ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.latinamericanjo.com

Latin American Journal of Ophthalmology

Case Report

Merkel cell carcinoma of the cornea and conjunctiva

Francisco Lucero Saá[1], Federico Andrés Cremona[1], Eugenia Páez Soria[1], Pablo Chiaradia[1]

[1]Department of Ophthalmology, Hospital de Clínicas José de San Martín, Universidad de Buenos Aires (UBA), Buenos Aires, Argentina.

***Corresponding author:**
Francisco Lucero Saá,
Department of Ophthalmology,
Hospital de Clínicas José de San Martín (UBA), Córdoba 2351,
Buenos Aires, Argentina.

franlucerosaa@gmail.com

Received : 31 August 2020
Accepted : 29 September 2020
Published : 17 October 2020

DOI
10.25259/LAJO_5_2020

Quick Response Code:

ABSTRACT

A 58-year-old woman presented with a corneoconjunctival tumor, first diagnosed as a squamous neoplasia. An excisional biopsy was performed. Histopathology revealed signs of MCC, which is a rare malignant tumor of the skin. It can affect the eyelids and is a differential diagnose of recurrent chalazion. The patient had a history of multiple chalazia excision. MCC is known to be highly aggressive and tends to metastasize early to regional lymph nodes. It is believed to originate from Merkel cells, which have not been identified in the conjunctiva or cornea. However, the tumor may originate from integration of Merkel cell polyomavirus (MCPyV) in other epithelial cells. Metastatic compromise of the conjunctiva by this tumor has been reported as well. We herein report a case of both corneal and conjunctival involvement by a previously misdiagnosed MCC. A correct histopathological analysis, including immunohistochemistry techniques oriented by clinical suspicion, is crucial for the diagnosis. Prognosis of this tumor is known to be poor, that is the reason why an accurate diagnosis and an early referral to an oncologist are essential to a successful management of the disease.

Keywords: Merkel cell carcinoma, Cornea, Ocular surface neoplasia, Oncology, Oncogenesis

INTRODUCTION

Merkel cell carcinoma (MCC) is an aggressive neoplasm of the skin. It was first described by Dr. Cyril Toker in 1972, referring to it as "trabecular carcinoma of the skin." Merkel cells are dermal mechanoreceptors that have been described as capable of malignant transformation and thought to be the origin of MCC.[1] Nevertheless, it has since been hypothesized that these malignancies may actually arise from abnormal proliferation of dermal pluripotent stem cells without mechanoreceptor function that have similar ultrastructure as Merkel cells.[2] In addition, MCC has also been linked to the infection and integration of Merkel Cell Polyomavirus (MCPyV), before the clonal expansion of tumor cells.[3] Even though it is infrequent, its incidence has increased in the past few years.[4] Many conditions, such as chronic exposure to sunlight, advanced age, and immunosuppression, have been identified as risk factors for the disease. MCC usually appears in areas exposed to the sun in the head and neck, sometimes as a painless erythematous or purple nodule; more rarely an ulcer.[5] These tumors have a poor prognosis, partly due to a delayed diagnosis related to its non-typical appearance, but also to a rapid and aggressive growth, high incidence of local recurrence, and early metastases.[6] Reports of ophthalmological involvement include mostly primary tumors of the eyelid, but also metastases to the orbit, choroid, ciliary body, iris and conjunctiva have been described.[7] We present a case of MCC with conjunctival and corneal involvement.

CASE REPORT

A 58-year-old female was referred to the Cornea Service at Hospital de Clinicas in Buenos Aires. In the past 6 months, she had been intervened several times for recurrent chalazion in her right upper eyelid. She presented with a temporal tumoral mass in conjunctiva and cornea that extended to the upper fornix of her right eye [Figure 1]. The lesion had been previously diagnosed as an ocular surface squamous neoplasia (OSSN) with an incisional biopsy in another center. We performed an excisional biopsy of the tumor and, except for Descemet membrane and endothelium, the rest of the cornea appeared to be compromised. Cryotherapy was performed at the margins of the excision. A bandage soft contact lens was placed at the end of surgery.

Histopathology revealed features of a high-grade non-differentiated carcinoma with a trabecular pattern [Figure 2]. Immunohistochemistry showed cytokeratin 20 and chromogranin expression [Figure 3]; thus, the tumor was diagnosed as a MCC. A computed tomography (CT) scan of the head, neck, chest, and abdomen was ordered, along with a sentinel lymph node (SLN) biopsy. The results were negative for metastasis. Even though being advised otherwise, the patient refused to continue further evaluation and treatment. Finally, she suffered from spontaneous perforation 2 weeks later and was enucleated. A 5-year follow-up has shown no signs of metastasis.

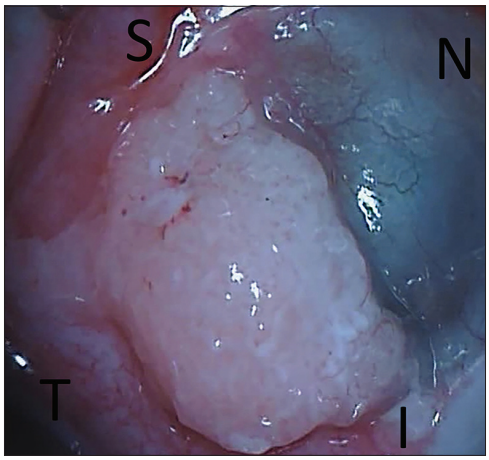

Figure 1: Right eye. Temporal tumor involving conjunctiva, cornea, and upper fornix. T: Temporal. N: Nasal. S: Superior. I: Inferior.

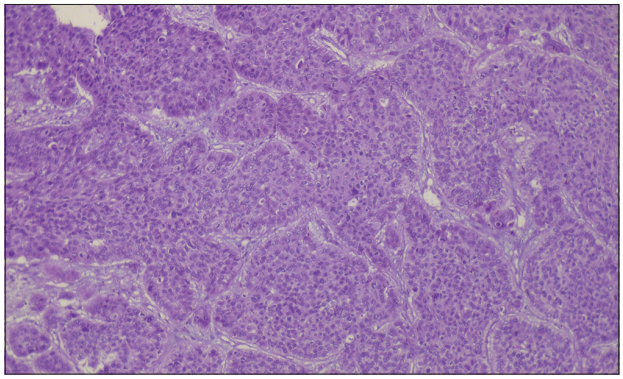

Figure 2: Histopathology (hematoxylin and eosin) showed a diffuse pattern with areas of trabecular aspect. Epithelioid cells arranged mainly in nests displayed severe nuclear atypia and atypical mitotic figures.

DISCUSSION

Ophthalmic primary involvement by this malignancy has been reported in the eyelid, where Merkel cells can be found. The clinical diagnosis of eyelid MCC can be difficult on account of its non-typical appearance and may on some cases be interpreted as a recurrent chalazion.

Histogenesis has not been completely understood yet. Even though historically MCC had been supposed to arise from Merkel cells, this hypothesis has been questioned lately. Feng *et al*. described MCPyV infection and integration into the host genome before clonal expansion of the malignant cells.[2] Furthermore, other epithelial cells, fibroblastic or B-cells, could be infected and induced to adopt a similar phenotype.[8]

Tumor extension to ocular surface and intraocular structures has been reported and appears to be originated by lymphatic dissemination. Alexander *et al.* presumed choroidal compromise in a patient with confirmed brain metastasis of MCC.[9] Purgason *et al*. documented a metastasis to the ciliary body in an enucleated blind eye, in a patient who had a history of a skin biopsy that proved to be MCC.[10] Kase *et al*. described a case of primary MCC of the upper eyelid that metastasized to the lower bulbar conjunctiva and demonstrated tumor cells in lymphatic vessels.[11] Kirwan *et al*. reported a rare case of metastasis to the iris in a 23-year-old female.[7]

To prevent recurrence and metastasis, wide surgical excision with adjuvant treatment is usually performed.

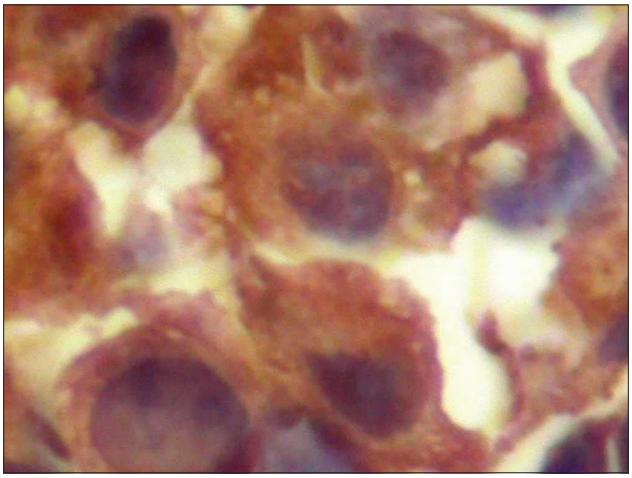

Figure 3: Immunohistochemistry showing positivity for chromogranin.

Assessing lymph node invasion with SLN biopsy followed by secondary complete node dissection in cases of positive histopathology is recommended.[12] Radiation therapy has shown benefits improving the survival rate. On the contrary, adjuvant chemotherapy for MCC has not shown benefits and has even been associated with increased morbidity and mortality. Even though patients may initially respond, resistance often develops.[13] The development of new alternative therapies, such as immunotherapy with checkpoint inhibitors (CPIs), is very promising for advanced disease.[14]

We present a case of a corneoconjunctival tumor that had been misdiagnosed as a squamous neoplasia and presented with a history of recurrent chalazion. A correct histopathological examination revealed MCC, a tumor that is much more aggressive than OSSN. Conjunctival and corneal compromise could be explained by two hypotheses: (1) The primary tumor was located in the eyelid and was misdiagnosed as a chalazion. In this case, extension to the conjunctiva and cornea could have happened either by seeding during surgery or by lymphatic metastasis. Unfortunately, there is no histopathological analysis of the eyelid tissue excised since the surgeries for recurrent chalazion were performed in another center with apparently no clinical suspicion of MCC. On the other hand, no signs of skin tumor were found in the eyelids when the patient was examined in our center; (2) as it has been mentioned before, MCC may arise from epithelial cells other than Merkel cells. Thus, the tumor could have been originated *de novo* from epithelial cells of the conjunctiva.

Another interesting finding in this case is the affection of almost the entire cornea, sparing Descemet membrane, and endothelium. To the best of our knowledge, this is the only report of MCC affecting corneal tissue.

CONCLUSION

Awareness of the existence and clinical presentation of ocular MCC is very important, as an early diagnosis could help to avoid future complications. A thorough histopathological analysis of every excised lesion by a trained pathologist cannot be overemphasized.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Toker C. Trabecular carcinoma of the skin. Arch Dermatol 1972;105:107-10.
2. Halata Z, Grim M, Bauman KI. Friedrich Sigmund Merkel and his Merkel cell, morphology, development, and physiology: Review and new results. Anat Rec A Discov Mol Cell Evol Biol 2003;271:225-39.
3. Feng H, Shuda M, Chang Y, Moore PS. Clonal integration of a polyomavirus in human Merkel cell carcinoma. Science 2008;319:1096-100.
4. Lemos B, Nghiem P. Merkel cell carcinoma: More deaths but still no pathway to blame. J Invest Dermatol 2007;127:2100-3.
5. Atamney M, Gutman D, Fenig E, Gutman H, Avisar I. Merkel cell carcinoma of the eyelid. Isr Med Assoc J 2016;18:126-8.
6. Yin VT, Merritt HA, Sniegowski M, Esmaeli B. Merkel cell carcinoma of the eyelid and periocular region. Cancers (Basel) 2014;6:1128-37.
7. Kirwan C, Carney D, O'Keefe M. Merkel cell carcinoma metastasis to the iris in a 23 year old female. Ir Med J 2009;102:53-4.
8. Kervarrec T, Samimi M, Guyétant S, Sarma B, Chéret J, Blanchard E, *et al*. Histogenesis of Merkel cell carcinoma: A Comprehensive review. Front Oncol 2019;9:451.
9. Alexander E 3rd, Rossitch E Jr., Small K, Rosenwasser GO, Abson P. Merkel cell carcinoma. Long term survival in a patient with proven brain metastasis and presumed choroid metastasis. Clin Neurol Neurosurg 1989;91:317-20.
10. Purgason PA, Hornblass A, Harrison W. Metastatic Merkel cell carcinoma to the eye. Ophthalmology 1991;98:1432-4.
11. Kase S, Ishijima K, Ishida S, Rao NA. Merkel cell carcinoma of the conjunctiva. Ophthalmology 2010;117:637.e1-2.
12. Maalouf TJ, Dolivet G, Angioi KS, Leroux A, Genin P, George JL. Sentinel lymph node biopsy in patients with conjunctival and eyelid cancers: Experience in 17 patients. Ophthalmic Plast Reconstr Surg 2012;28:30-4.
13. Garneski KM, Nghiem P. Merkel cell carcinoma adjuvant therapy: Current data support radiation but not chemotherapy. J Am Acad Dermatol 2007;57:166-9.
14. Villani A, Fabbrocini G, Costa C, Annunziata MC, Scalvenzi M. Merkel cell carcinoma: Therapeutic update and emerging therapies. Dermatol Ther (Heidelb) 2019;9:209-22.

How to cite this article: Lucero Saá F, Cremona FA, Páez Soria E, Chiaradia P. Merkel cell carcinoma of the cornea and conjunctiva. Lat Am J Ophthalmol 2020;3:7.