Case Report

Unusual Metastasis to Eyelid from Extraocular Merkel Cell Carcinoma

Ahmet Özdemir, Volkan Yeter, Nurullah Koçak, Sultan Çalışkan

Ondokuz Mayıs University, Department of Ophthalmology, Samsun, Türkiye

Abstract

Merkel cell carcinoma (MCC) is an unusual skin tumor that has a significant rate of distant and local metastases. It is known that primary MCC of the eyelid usually occurs at the upper eyelid. Here we report an unusual case of MCC metastasis to the eyelid. A 63-year-old male was diagnosed with MCC three years earlier after initially presenting with a mass in his right thigh. After histopathological diagnosis, the patient received medical therapy. During treatment, he developed multiple distant metastases and a firm, purple, vascularized lesion on the upper eyelid. We confirmed the lesion was an eyelid metastasis of MCC by histopathological examination and imaging methods. This case shows that extraocular MCC can metastasize to the eyelids, particularly the upper eyelid, where primary periocular MCC usually appears.

Keywords: Merkel cell carcinoma, eyelid, metastasis

Cite this article as: : Özdemir A, Yeter V, Koçak N, Çalışkan S. Unusual Metastasis to Eyelid from Extraocular Merkel Cell Carcinoma. Turk J Ophthalmol 2024;54:116-119

Address for Correspondence: Ahmet Özdemir, Ondokuz Mayıs University, Department of Ophthalmology, Samsun, Türkiye
E-mail: dr_ahmet_ozdemir@hotmail.com **ORCID-ID:** orcid.org/0000-0002-0728-6027
Received: 14.08.2023 **Accepted:** 02.02.2024

DOI: 10.4274/tjo.galenos.2024.25686

Introduction

Merkel cells are deep epidermal cells that function as mechanoreceptors. They are essential for light touch sensation and are also capable of malignant transformation.[1] Merkel cell carcinoma (MCC) is a rare, destructive tumor that has a mortality rate of up to 40%.[2] MCC tumors are generally observed on sun-exposed skin areas in older whites and usually present as painless, bluish red, expansive nodules. Immunosuppression is an important risk factor, especially in people with solid organ transplants, chronic lymphocytic leukemia, or human immunodeficiency virus.[2]

A literature review of eyelid MCCs in 2019 reported nearly 200 published cases, which included 127 women (64.1%) and 67 men (33.8%), with a median age of 77 years.[2] As approximately 50% of the cases occurred on the head or neck, the cancer now ranks among the five most common malignant tumors found at these sites, preceded in frequency only by basal cell, squamous cell, and sebaceous carcinomas and melanoma.[3] After diagnosis, appropriate staging is necessary to develop a treatment course and effectively counsel patients.[3] Treatment usually includes wide local excision, commonly with the addition of radiotherapy for improved loco-regional disease control.[4] Adjuvant chemotherapy had been reserved for metastatic disease, but immunotherapy and targeted chemotherapies are currently being investigated for use in primary cases.[4]

There have been previous reports of metastases from the eyelid to the regional lymph nodes, parotid lymph nodes, preauricular nodes, submandibular nodes, and distant sites such as the lungs with larger tumors.[5] However, MCC of the ocular adnexa remains a very rare condition.

This is the first case report of the metastasis of MCC from an extraocular region to the eyelid. Another interesting feature of this case is the appearance of metastasis only on the upper eyelid, where primary eyelid MCC usually occurs, without any concomitant uveal or orbital metastasis.

Case Report

A 63-year-old man who underwent kidney transplantation nine years earlier and had diabetes and hypertension reported a history of a mass in the outer center of the right thigh that had first emerged about three years ago. The histopathological examination of the excisional biopsy was reported as malignant neuroendocrine tumor infiltration of MCC (grade 3). The first surgical (extensive) resection was then performed, and six cycles of chemotherapy (etoposide + carboplatin) were administered.

Nine months later, a new mass and lymph node involvement were detected, and surgical resection and lymph node dissection were performed again. After surgery, 31 radiotherapy sessions were administered. Positron emission tomography with computed tomography (PET/CT) performed four months after the second surgery revealed new and widespread metastatic lesions. Off-label pembrolizumab was initiated for immunotherapy. After four courses of this treatment, there was a decrease in the metabolic activity of the existing metastatic lesions on PET/CT, and this was accepted as a response to the treatment. However, a significantly low platelet count (PLT: 11,000 cell/mL) and tumor infiltration in the bone marrow biopsy were observed during this follow-up period. Chemotherapy (carboplatin + irinotecan) was started by the oncologist. After the patient received four cycles of this treatment, the oncologist discontinued immunotherapy and further chemotherapy was planned.

While the patient was hospitalized in the oncology unit, the ophthalmology department was consulted because of the onset of discharge and redness in the right eye. On examination, a mass in the form of a vascularized nodule approximately 1.5 × 1 cm in size was observed on the midline of the left upper lid (Figure 1). According to information received from the patient's relatives, the nodule had appeared in the last 15 days and was growing rapidly. A comparison of recent magnetic resonance images to those obtained six months earlier (Figure 2) revealed a new enhancing mass on the left upper eyelid and multiple intracranial metastases. Apart from the eyelid metastasis, PET/CT imaging from the same period also detected multiple metastases at sites including the C7, T3, T8, and T9 vertebrae, the bone marrow of the left femur, the fourth rib on the right and third rib on the left, the posterior left iliac bone, the left sacrum, right superior scapula, sternum, abdomen, and pelvis region. In addition, there were multiple hypodense lesions widespread in both lobes of the liver.

Total excision of the eyelid tumor and upper eyelid reconstruction were recommended but could not be performed because the patient's general condition was unsuitable for surgery. Approximately one day after the patient's ophthalmological consultation, a local incisional biopsy of the center of the upper eyelid lesion was performed bedside under sterile conditions for histopathologic evaluation. However, the patient's general condition deteriorated further and he died approximately two days after the biopsy. Histopathologic examination subsequently confirmed the upper eyelid lesion was a metastasis of MCC (Figure 3).

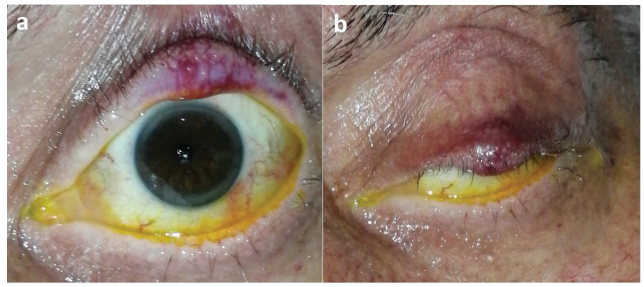

Figure 1. A vascularized, purplish nodule approximately 1.5 x 1 cm in diameter was observed in the center of the upper eyelid (a, b)

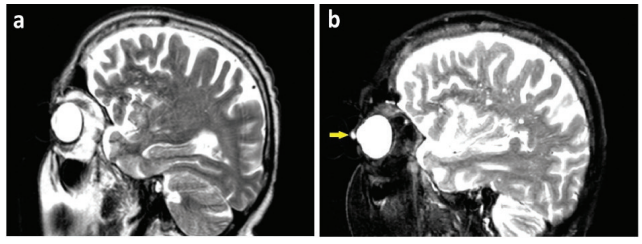

Figure 2. Comparison of magnetic resonance imaging performed 6 months ago (a) with recent scans (b) confirmed the development of a well-confined hyperreflective nodule (yellow arrow) in the left eyelid, as well as multiple intracranial metastases

Discussion

MCC of the eyelid is a rare and extremely malignant tumor with distinctively rapid progression, a high recurrence rate after resection, and early local or metastatic spread.[2] It usually appears in the upper eyelid (76%) as a solitary, painless, multilobulated, violaceous (bluish-purple) nodule near the lid margin (Figure 1).[6] Ulcerations, madarosis, abnormal vascular configuration, and local invasion are often associated with MCC of the eyelid.[6] The eyelid mass may be accompanied by early regional lymph node metastasis in the initial presentation of MCC. MCC of the eyelid may be misdiagnosed as a dermal cyst, chalazion, or hemangioma, and differentiation from other similarly presenting cancerous masses, such as basal cell carcinoma, lymphoma, keratoacanthoma, or metastases, may be difficult in some cases.[6] Thus, a biopsy for histopathologic evaluation should be performed to confirm the clinical diagnosis.

Several risk factors have been identified, such as Merkel cell polyomavirus (MCPyV) infection, sun (ultraviolet light) exposure, acquired immunodeficiency syndrome, chronic lymphocytic leukemia, and immunosuppression.[7] In 2008, Feng et al.[8] detected genomic integration of polyomavirus DNA in 40% of patient samples, leading to the conclusion that MCPyV may be involved in the etiology of MCC. High rates of local recurrence (27-60%), lymph node involvement (45-91%), and distant metastasis (18-52%) have been reported in groups infected with the virus.[8] Recently, Komatsu et al.[7] evaluated the MCPyV status of 10 cases of MCC arising from the eyelid and elucidated the clinical and histopathological characteristics of MCPyV-positive MCC in a literature review.

MCC occurs more commonly on sun-exposed skin. Half of cases are located on the head and neck, 40% on the extremities,

and 10% on the trunk.[7] However, some exceptional tumor sites that are not exposed to sunlight have also been reported, such as the vulva, penis, pharynx, oral mucosa, and thigh, as in our patient.

Poor prognostic factors of MCC are a tumor diameter larger than 2 cm, male sex, immunosuppression, and location on the lower extremities.[5] The average survival time is about eight months from diagnosis in patients with widespread disease. Regional metastases are quite common, and distant metastases do sometimes arise, especially in the liver, bones, lungs, and brain. In the literature, there are no cases of MCC metastasizing to the eyelid from extraocular tissues; this is the first case that showed metastasis of MCC from another region to the eyelid.

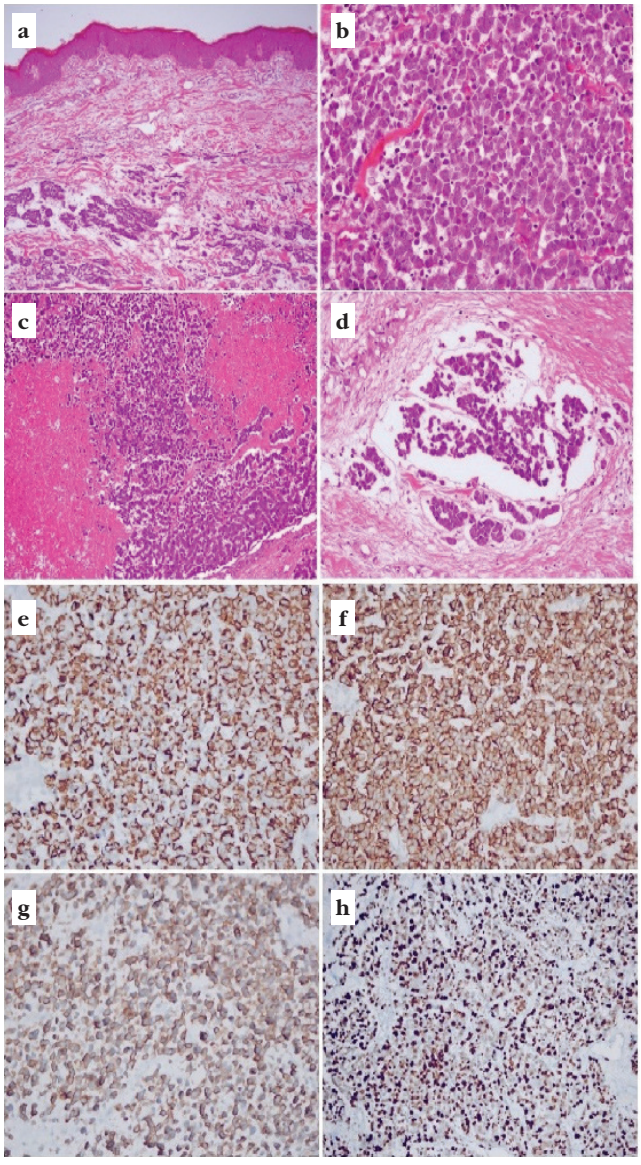

Figure 3. At low magnification, the tumor is seen to be localized to the dermis, unrelated to the epidermis, and arranged as cords and islands (hematoxylin-eosin [H&E], x100) (a). High magnification shows the nuclear features of the tumor cells: neuroendocrine cells with a uniform round nucleus, scant cytoplasm, nuclear molding, and salt and pepper chromatin; mitoses and apoptotic bodies are present (H&E, x400) (b). Areas of necrosis in the tumor (H&E, x200) (c). Tumor cells with lymphatic invasion (H&E, x200) (d). Immunohistochemical features of tumor: cytoplasmic staining with CK20 (e), chromogranin (f), and synaptophysin (g). The proliferative index is very high with Ki-67 (h)

The National Comprehensive Cancer Network Guidelines propose that baseline imaging with CT or whole-body PET/CT may be useful for MCC, especially in cases of lymph node-positive disease.[9] Eyelid metastasis of MCC can occur in various clinical circumstances and should be considered in patients with systemic cancer. These patients usually have multiple metastatic lesions of an ocular and extraocular nature.[10] In our patient, PET/CT imaging revealed multiple extraocular metastases concurrent with the eyelid metastasis in areas such as the vertebral bodies, bone marrow, ribs, iliac bone, sacrum, scapula, sternum, abdomen, pelvis region, liver, and brain.

Metastases from distant primary sites to the eyelids are very rare and comprise less than 1% of all malignant eyelid lesions.[10] The most common primary tumors that metastasize to the eyelids are breast carcinoma, followed by skin melanoma, gastric carcinoma, and lung carcinoma.[10] Half of these metastatic lesions have concomitant ocular sites, which include the uvea and orbit.[10] In the present case, MCC metastasized to multiple body sites, while the only ocular metastasis was to the upper eyelid, the site where primary eyelid MCC frequently arises.

In conclusion, MCC is a rare skin tumor with a significant rate of distant and local metastasis. This case shows that the eyelids are also a possible site for the metastasis of extraocular MCC.

Ethics

Informed Consent: Written consent was obtained from the patient's relatives.

Authorship Contributions

Surgical and Medical Practices: A.Ö., Concept: V.Y., Design: V.Y., N.K., Data Collection or Processing: A.Ö., V.Y., S.Ç., Analysis or Interpretation: A.Ö., N.K., V.Y., Literature Search: A.Ö., V.Y., Writing: A.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Maksimovic S, Nakatani M, Baba Y, Nelson AM, Marshall KL, Wellnitz SA, Firozi P, Woo SH, Ranade S, Patapoutian A, Lumpkin EA. Epidermal Merkel cells are mechanosensory cells that tune mammalian touch receptors. Nature. 2014;509:617-621.
2. North VS, Habib LA, Yoon MK. Merkel cell carcinoma of the eyelid: A review. Surv Ophthalmol. 2019;64:659-667.
3. Lemos BD, Storer BE, Iyer JG, Phillips JL, Bichakjian CK, Fang LC, Johnson TM, Liegeois-Kwon NJ, Otley CC, Paulson KG, Ross MI, Yu SS, Zeitouni NC, Byrd DR, Sondak VK, Gershenwald JE, Sober AJ, Nghiem P. Pathologic nodal evaluation improves prognostic accuracy in Merkel cell carcinoma: analysis of 5823 cases as the basis of the first consensus staging system. J Am Acad Dermatol. 2010;63:751-761.

4. Abbasi AN, Ahmed SM, Qureshi BM. Recent updates in the management of Merkel Cell Carcinoma. J Pak Med Assoc. 2019;69:1693-1699.
5. Herbert HM, Sun MT, Selva D, Fernando B, Saleh GM, Beaconsfield M, Collin R, Uddin J, Meligonis G, Leatherbarrow B, Ataullah S, Irion L, McLean CJ, Huilgol SC, Davis G, Sullivan TJ. Merkel cell carcinoma of the eyelid: management and prognosis. JAMA Ophthalmol. 2014;132:197-204.
6. Walsh NM. Merkel cell carcinoma of the eyelid and periocular region: A review. Saudi J Ophthalmol. 2021;35:186-192.
7. Komatsu H, Usui Y, Sukeda A, Yamamoto Y, Ohno SI, Goto K, Kuroda M, Nagao T, Goto H. Prevalence of Merkel Cell Polyomavirus in Primary Eyelid Merkel Cell Carcinomas and Association With Clinicopathological Features. Am J Ophthalmol. 2023;249:49-56.
8. Feng H, Shuda M, Chang Y, Moore PS. Clonal integration of a polyomavirus in human Merkel cell carcinoma. Science. 2008;319:1096-1100.
9. Sachpekidis C, Sidiropoulou P, Hassel JC, Drakoulis N, Dimitrakopoulou-Strauss A. Positron Emission Tomography in Merkel Cell Carcinoma. Cancers (Basel). 2020;12:2897.
10. Bianciotto C, Demirci H, Shields CL, Eagle RC Jr, Shields JA. Metastatic tumors to the eyelid: report of 20 cases and review of the literature. Arch Ophthalmol. 2009;127:999-1005.