensitive areas. We present 2 cases of EMPSGC and 3 cases of PCMC and review their clinical and histopathologic features, differential diagnoses, and treatment.

Cutis. 2023;112:E6-E10.

Endocrine mucin-producing sweat gland carcinoma (EMPSGC) and primary cutaneous mucinous carcinoma (PCMC) are rare low-grade neoplasms thought to arise from apocrine glands. These neoplasms share many histologic features and are proposed to be on a single histopathologic continuum, with EMPSGC as the in situ form that may progress to the invasive PCMC,¹ which is analogous to ductal carcinoma in situ and mucinous carcinoma of the breast, respectively.²⁻⁵ Management involves a metastatic workup and either wide local excision (WLE) with margins greater than 5 mm or Mohs micrographic surgery (MMS) in anatomically sensitive areas.² We present 2 cases of EMPSGC and 3 cases of PCMC. We also review the clinical and histopathological features, differential diagnoses, and treatments.

Methods

Following institutional review board approval, we conducted a retrospective, single-institution case series. We searched electronic medical records dating from 2000 to 2019 for tumors diagnosed as PCMC or extramammary Paget disease treated with MMS. We gathered demographic, clinical, pathologic, and follow-up information from the electronic medical records for each case (Tables 1 and 2). Two dermatopathologists (B.P. and B.F.K.) reviewed the hematoxylin and eosin-stained

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The authors report no conflict of interest.

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doi:10.12788/cutis.0856

TABLE 1. Clinical Features of Patients With EMPSGC and PCMC

Case no.	Sex	Age at diagnosis, y	Site	Pathologic diagnosis	Treatment	Preoperative size, mm	Postoperative size, mm	Initial margin, mm	Mohs stages	Workup	Follow-up, mo	Recurrence
1	F	68	Right lower eyelid	EMPSGC	WLE	12×10	16×14	2	N/A	MRI	15	No
2	M	62	Left lower eyelid margin	EMPSGC	MMS, perms	7×5	22×12	3×6	1	CT	9	No
3	M	72	Right lateral canthus	PCMC	MMS, perms	N/A	N/A	N/A	1	N/A	112	No ^a
4	F	87	Left lower abdomen	PCMC	WLE	25×25	60×40	20–30	N/A	PET/CT	11	No
5	F	66	Left scalp	PCMC	MMS, frozen	23×18	45×40	1–3	1	MRI	1	No

Abbreviations: CT, computed tomography; EMPSGC, endocrine mucin-producing sweat gland carcinoma; F, female; M, male; MMS, Mohs micrographic surgery; MRI, magnetic resonance imaging; N/A, not available; PCMC, primary cutaneous mucinous carcinoma; perms, permanent en face section processing; PET, positron emission tomography; WLE, wide local excision.

^aPatient died of unrelated causes.

TABLE 2. Immunohistochemical Staining Results

Case no.	Tumor	Mucin	CK7	CAM5.2	CK20	GATA3	GCDFP-15	Chromogranin	Synaptophysin	ER	PR
1	EMPSGC	Focal	N/A	N/A	N/A	N/A	N/A	+	+	+	+
2	EMPSGC	No	N/A	N/A	N/A	N/A	N/A	+	+	+	N/A
3	PCMC	Yes	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
4	PCMC	Yes	+	+	–	+	+	N/A	N/A	+	+
5	PCMC	Yes	+	N/A	–	+	+	–	–	N/A	N/A

Abbreviations: CK7, cytokeratin 7; CK20, cytokeratin 20; EMPSGC, endocrine mucin-producing sweat gland carcinoma; ER, estrogen receptor; GATA3, GATA binding protein 3; GCDFP-15, gross cystic disease fluid protein 15; N/A, not available; PCMC, primary cutaneous mucinous carcinoma; PR, progesterone receptor.

slides of each tumor as well as all available immunohistochemical stains. One of the reviewers (B.F.K.) is a board-certified dermatologist, dermatopathologist, and fellowship-trained Mohs surgeon.

Results

Demographic and Clinical Information—We identified 2 cases of EMPSGC and 3 cases of PCMC diagnosed and treated at our institution; 4 of these cases had been treated within the last 2 years. One had been treated 18 years prior; case information was limited due to planned institutional record destruction. Three of the patients were female and 2 were male. The mean age at presentation was 71 years (range, 62–87 years). None had experienced recurrence or metastases after a mean follow-up of 30 months.

Case 1—A 68-year-old woman noted a slow-growing, flesh-colored papule measuring 12×10 mm on the right lower eyelid. An excisional biopsy was completed with 2-mm clinical margins, and the defect was closed in a linear fashion. Histologic sections demonstrated EMPSGC with uninvolved margins. The patient desired no further intervention and was clinically followed. Magnetic resonance imaging (MRI) of the head and neck found no evidence of metastasis. She has had no recurrence after 15 months.

Case 2—A 62-year-old man presented with a 7×5-mm, flesh-colored papule on the left lower eyelid margin (Figure 1). It was previously treated conservatively as a hordeolum but was biopsied after it failed to resolve with 3-mm margins. Histopathology demonstrated an EMPSGC (Figure 2). The lesion was treated with modified MMS with permanent en face section processing and cleared after 1 stage. Computed tomography of the head and neck showed no abnormalities. He has had no recurrence after 9 months.

Case 3—A 72-year-old man presented with a nontender papule near the right lateral canthus. A punch

biopsy demonstrated PCMC. He was treated via modified MMS with permanent en face section processing. The tumor was cleared in 1 stage. He showed no evidence of recurrence after 112 months and died of unrelated causes. The rest of his clinical information was limited because of planned institutional destruction of records.

Case 4—An 87-year-old woman presented with a 25×25-mm, slow-growing mass of 12 months' duration on the left lower abdomen (Figure 3). A biopsy demonstrated PCMC (Figure 4). Because of the size of the lesion, she underwent WLE with 20- to 30-mm margins by a general surgeon under general anesthesia. Positron emission tomography/computed tomography was unremarkable. She has remained disease free for 11 months.

Case 5—A 66-year-old woman presented for evaluation of a posterior scalp mass measuring 23×18 mm that had grown over the last 24 months. Biopsy showed mucinous carcinoma with lymphovascular invasion consistent

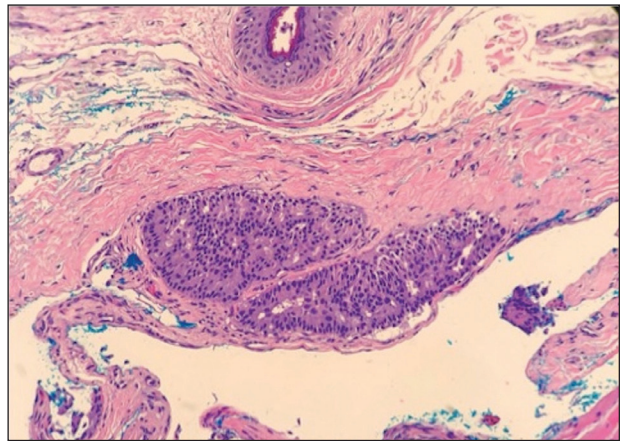


FIGURE 2. Histopathology revealed a well-circumscribed papillary nodule without apparent mucin in the dermis, consistent with an endocrine mucin-producing sweat gland carcinoma (case 2) (H&E, original magnification ×20).

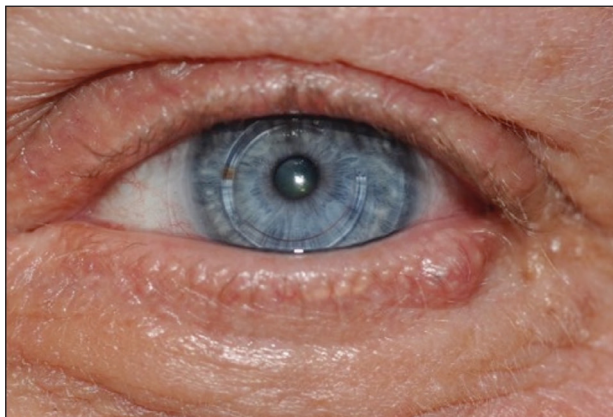


FIGURE 1. A flesh-colored papule on the left lower eyelid margin diagnosed as an endocrine mucin-producing sweat gland carcinoma (case 2).



FIGURE 3. A painful pink, poorly circumscribed, subcutaneous nodule on the left lower abdomen diagnosed as a primary cutaneous mucinous carcinoma (case 4).

with PCMC (Figure 5) confirmed on multiple tissue levels and with the aid of immunohistochemistry. She was sent for an MRI of the head, neck, chest, abdomen, and pelvis, which demonstrated 2 enlarged postauricular lymph nodes and raised suspicion for metastatic disease vs reactive lymphadenopathy. Mohs micrographic surgery with frozen sections was performed with 1- to 3-mm margins; the final layer was sent for permanent processing and confirmed negative margins. Sentinel lymph node biopsy and lymphadenectomy of the 2 nodes present on imaging showed no evidence of metastasis. The patient had no recurrence in 1 month.

Comment

Endocrine mucin-producing sweat gland carcinoma and PCMC are sweat gland malignancies that carry low

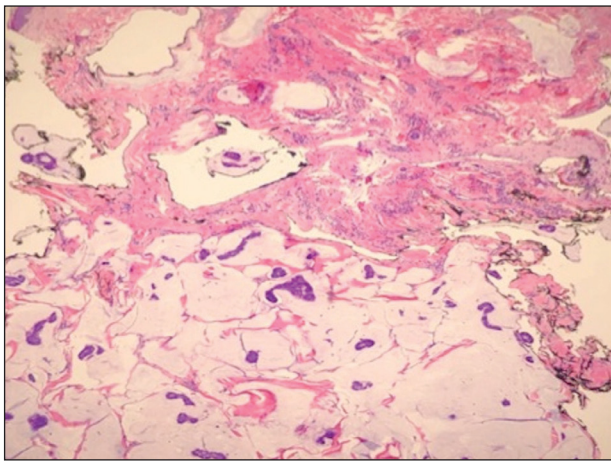


FIGURE 4. Histopathology revealed basaloid tumors infiltrating the dermis surrounded by pools of mucin, consistent with a primary cutaneous mucinous carcinoma (case 4)(H&E, original magnification $\times 20$).

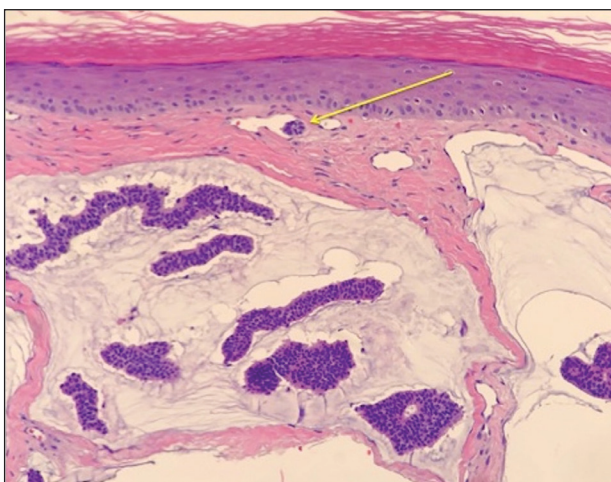


FIGURE 5. Histopathology revealed a primary cutaneous mucinous carcinoma with lymphovascular invasion (yellow arrow)(case 5) (H&E, original magnification $\times 20$).

metastatic potential but are locally aggressive. Endocrine mucin-producing sweat gland carcinoma has a strong predilection for the periorbital region, especially the lower eyelids of older women.³ Primary cutaneous mucinous carcinoma may arise on the eyelids, scalp, axillae, and trunk and has been reported more often in older men. These slow-growing tumors appear as nonspecific nodules.³ Lesions frequently are asymptomatic but rarely may cause pruritus and bleeding. Histologically, EMPSGC appears as solid or cystic nodules of cells with a papillary, cribriform, or pseudopapillary appearance. Intracellular or extracellular mucin as well as malignant spread of tumor cells along pre-existing ductlike structures make it difficult to histologically distinguish EMPSGC from ductal carcinoma in situ.³

A key histopathologic feature of PCMC is basophilic epithelioid cell nests in mucinous lakes.⁴ Rosettelike structures are seen within solid areas of the tumor. Fibrous septae separate individual collections of mucin, creating a lobulated appearance. The histopathologic differential diagnosis of EMPSGC and PCMC is broad, including basal cell carcinoma, hidradenoma, hidradenocarcinoma, apocrine adenoma, and dermal duct tumor. Positive expression of at least 1 neuroendocrine marker (ie, synaptophysin, neuron-specific enolase, chromogranin) and low-molecular cytokeratin (cytokeratin 7, CAM5.2, Ber-EP4) can aid in the diagnosis of both EMPSGC and PCMC.⁴ The use of p63 immunostaining is beneficial in delineating adnexal neoplasms. Adnexal tumors that stain positively with p63 are more likely to be of primary cutaneous origin, whereas lack of p63 staining usually denotes a secondary metastatic process. However, p63 staining is less reliable when distinguishing primary and metastatic mucinous neoplasms. Metastatic mucinous carcinomas often stain positive with p63, while PCMC usually stains negative despite its primary cutaneous origin, decreasing the clinical utility of p63. The tumor may be identical to metastatic mucinous adenocarcinoma of the breast, gastrointestinal tract, lung, ovary, and pancreas. Tumor islands floating in mucin are identified in both primary cutaneous and metastatic disease to the skin.^{3,6} Areas of tumor necrosis, notable atypia, and perineural or lymphovascular invasion are infrequently reported in EMPSGC or PCMC, though lymphatic invasion was identified in case 5 presented herein.

A metastatic workup is warranted in all cases of PCMC, including a thorough history, review of systems, breast examination, and imaging. A workup may be considered in cases of EMPSGC depending on histologic features or clinical history.

There is uncertainty regarding the optimal management of these slow-growing yet locally destructive tumors.⁵ The incidence of local recurrence of PCMC after WLE with narrow margins of at least 1 cm can be as high as 30% to 40%, especially on the eyelid.⁴ There is no consensus on surgical care for either of these tumors.⁵ Because of the high recurrence rate and the

predilection for the eyelid and face, MMS provides an excellent alternative to WLE for tissue preservation and meticulous margin control. We advocate for the use of the Mohs technique with permanent sectioning, which may delay the repair, but reviewing tissue with permanent fixation improves the quality and accuracy of the margin evaluation because these tumors often are infiltrative and difficult to delineate under frozen section processing. Permanent en face sectioning allows the laboratory to utilize the full array of immunohistochemical stains for these tumors, providing accurate and timely results.

Limitations to our retrospective uncontrolled study include missing or incomplete data points and short follow-up time. Additionally, there was no standardization to the margins removed with MMS or WLE because of the limited available data that comment on appropriate margins.

REFERENCES

1. Held L, Ruetten A, Kutzner H, et al. Endocrine mucin-producing sweat gland carcinoma: clinicopathologic, immunohistochemical and molecular analysis of 11 cases with emphasis on MYB immunoeexpression. *J Cutan Pathol*. 2018;45:674-680.
2. Navrazhina K, Petukhova T, Wildman HF, et al. Endocrine mucin-producing sweat gland carcinoma of the scalp treated with Mohs micrographic surgery. *JAAD Case Rep*. 2018;4:887-889.
3. Scott BL, Anyanwu CO, Vandergriff T, et al. Endocrine mucin-producing sweat gland carcinoma treated with Mohs micrographic surgery. *Dermatol Surg*. 2017;43:1498-1500.
4. Chang S, Shim SH, Joo M, et al. A case of endocrine mucin-producing sweat gland carcinoma co-existing with mucinous carcinoma: a case report. *Korean J Pathol*. 2010;44:97-100.
5. Kamalpour L, Brindise RT, Nodzenski M, et al. Primary cutaneous mucinous carcinoma: a systematic review and meta-analysis of outcomes after surgery. *JAMA Dermatol*. 2014;150:380-384.
6. Bulliard C, Murali R, Maloof A, et al. Endocrine mucin-producing sweat gland carcinoma: report of a case and review of the literature. *J Cutan Pathol*. 2006;33:812-816.