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## Case Report

# Primary mucinous carcinoma of the skin arising from the upper eyelid: A case report and literature review

Yaso Saito<sup>a,\*</sup>, Katsuya Ota<sup>b</sup>, Yusuke Sumita<sup>c</sup>

<sup>a</sup>Shinoda General Hospital, Department of Plastic Surgery, 2-68 Sakuracho, Yamagata City, Yamagata, 9900045, Japan

<sup>b</sup>Aomori Prefectural Central Hospital, Plastic and Reconstructive Surgery Unit, 2-1-1, Higashi-Tsukurimichi, Aomori City, Aomori, 0308553, Japan

<sup>c</sup>Nagaoka Red Cross Hospital, Department of Plastic Surgery, Senshu-2 297-1, Nagaoka City, Niigata, 9402085, Japan

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## ABSTRACT

Primary mucinous carcinoma of the skin (PMCS) is a rare malignant neoplasm of the sweat glands that has an incidence of 1 per 150,000 population. Because of the lack of typical characteristics, it is often misdiagnosed as an epidermoid cyst, pilomatixoma, or chalazion before resection, with subsequent enucleation performed unintentionally. We present a case of a 51-year-old patient with PMCS in the upper eyelid that was successfully treated at our hospital. Additionally, we reviewed the literature and discussed the diagnosis, primary and adjuvant therapy, and follow-up procedure.

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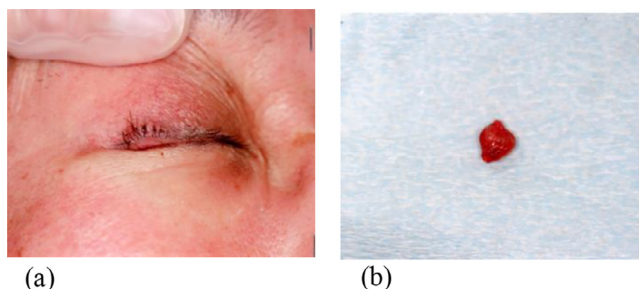
\* Corresponding author.

E-mail address: [yaso.s@shinoda-hp.or.jp](mailto:yaso.s@shinoda-hp.or.jp) (Y. Saito).

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**Figure 1.** Clinical photographs (taken at a plastic surgery clinic before the patient was referred to our hospital). (a) The right upper eyelid before enucleation was performed (b) The enucleated specimen.

## Introduction

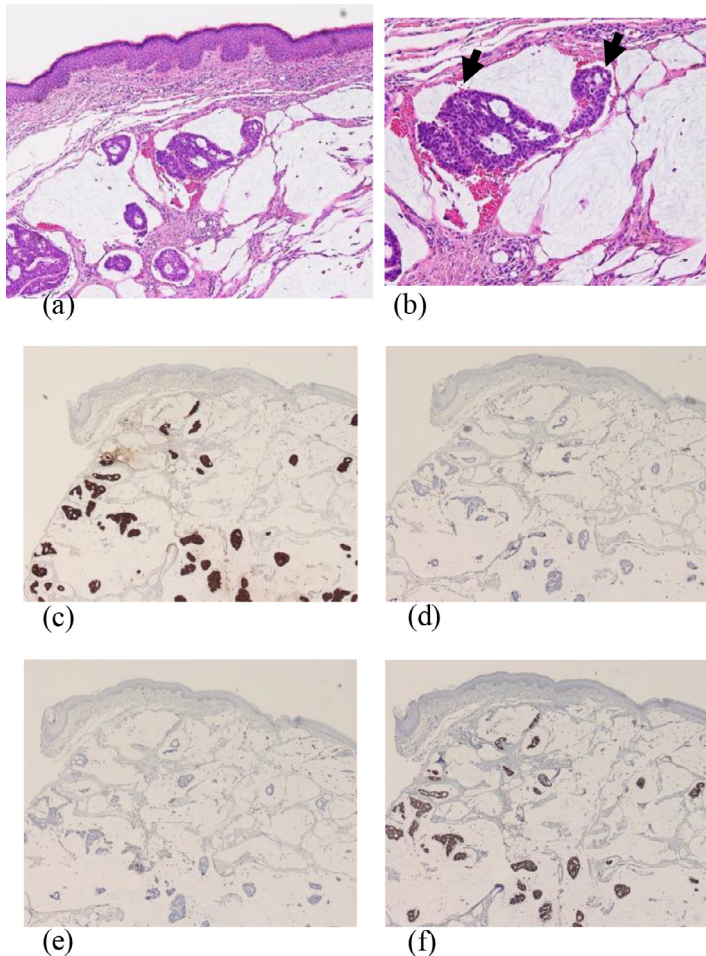
Primary mucinous carcinoma of the skin (PMCS) is a rare malignant neoplasm of the sweat glands<sup>1,2</sup> with an incidence of 1 per 150,000 population.<sup>3</sup> PMCS primarily affects middle-aged or older individuals; 54.7–70% of cases occur in men, and periorbital involvement is seen in 40–49.7% of cases.<sup>4,5</sup> It is a slow-growing, small, flesh-colored or pale blue, smooth nodule. Because of the lack of typical characteristics, it is often misdiagnosed as an epidermoid cyst, pilomatrixoma, or chalazion before resection,<sup>6,7</sup> with subsequent enucleation carried out unintentionally. PMCS should be regarded as a differential diagnosis of periorbital tumors because of its frequent occurrence at that site. Wide local excision with adequate surgical margin is the recommended treatment because of its high local recurrence rate.<sup>7</sup> Additionally, treatment of hormone receptor-positive PMCS with aromatase inhibitors as adjuvant therapy was reported in recent years.<sup>8–10</sup> We report a case of PMCS arising from the upper eyelid. Additionally, we reviewed the related literature.

## Case report

A 51-year-old man with a two-year history of a palpable mass in the right upper eyelid presented to a plastic surgery clinic. He had a past medical history of diabetes, hypertension, and cholelithiasis. Clinical examination revealed a subcutaneous, skin-colored, 5-mm-sized mass on his lateral upper eyelid. Enucleation was performed (Figures 1a and b), and histopathological examination revealed mucinous carcinoma of the skin. Two weeks later, he was referred to our hospital for further investigation, and wide local excision was performed. Blood test results revealed slightly high alanine aminotransferase (51 IU/l), uric acid (7.2 mg/dl), and hemoglobin A1c (6.3%, National Glycohemoglobin Standardization Program) levels, and normal carcinoembryonic antigen (2.0 ng/ml), prostate-specific antigen (0.35 ng/ml), cancer antigen (CA) 125 (5.7 U/ml), CA19-9 (4.0 U/ml), CA15-3 (5.6 U/ml), and alpha-fetoprotein (3.4 ng/ml) levels.

Histopathological analysis showed islands of epithelial cells floating in an intradermal lake of extracellular mucin. The tumor was composed of low-grade atypical cells, some of which formed small lumens (Figures 2a and b). Tumor cells were present at the edge of the resection specimen, resulting in a positive surgical margin. Immunohistochemical (IHC) staining was positive for cytokeratin 7 (CK7) but negative for cytokeratin 20 (CK20) and caudal-type homeobox 2 (CDX-2) (Figures 2c, d, and e). Estrogen receptor (ER) was strongly expressed in >90% of cells (Figures 2f). Computed tomography of the head and neck, chest, abdomen, and pelvis revealed no lymph node or distant metastases. Gallium scintigraphy detected no abnormalities. Upper gastrointestinal tract endoscopy and colonoscopy revealed chronic gastritis and duodenitis. Based on these results, the PMCS diagnosis was confirmed.

Nineteen days after the first visit to our hospital, wide local excision was performed. The tumor was dissected over the orbital septum with a caudal incision 2 mm from the scar toward the free margin of the eyelid and a cranial incision 8 mm from the scar toward the eyebrow (Figures 3a, b, and c). Subsequently, the skin defect site was covered with artificial dermis. Histopathology revealed that the

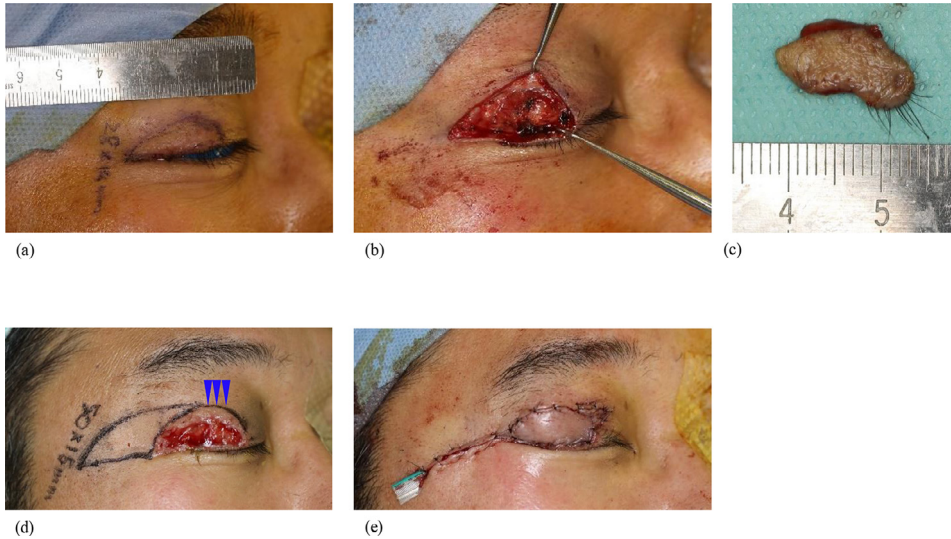


**Figure 2.** Histological features of primary mucinous carcinoma of the skin. (a) Hematoxylin and eosin (H&E) staining of the enucleated specimen viewed at 10× magnification (b) H&E staining of the specimen viewed at 20× magnification: arrows indicate islands of epithelial cells floating in an intradermal lake of extracellular mucin. (c) Immunohistochemical staining for cytokeratin 7: positively stained cells appear brown. (d) Immunohistochemical staining for cytokeratin 20: no positively stained cells (e) Immunohistochemical staining for caudal-type homeobox 2 (CDX-2): no positively stained cells (f) Immunohistochemical staining for estrogen receptor (ER): ER was strongly expressed in >90% of the cells.

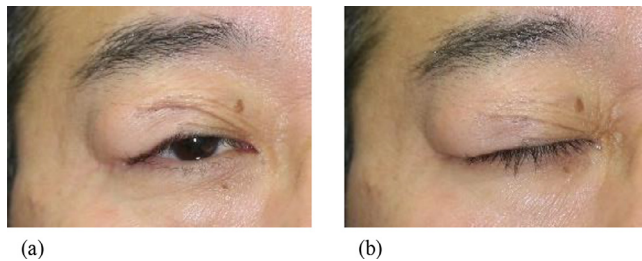
cranial horizontal edge of the specimen was 0.2 mm from the intradermal lake of mucin that exposed a mass of foreign-body giant cells. Therefore, we performed an additional wide local excision 30 days after the first visit. The tumor was additionally excised with a 5-mm surgical margin from the cranial edge of the skin defect. Next, a V-Y advancement flap with the orbicularis oculi muscle pedicle was harvested from the lateral side of the skin defect, and the eyelid defect was repaired (Figure 3d and e). Subsequent histopathology was negative. The patient remains under follow-up with no evidence of recurrence at 7 months post-reconstruction and no functional eyelid disability (Figures 4a and b).

## Discussion

PMCS is characterized by islands of tumor cells that float in pools of mucin demarcated by fibrous septa.<sup>3,6,11</sup> Moreover, this feature is common in metastatic mucinous carcinoma of other ori-



**Figure 3.** Intraoperative photographs. (a) Before wide local excision (b) After wide local excision (c) Excised specimen (d) Before an additional wide local excision: arrowheads indicate the additional excised part. (e) After reconstruction with a V-Y advancement flap.



**Figure 4.** Clinical photographs at 7 months post-reconstruction. (a) With open eyelids (b) With closed eyelids.

gins. Therefore, excluding metastasis or direct invasion from an underlying neoplasm is necessary.<sup>11</sup> In the present case, IHC examination showed positive staining for CK7 and was strongly positive for ER (>90%) and negative for CK20 and CDX-2. Mammary mucinous carcinoma was ruled out based on physical findings, tumor markers, and image analysis. Kazakov et al. described several useful criteria for distinguishing primary from secondary mucinous carcinoma, including the thickness of fibrous septae, epithelial-mucin ratio, CK7/CK20 expression pattern, and presence of an *in situ* component.<sup>11</sup> They stated that the presence of an *in situ* component, which denotes a tumor of skin origin, is the most logical criterion since a metastatic carcinoma from a distant site cannot contain an *in situ* component.<sup>11</sup> Moreover, tumor location could be helpful in the differential diagnosis as mammary neoplasms show a strong predilection for the chest, breast, and axilla.<sup>11</sup> In our case, the presence of low-grade atypical cells in the tumor and its location on the upper eyelid support the PMCS diagnosis.

IHC examination revealed strong ER expression in >90% of tumor cells. Although we used ER for differential diagnosis, treatment of hormone receptor-positive PMCS with aromatase inhibitors was reported.<sup>8–10</sup> Thus, detecting ER by IHC is important for PMCS diagnosis and perioperative adjuvant therapy because some cases achieved a stable disease status with aromatase inhibitor treatment.<sup>8–9</sup>

Wide local excision is regarded as the primary therapy for PMCS because PMCS is resistant to chemotherapy and radiation therapy.<sup>7</sup> Additionally, an adequate surgical margin is necessary because

of a relatively high local recurrence rate (approximately 30%)<sup>4</sup> and some distant metastases (2.7–6.1%).<sup>4,5</sup> Surgical margins were reported in 11 of 100 (11%) PMCS cases, with an average margin of 12.5 mm.<sup>7</sup> Since local recurrence is a significant factor, excisions with at least 1 cm margins would be reasonable. Mohs surgery may be helpful for small, superficial lesions in the eyelid where wide resection is difficult due to anatomic or cosmetic restraints. In PMCS cases including non-periorbital locations, among 15 cases treated with Mohs surgery, only 2 had a recurrence and none had metastasis. However, among 136 cases treated with traditional surgery, 46 (34%) recurred or metastasized.<sup>5</sup> Our literature review showed no reported cases of periorbital PMCS treated with Mohs surgery in Japan. However, periorbital PMCS could be treated with Mohs surgery because of low local recurrence and metastasis rates with surgery.

Although we performed local excision with an 8-mm surgical margin, the tumor was close to the resection stump requiring an additional 5-mm horizontal resection. Moreover, Horibe et al.<sup>12</sup> suggested that a >10 mm surgical margin is desirable because satellite tumors may spread beyond the range of surgical excision. Mohs surgery may be useful in cases with <10 mm surgical margins in terms of functional and aesthetic aspects.<sup>11</sup> Adjuvant therapy with aromatase inhibitors should be considered in similar cases. Long-term follow-up after tumor resection using modalities with high-detection sensitivity, including positron emission tomography-computed tomography, may be necessary since a case of metastasis after 10 years of disease-free survival was reported.<sup>13</sup>

## Conclusion

PMCS has a relatively high local recurrence rate and the potential for distant metastases. We, therefore, recommend an adequate surgical margin for the treatment of PMCS. Perioperative adjuvant therapy with aromatase inhibitors may be considered in cases with <10 mm surgical margins and with local recurrence or distant metastasis. Finally, long-term follow-up may be necessary since a case of metastasis after 10 years of disease-free survival was reported in the literature.

## Declaration of Competing Interest

None declared.

## Funding sources

None

## Ethical approval and patient consent

Ethical approval for this study was obtained from our institution. Additionally, patient consent was obtained, although we did not use any personal or identifying information of the patients.

## STROBE guidelines

Our case report follows the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

## Acknowledgments

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