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Primary mucinous carcinoma of the lower eyelid treated with wide excision and postoperative radiotherapy: a case report and literature review

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Primary cutaneous mucinous carcinoma (PCMC) is a rare malignant neoplasm that originates from the deepest part of the eccrine sweat glands. Characterized by slow growth, PCMC often appears on the head and neck of older patients. Although it rarely metastasizes, its high recurrence rate leads to significant morbidity. Clinically differentiating PCMC from benign tumors is challenging due to its slow growth and asymptomatic nature, and a biopsy is often required for a definitive diagnosis. A 77-year-old man presented with a non-tender lesion on his left lower eyelid that had been gradually progressing over a decade. The lesion was excised, and histological examination confirmed it as PCMC. A positron emission tomography-computed tomography scan conducted to differentiate between primary and metastatic cancer showed no abnormal findings. Computed tomography was then performed to assess the remaining primary site, followed by a wide excision. The frozen biopsy revealed no cancer in the margins from five directions; however, the permanent biopsy confirmed the presence of cancer in the base margin. After consultation with the hematology-oncology department, the patient underwent additional radiation therapy. One year post-surgery, there were no signs of recurrence.

Abbreviations: CK7, cytokeratin 7; MRI, magnetic resonance imaging; PCMC, primary cutaneous mucinous carcinoma; PET-CT, positron emission tomography-computed tomography

Keywords: Case reports / Eyelid neoplasms / Mucinous carcinoma

Case Report and Literature Review

INTRODUCTION

Primary cutaneous mucinous carcinoma (PCMC) is a rare form of skin cancer originating from the eccrine sweat glands. This type of cancer was first identified by Lennox et al. in 1952 and was officially named in 1972 [1,2]. Although PCMC has a high local recurrence rate, it does not typically metastasize to distant parts of the body. The mean annual age-standardized incidence rate of PCMC is extremely low, at 0.07 per million person-years [3]. According to a recent report by Jhunjhunwala et al. [4], only approximately 380 cases of PCMC have been documented as of 2022. A meta-analysis that examined 215 cases found that the average age of patients was 63.5 years, and 54.7% were male [5]. Among the total cases, 49.7% of PCMCs were found around the eye, including the eyelid, canthus, and brow. Clinically, PCMC presents as a slow-growing, asymptomatic, solitary lesion that is flesh-colored or pale blue, and it may be ulcerative. Given its high local recurrence rate, a sufficient surgical margin is recommended.

We report the case of a 77-year-old man who presented with a

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non-tender lesion on his left lower eyelid. This lesion had gradually progressed over 10 years. Following wide excision and postoperative radiotherapy, there has been no sign of recurrence or metastasis. The patient recovered well, with his vision and eye movement unaffected by the treatment. He is currently under outpatient follow-up.

CASE REPORT

A 77-year-old male patient presented with a mass on his left lower eyelid, which first appeared about 10 years ago and had gradually increased in size. At the patient's initial outpatient visit, a slightly red, non-tender, raised nodule measuring approximately 3 cm was observed (Fig. 1). Preoperative ultrasonography, performed in the outpatient clinic, revealed an ill-defined hypoechoic infiltrative lesion with internal vascularity in the subcutaneous layer of the left lower eyelid. An excisional biopsy was performed under local anesthesia, and histopathology confirmed the diagnosis of mucinous carcinoma. The excised mass measured 2.5×2.3 cm. Hematoxylin and eosin staining showed dermal nests of epithelial cells floating in a pale-staining mucin pool (Fig. 2A). Immunohistochemical staining revealed that the tumor cells were positive for cytokeratin 7 (CK7) and negative for cytokeratin 20 (CK20) and CDX-2 (Fig. 2B).

A positron emission tomography-computed tomography (PET-CT) scan was conducted to determine whether the PCMC in the left lower eyelid was primary or metastatic, and the results were negative. An enhanced CT scan of the remaining primary lesion revealed a 1.5-cm peripheral enhancing thin-walled cystic mass in the left lower eyelid (Fig. 3). The radiologist suggested that while this was likely a postoperative change, the possibility of residual PCMC could not be dismissed. No lymphadenopathy was detected on a magnetic resonance imaging (MRI) scan. Two weeks following the initial excision, the patient underwent a wide excision of the PCMC with a safety margin of 3 mm (Fig. 4A). Frozen biopsies from

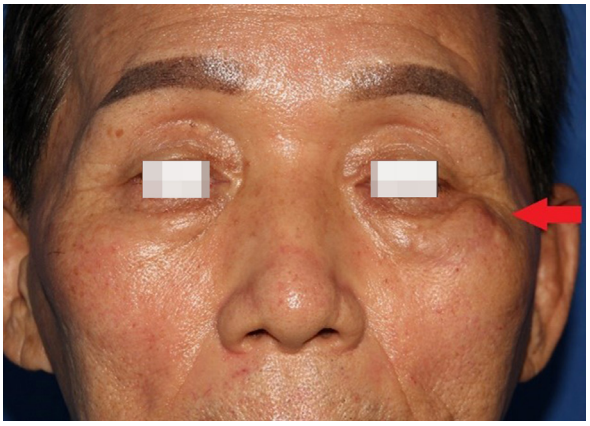

Fig. 1. A 77-year-old man with a protruding nodular mass (red arrow) on the left lower eyelid.

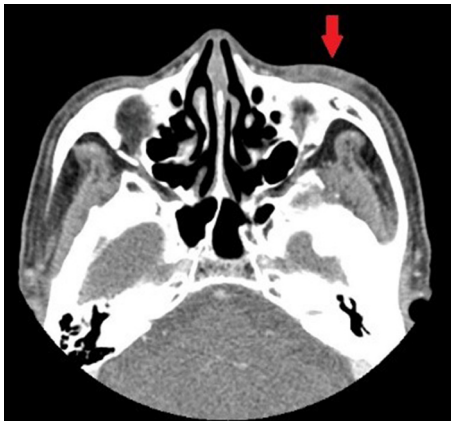

Fig. 3. Orbital computed tomography after excision surgery showing a 1.5 cm cystic mass and perilesional soft tissue infiltration (red arrow).

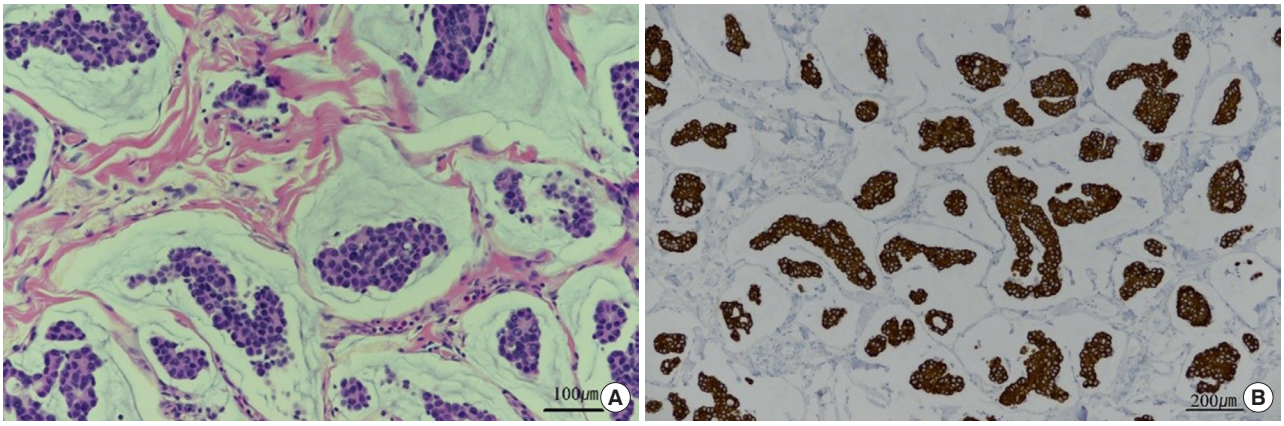

Fig. 2. Histological examination. (A) Tumor cells are floating within the pools of extracellular mucin (hematoxylin and eosin, ×200). (B) Immunohistochemical staining displays tumor cells that are positive for cytokeratin 7 (CK7) (×100).

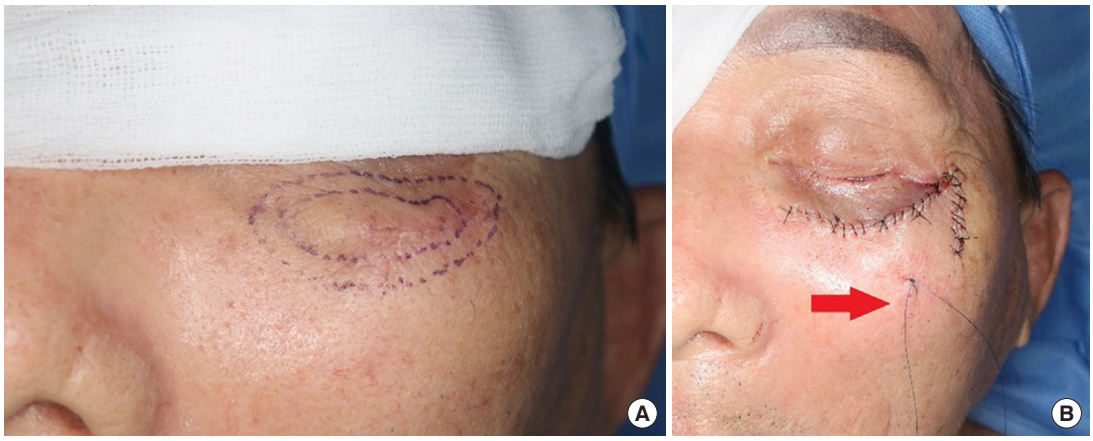

Fig. 4. Intraoperative photographs. (A) The design for wide excision with a 3 mm safety margin. The scar from the previous excision was included in the wide excision boundary. (B) After the rotation flap, a suspension suture (red arrow) was made and fixed with the forehead to prevent downward retraction of the lower eyelid.

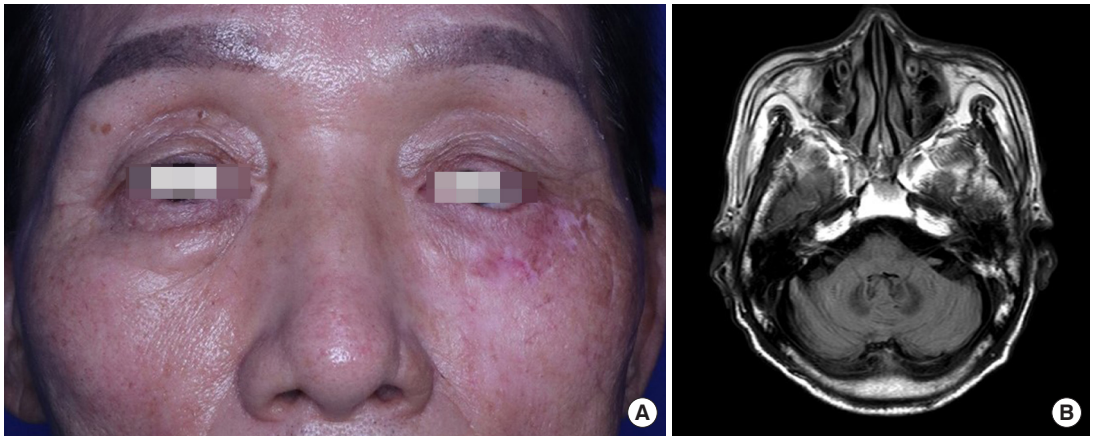

Fig. 5. One-year postoperative images. (A) A photograph showing that there is no problem opening and closing his eyes. (B) T2-weighted magnetic resonance imaging with no evidence of recurrence.

five locations of the skin margin (12, 3, 6, and 9 o'clock, and the deep margin) were conducted. The frozen sections showed clear surgical margins. In the resected deep margin, the orbicularis oculi muscle and tarsal plate were preserved. A rotation flap from the left cheek was created to reconstruct the soft tissue defect (Fig. 4B). To prevent excessive downward retraction of the lower eyelid, a suspension suture was positioned below the suture line, then drawn upward towards the patient's forehead and secured with skin tape.

Unfortunately, the permanent biopsy revealed that cancer was present in the deep margin. We sought advice from the hematology-oncology department regarding the patient's further treatment. The decision was made for the patient to undergo postoperative radiation therapy 29 times (daily tumor dose: 210 cGy, total tumor dose: 6,090 cGy). Following surgery and radiation therapy, the patient experienced no problems with opening and closing his eyes (Fig. 5A). One year post-surgery, there is no evidence of recurrence, and the patient is currently receiving follow-up care on an outpatient basis (Fig. 5B).

LITERATURE REVIEW

PCMC is an extremely rare form of skin cancer that originates from the sweat glands. The histogenesis of this cancer remains a subject of debate, with uncertainty surrounding whether it arises in the apocrine or eccrine glands. Some studies have found that PCMC cells resemble the dark cells of normal eccrine glands, while others have suggested that PCMC cells undergo apocrine differentiation [6]. According to a systematic review and meta-analysis conducted by Kamalpour et al. [5], PCMC most commonly occurs in the eyelid/canthus/brow area (49.7%), followed by the non-periorbital area and neck (19.5%), and the scalp (17.0%). Most cases were found in white individuals (77.2%), followed by Asians (12.7%), and African Ameri-

cans (10.1%). PCMC typically presents in individuals in their 60s and 70s as a solitary, painless, slowly growing flesh-colored nodule, ranging in size from 0.7 cm to 8 cm [2,3,5,6]. However, the clinical appearance can vary significantly. There are no characteristic clinical features that make PCMC easily recognizable; therefore, it is challenging to differentiate PCMC from other neoplasms before pathological confirmation [6,7]. The average diameter of the cancer prior to excision was 1.8 cm, with an average interval of 37.4 months from symptom onset to clinical consultation [5].

Mucinous carcinoma generally has a favorable prognosis, with distant metastasis occurring in fewer than 3% of cases [5,7]. However, mucinous carcinoma of the skin often presents as metastatic cancer, making it crucial to conduct a comprehensive examination to rule out the presence of primary cancer prior to surgery. The recommended diagnostic procedures include CT scans of the chest, abdomen, and pelvis. Additionally, upper gastrointestinal endoscopy and colonoscopy should be performed to eliminate the possibility of gastrointestinal mucinous carcinoma. PET-CT is highly effective in detecting nodal metastasis, although false negatives have been reported in patients with early micro-metastasis [8]. Fluorodeoxyglucose uptake may be impeded by low cellularity when the mucin ratio is high, which is a key histological characteristic [9]. MRI is a useful tool for delineating the border of the PCMC, as it displays high signal intensity on T2-weighted images due to its mucin component.

Immunohistochemical staining (CK7, CK20, CDX-2, and p63) can assist in distinguishing primary mucinous carcinoma from metastatic mucinous carcinoma. PCMC is CK7-positive and CK20-negative, similar to mucinous carcinoma of the breast, gallbladder, and lung. In contrast, gastrointestinal mucinous carcinoma is CK7-negative and CK20-positive. p63 is more highly expressed in PCMC than in metastatic cancer, making it a valuable diagnostic marker [10].

The prognosis for PCMC is generally favorable because its avascular nature makes distant metastases rare. However, the local recurrence rate for PCMC is quite high, at around 30%. Therefore, to prevent recurrence, it is crucial to completely excise the lesion during surgery [5,6]. The current recommendation is to perform a wide local excision using an intraoperative frozen section. Typically, a margin of 1 cm is advised due to the high local recurrence rate. However, there have been successful treatments following excision with a margin of 3–5 mm, depending on the lesion's location and size [11,12]. Some case reports have indicated a low local recurrence rate following Mohs micrographic surgery, but the number of such cases remains limited [5,13]. Due to the rarity of this tumor, there are no prospective randomized controlled trials, and consequently, no evidence-based guidelines have been established. PCMC is generally considered resistant to radiotherapy and chemotherapy, which are not commonly used in its management. However, some case reports have described the use of postoperative adjuvant radiotherapy in cases of recurrent PCMC [12,14,15].

DISCUSSION

In this case, a 77-year-old male patient presented with a left lower eyelid mass that had been slowly growing for 10 years. The size of the cancer removed from this patient was approximately 1.1 × 1.8 cm at the time of the initial excisional biopsy, and 3.1 × 1.3 cm following an additional wide excision. A meta-analysis reported that the average cancer diameter prior to excision was 1.8 cm, making the size of the cancer in this case larger than most. This is believed to have been because the patient sought medical attention later than the average time from symptom recognition to doctor visit, as reported in the meta-analysis (37.4 months) [5].

The patient underwent an excisional biopsy of a mass located in the left lower eyelid, due to the suspicion of a benign tumor. Following a histologic diagnosis of PCMC, a wide excision with 3 mm margins was performed, given the lesion's location. Neither sentinel lymph node biopsy nor neck node dissection was performed due to the lack of established evidence supporting the effectiveness of these procedures in patients without clinical lymphadenopathy [10]. Additionally, preoperative imaging, including orbital CT, MRI, and PET-CT, showed no signs of lymphadenopathy beyond the primary site, further supporting the decision to omit these procedures. An upper and lower gastrointestinal endoscopy to determine whether the cancer was primary or metastatic had already been performed at another hospital 3 months before the first visit, and no specific abnormal findings were found. The deep margin was determined by the results of the frozen biopsy, based on studies showing no significant difference in recurrence and survival rates between Mohs surgery and wide excision with frozen section control [16,17]. The intraoperative frozen biopsy incorrectly concluded that cancer was absent in five margins, and a rotation flap was utilized to cover the defect [18]. To prevent the lower eyelid from retracting downwards and to avoid postoperative ectropion, a suspension suture, which is a modification of the Frost suture, was applied over the skin of the rotation flap and secured to the forehead using skin tape [19,20]. This suspension was removed on the third day after the operation. The permanent biopsy revealed cancer-positive findings in the deep margin. In this case, the difficulty in distinguishing cancerous tissue from normal

tissue made intraoperative decision-making particularly challenging. This complexity raised the risk of unnecessarily removing healthy tissue, including the orbicularis oculi muscle and tarsal plate, which could have severely impacted the patient's ability to blink his eye. After careful consideration and consultation with the patient and a hematologist-oncologist, it was decided that radiation therapy would be the best course of action. The patient has been attending outpatient follow-ups for 1 year, with no evidence of recurrence or postoperative complications.

Diagnosing PCMC based on its morphology can be challenging; thus, histologic confirmation is crucial. PCMC grows slowly and is painless, which can lead to misdiagnosis as a benign cystic lesion or delayed diagnosis. Even after histologic confirmation, it is necessary to distinguish between primary and metastatic lesions through a comprehensive body examination to detect potential metastasis from other organs. Some reports have described wide local excision or Mohs surgery with clear resection margins followed by adjuvant radiotherapy to lower the risk of local recurrence [12,14,15,21,22]. This case is the first report of an attempt to reduce the likelihood of local recurrence with postoperative radiotherapy, even though the primary mucinous carcinoma was not clearly excised at the base margin. Long-term follow-up is necessary after surgery, and further studies on the prognostic impact of postoperative radiotherapy will help guide treatment decisions.

NOTES

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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Ethical approval

The report was approved by the Institutional Review Board of Inha University Hospital (IRB No. 2023-05-022).

Patient consent

The patient provided written informed consent for the publication and use of his images.

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