

Primary Mucinous Carcinoma of the Eyelid Treated With Mohs Micrographic Surgery



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PRACTICE POINTS

- Primary mucinous carcinoma (PMC) of the skin is a rare adnexal tumor.
- Prior to treatment, the diagnostic importance lies in distinguishing PMC from metastatic mucinous malignancies, which portend a poorer prognosis.
- Treatment primarily is surgical, with Mohs micrographic surgery offering improved tissue conservation and reduced recurrence rates.

To the Editor:

Primary mucinous carcinoma (PMC) is an exceedingly rare adnexal tumor with an incidence of 0.07 cases per million individuals.^{1,2} First described by Lennox et al³ in 1952, this entity often presents as slow-growing, solitary nodules that often are soft on palpation but may have an indurated quality and range in color from reddish blue to flesh colored to white.⁴ Primary mucinous carcinoma most commonly is found on the eyelid (38%) but may affect other sites on the face (20.3%), scalp (16%), and axilla (10%).⁵ Historically, it has been thought to be more common among men; however, a 2005 large case series by Kazakov et al⁵ found that women were twice as likely to be affected. Primary mucinous carcinoma most frequently is diagnosed in the fifth through seventh decades of life, with a median age at onset of 63 years.^{6,7} Because of its rarity, PMC is most frequently confused clinically with basal cell carcinoma, keratoacanthoma, apocrine hidrocystoma, epidermoid cyst, Kaposi sarcoma, neuroma,

lacrimal sac tumor, squamous cell carcinoma, granulomatous tumors, and metastatic adenocarcinoma.^{1,8-10}

Primary mucinous carcinoma is thought to be derived from sweat glands, and select features such as decapitation secretion are more suggestive of apocrine than eccrine differentiation.^{5,8} On histopathology, PMC classically is described as nests of epithelial cells floating in lakes of extracellular mucin, primarily in the dermis and subcutis. The nests are composed of basaloid cells in solid to cribriform arrangements, usually with a low mitotic count and little nuclear atypia. These nests are suspended within periodic acid–Schiff positive mucinous pools partitioned by delicate fibrous septa. The mucin produced by PMC is sialomucin, and as such it is hyaluronidase resistant and sialidase labile.⁶ At least 1 report has been made of the presence of psammoma bodies in PMC.¹¹

The neoplasm is characterized by an indolent course with frequent recurrence but rare metastasis.^{5,12} Treatment is primarily surgical, with Mohs micrographic surgery (MMS) offering improved tissue conservation and reduced recurrence rates.¹² The diagnostic challenge lies in distinguishing PMC from a variety of metastatic mucinous internal malignancies that portend a notably greater morbidity and mortality to the patient. We describe a case of PMC, discuss the differentiation of PMC from metastatic mucinous carcinoma, and review the literature regarding treatment of this rare neoplasm.

A 65-year-old white woman was referred to our tertiary-care dermatologic surgery clinic for treatment of an incompletely excised mucinous carcinoma of the right lateral canthus (Figure 1). The clinically evident scar measured 0.5×0.5 cm. Although difficult to appreciate in Figure 1, a slight textural change of the surrounding skin, including the upper and lower eyelid, was apparent.

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Prior to her arrival to our clinic, the referring physician had completed a thorough review of systems and physical examination, which did not suggest an underlying malignancy. Computed tomography of the head, neck, chest, abdomen, and pelvis revealed a mass in the thyroid that was removed and found to be benign. The patient's cutaneous lesion was therefore considered to be a PMC of the skin.

Given the prior incomplete excision of the lesion and its periocular location, we treated the patient with MMS. After 6 surgical stages, we continued to see evidence of the neoplasm as it tracked medially along the orbicularis oculi muscle (Figure 2). Due to the patient's physical and emotional exhaustion at this point, we



FIGURE 1. Primary mucinous carcinoma of the right lateral canthus (clinical lesion within red circle) that was incompletely excised.

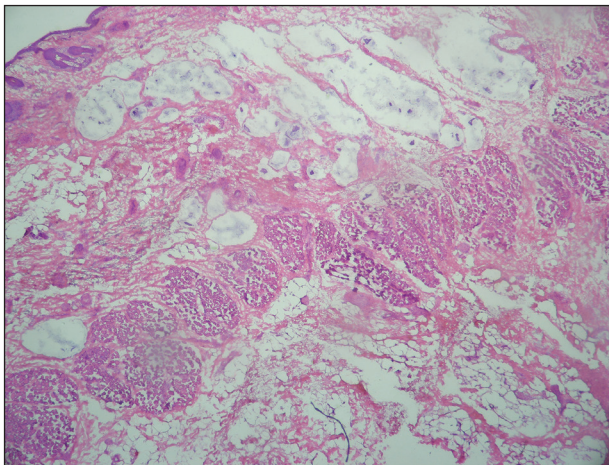


FIGURE 2. Primary mucinous carcinoma tracking medially along the orbicularis oculi muscle (H&E, original magnification $\times 40$).

discontinued MMS and referred her to a colleague in plastic surgery for further excision of the remaining focus of positivity as well as repair. The final Mohs defect measured 4.2×4.0 cm (Figure 3). Approximately 2.3×1.0 cm of tissue in the area of remaining tumor was excised by plastic surgery, and the defect was repaired with a cervicofacial advancement flap closure of the right cheek and lower eyelid and full-thickness skin graft of the left upper eyelid. Histopathologic investigation found the additional tissue resected to be free of residual tumor.

To diagnose a patient with PMC, one must first rule out cutaneous metastasis of various internal malignancies that may appear similar on histopathology. A full clinical investigation consisting of a thorough history, physical examination, and appropriate radiographic imaging is required. Cutaneous metastases most commonly arise from the breast or gastrointestinal tract (GIT) but also can originate from the prostate, lungs, ovaries, pancreas, and kidneys.⁵ Histologically, PMC may be identical to metastatic adenocarcinoma.¹³ Location on the body may be a clue to a lesion's origin, as metastases from a mucinous adenocarcinoma of the breast typically occur on the chest, breast, or axilla,⁵ whereas PMC primarily is found on the head and neck.

Certain histopathologic features may be suggestive of either a primary or metastatic etiology. Lesions arising in the skin may reveal an in situ component representing ductal hyperplasia, atypical ductal hyperplasia, or ductal carcinoma in situ. Identification of an in situ component defines a cutaneous primary neoplasm, but its absence does not exclude PMC.⁵ Additionally, metastatic lesions from the GIT typically have greater pleomorphism and "dirty" necrosis defined as eosinophilic foci containing nuclear debris.⁵

The expression pattern of cytokeratins (CKs) also can be suggestive. Primary mucinous carcinoma and



FIGURE 3. The final Mohs defect from the primary mucinous carcinoma measured 4.2×4.0 cm.

metastatic breast adenocarcinoma are both CK7⁺ and CK20⁻. By contrast, mucinous adenocarcinoma of the GIT stains CK20⁺ and CK7⁻.¹⁴ Another marker that stains PMC is CK5 and CK6, though infrequently present. Levy et al¹⁵ reported positive staining for CK5 and CK6 in only 1 of 5 PMC cases. Positive staining for CK5 and CK6 has not been reported in any metastatic mucinous carcinoma.

The role of p63 immunostaining in the setting of mucinous carcinoma is controversial.¹⁶⁻¹⁸ Some practitioners have reported using p63 immunostaining to assist in establishing the diagnosis of PMC but only after performing a clinical workup to search for any primary sites of mucinous carcinoma in other organs.¹¹ Other studies, however, have found select metastatic lesions from the breast^{17,18} and GIT¹⁸ to stain positively with p63. It is important to remember that these clinical and pathologic features are only suggestive of the primary etiology and are not replacement for a full clinical investigation.

Primary mucinous carcinoma is considered an indolent tumor with the majority of patient morbidity attributable to local recurrence and regional metastasis. Although uncommon, regional and distant metastasis rates have been reported to be 11% and 3%, respectively.¹⁹ Direct lymphatic invasion has been reported and indicates a more aggressive tumor with shorter recurrence-free intervals and predicts nodal metastases. Paradela et al²⁰ recommended the use of D2-40, a monoclonal antibody and specific marker for lymphatic endothelium, to detect lymphatic invasion, particularly in node-negative primary tumors.

In one case of PMC on the jaw of a 39-year-old Japanese man, no recurrence or metastases were discovered until the 11th year of follow-up. At that time, he was found to have lung and bone metastases and died after 3 years.²¹ Other investigators report death occurring 4 to 24 months following diagnosis of distant metastases.^{7,22} Direct extension of the tumor into skeletal muscle, periosteum, bone, and dura also has been documented.⁷

Treatment principally is surgical, with PMC known to be resistant to both chemotherapy and radiation therapy.^{19,22} The recommended margins for simple excision range from 1 to 2 cm, but this method of treatment yields recurrence rates upward of 30% to 40%, especially for lesions located on the eyelid.^{12,13} First utilized in PMC of the eyelid to conserve tissue, MMS is rapidly becoming the treatment of choice because of its notably improved recurrence rate. A case series of 4 PMCs of the eyelid treated via MMS or frozen section control found the recurrence rate to be 7%.²³ Another report of 2 cases of PMC treated by MMS reported no recurrence after 42 and 26 months.¹³ Ortiz et al⁷ reported an additional case of a patient treated by MMS that was recurrence free for 30 months at the time of publication. Further investigation is required to definitively recommend MMS on the basis of improved recurrence rate but should now be considered standard of care in recurrent, sizeable, or eyelid PMC.

Despite its ascension as treatment of choice in many cases of PMC, MMS is not without its risk of metastasis and recurrence. Tam et al²⁴ reported a case of PMC with multiple recurrences and metastases following 3 simple excisions and 2 excisions via MMS. Although the lesion's previously recurrent nature increased the likelihood of failure of MMS, this case demonstrates that all patients should be followed periodically after the treatment of PMC.

We presented a case of PMC in which standard surgical margins would have been insufficient to clear the lesion. Mohs micrographic surgery was used to remove the majority of the tumor. As is common in PMC, the lesion was indolent and periocular in location. It also was incompletely excised due to notable subclinical extension, which is common for PMC. The distinction of PMC from metastatic mucinous carcinoma is paramount but sometimes difficult. Randomized controlled trials are lacking with regards to preferred method of treatment, but MMS has shown benefit and should be considered for recurrent lesions and lesions in cosmetically sensitive areas.

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