American Journal of Ophthalmology Case Reports 11 (2018) 95–97

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.elsevier.com/locate/ajoc

Case report

Corneal infiltration and xanthoma formation in mycosis fungoides

Caleb Busch, Noriyasu Hashida*, Kohji Nishida

Department of Ophthalmology, Osaka University Graduate School of Medicine, Osaka, Japan

ARTICLE INFO

Keywords:
Mycosis fungoides
Cutaneous T cell lymphoma
Corneal infiltration
Xanthoma
Optical coherence tomography
Short running title

ABSTRACT

Purpose: To report a case of corneal infiltration and xanthoma formation in mycosis fungoides (cutaneous T-cell lymphoma).

Observations: A middle aged Japanese man with mycosis fungoides (MF) involving the face was referred to Ophthalmology for evaluation of unilateral, painless conjunctival injection. Biopsy of the conjunctiva revealed a malignant T cell population consistent with MF tumor invasion. Years later, he returned following several episodes of infectious keratitis with a painless, yellow, rapidly forming mass in the left eye over two weeks. Corneal biopsy showed foamy histiocytes and positive staining for CD68, and a diagnosis of corneal xanthoma was made.

Conclusions and importance: Severe ocular surface disease can rarely occur in MF by direct invasion of tumor cells. Corneal infiltration and xanthoma development may be avoidable by careful monitoring for infectious keratitis in patients with conjunctival involvement, as in our case.

1. Introduction

Mycosis fungoides (MF) is a neoplastic proliferation of helper T lymphocytes that initially presents as itchy patches on the skin that may progress internally.[1] Ocular abnormalities are infrequent and occur in 2% of patients.[2] Eyelid tumors are the most common finding and typically manifest as ectropion.[3] While most ophthalmic findings are related to the eyelid, direct infiltration of the ocular surfaces by tumor cells may be seen in severe cases. Herein, we describe a rare case of corneal infiltration and xanthoma formation in MF. To our knowledge, this is the first report of corneal xanthoma formation associated with MF.

2. Case report

2.1. Findings

A 42-year-old Japanese male with a one-year diagnosis of MF affecting the face was referred to the Ophthalmology Department for evaluation of persistent, painless conjunctival injection of the left eye. Conjunctival biopsy was taken to investigate ocular involvement of MF due to lack of improvement with topical treatment and, with immunohistochemistry, was suggestive of the malignant T-cell population seen in MF (Fig. 1A–D). His ocular disease was observed until years later when he developed recurrent *Staphylococcus aureus* keratitis of the left eye, which was treated topically. The next year he presented to our clinic with a two-week history of a painless, rapidly forming, yellow, ring-shaped abnormality in the left eye after a previously inconspicuous slit lamp examination (Fig. 2A–C).

On examination visual acuity was 20/22 in the right eye and 20/225 and aphakia in the left eye with normal intraocular pressures in both eyes. Slit lamp biomicroscopy of the left eye revealed an area of corneal vascularization surrounded by a ring-shaped yellow band in the inferior nasal quadrant of the cornea. The adjacent conjunctiva was hyperemic with evidence of corneal infiltration by conjunctival vessels. There was no apparent eyelid abnormality. Fundus examination was normal in both eyes. Anterior Segment Optical Coherence Tomography (ASOCT) revealed a hyper reflective area in the left corneal stroma (Fig. 2G). Over the next several months the ring-shaped lesion transformed into a solid yellow mass (Fig. 2D), and one year after presentation a second mass appeared in the left, temporal cornea (Fig. 2E–F). At this time corneal biopsy of the initial lesion was obtained, which revealed numerous foamy histiocytes that stained positively for CD68 on immunohistochemistry (Fig. 1E–F). A diagnosis of corneal xanthoma was made. Currently, he is receiving chemotherapy for his systemic disease and conservative management of his ocular disease due to patient wishes.

2.2. Materials and methods

Informed consent was obtained from the patient.

Conjunctival and corneal biopsies were performed to confirm ocular

* Corresponding author. Department of Ophthalmology, Osaka University Medical School, E7, 2-2 Yamadaoka, Suita, Osaka, 565, Japan.
E-mail addresses: cbusch2@kumc.edu (C. Busch), nhashida@ophthal.med.osaka-u.ac.jp (N. Hashida), knishida@ophthal.med.osaka-u.ac.jp (K. Nishida).

https://doi.org/10.1016/j.ajoc.2018.06.008
Received 11 November 2017; Received in revised form 26 March 2018; Accepted 18 June 2018
Available online 20 June 2018

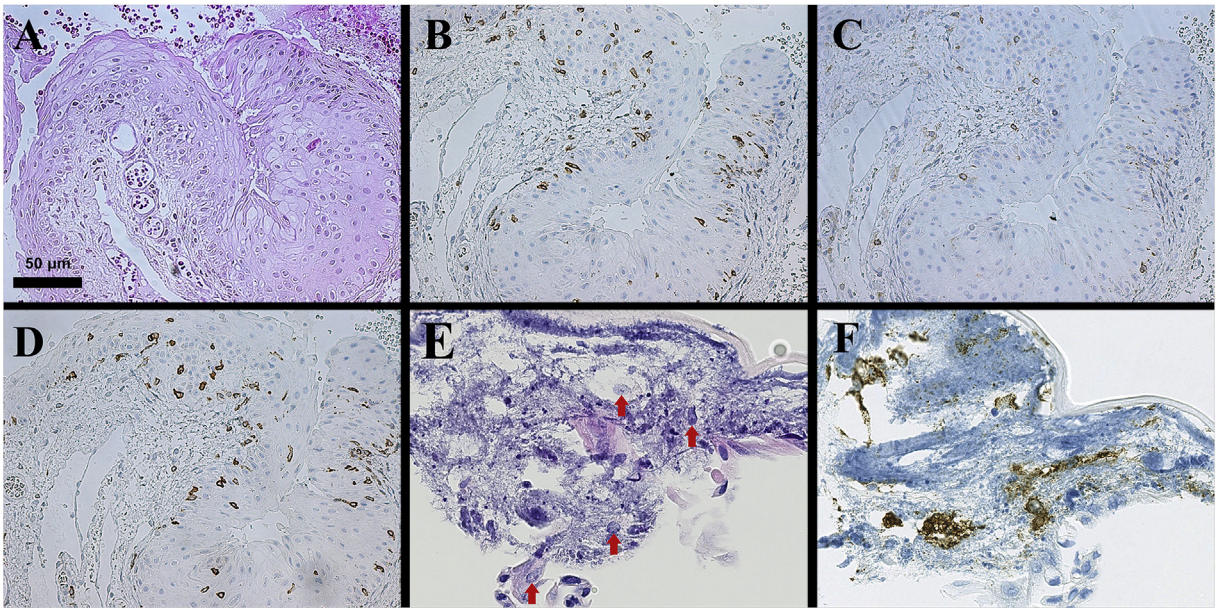

Fig. 1. Conjunctival Biopsy at Referral and Corneal Biopsy at Appearance of Second Mass. Conjunctival biopsy taken at presentation for conjunctivitis shows inflammation and malignant T cell invasion (A). Immunohistochemical staining of conjunctival tissue reveals positive staining for CD3 (B), CD4 (C), and CD8 (D), which is suggestive of the malignant T-cell population seen in MF. Corneal biopsy after formation of the yellow masses reveals numerous foamy histiocytes (red arrowheads) (E) which stained positive for CD68 on immunohistochemistry (F). These corneal biopsy findings in combination with the clinical scenario were suggestive for the diagnosis of corneal xanthoma. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

involvement of MF. Hematoxylin and Eosin and immunohistochemical staining were implemented for both conjunctival (Fig. 1A–D) and corneal specimen (Fig. 1E–F). Immunohistochemical markers for conjunctiva were CD3, CD4, and CD8 for the diagnosis of MF (Fig. 1B–D). The immunohistochemical marker for cornea was CD68 for the diagnosis of xanthoma (Fig. 1F).

ASOCT (CASIA2, TOMEY Co. Ltd., Tokyo, Japan) was performed to evaluate extent of involvement and progression of the corneal abnormality.

3. Discussion

MF is the most common type of cutaneous T-cell lymphoma with an annual incidence of 6.4 cases per million.[4] Ocular involvement is uncommon and is typically related to the eyelid and ocular surface disease.[5] Ectropion is the most common finding and is indirectly caused by tumor cell infiltration of the overlying facial or eyelid skin. Moreover, the ocular surface may be directly infiltrated by tumor cells resulting in lesions of the conjunctiva and caruncle.[6,7] These abnormalities usually appear late in the disease course and are secondary lesions.[8] Historically corneal involvement has been reported as keratitis and corneal scarring, a sequelae to eyelid disease and lagophthalmos. To our knowledge, this is the first report of corneal infiltration and xanthoma formation in MF.

Evidence of corneal infiltration was observed on slit lamp and ASOCT findings. The mechanism of infiltration seen in this case could be explained by direct spread of malignant cells from the conjunctiva to the cornea. Although not nodular in form, our patient had tumor cell infiltration of the conjunctiva confirmed on biopsy. It was speculated that keratitis-associated epithelial damage allowed conjunctival vessels carrying malignant T cells to cross the limbus to seed the exposed corneal stroma. Accordingly, lesions developed in peripheral areas of the cornea affected by keratitis. The appearance of two separate corneal lesions, divided spatially and temporally may be explained by the sporadic nature of the patient's infective keratitis.

Rarely, xanthomatosis has been reported in association with MF.[9] It is thought that malignant T-cell infiltration causes lipoprotein leakage which, after tumor regression, is phagocytosed by macrophages causing xanthoma development around the tumor plaque.[9] The characteristic ring-like growth pattern around corneal vascular lesions in our patient could be explained by this phenomenon, wherein the xanthomatous ring slowly advanced inward as centralized malignant cells regressed. As such, corneal biopsy in our patient did not reveal malignant cells but rather foamy histiocytes and positive staining for CD68. These findings in combination with yellow, annular lesion growth was highly suggestive for the diagnosis of corneal xanthoma. Thus, hyper reflective areas in the corneal stroma observed on ASOCT were thought to be due to the accumulation of lipids.

Lipid Keratopathy (LK) refers to corneal lipid deposition, occurring most commonly secondary to prolonged keratitis, and manifests as a yellow-white corneal abnormality.[10] Chronic inflammation, classically by herpes keratitis or trachoma infection, causes blood vessel extension into damaged corneal tissue and results in lipid exudation, called lipoidal degeneration.[11] Cogan et al. in their description of LK and review of the literature included reports using the term corneal xanthomatosis, among others, which is consistent with our patient's diagnosis.[10] Thus, corneal lipid deposition in our patient could also be explained by lipoidal degeneration owing to prolonged inflammatory insult by resident malignant T cells in the anterior chamber. Our patient's recurrent *staphylococcus aureus* keratitis may have also contributed to a predisposing inflammatory state. Therefore, much the same as neovascularization in LK provides an easy route for lipid access into the cornea,[12] it was thought that in our case it also provided an easy route for malignant cells into the cornea, thereby promoting corneal xanthoma formation by two synergistic phenomena: chronic inflammation with lipoidal degeneration and augmentation of lipoprotein leakage into the cornea by tumor cell invasion. In summary, this case highlights the possible corneal infiltration and xanthoma formation that can occur in MF due to direct invasion of tumor cells. Although rare, careful monitoring for infective keratitis in MF patients with conjunctival involvement may prevent ocular disease progression.

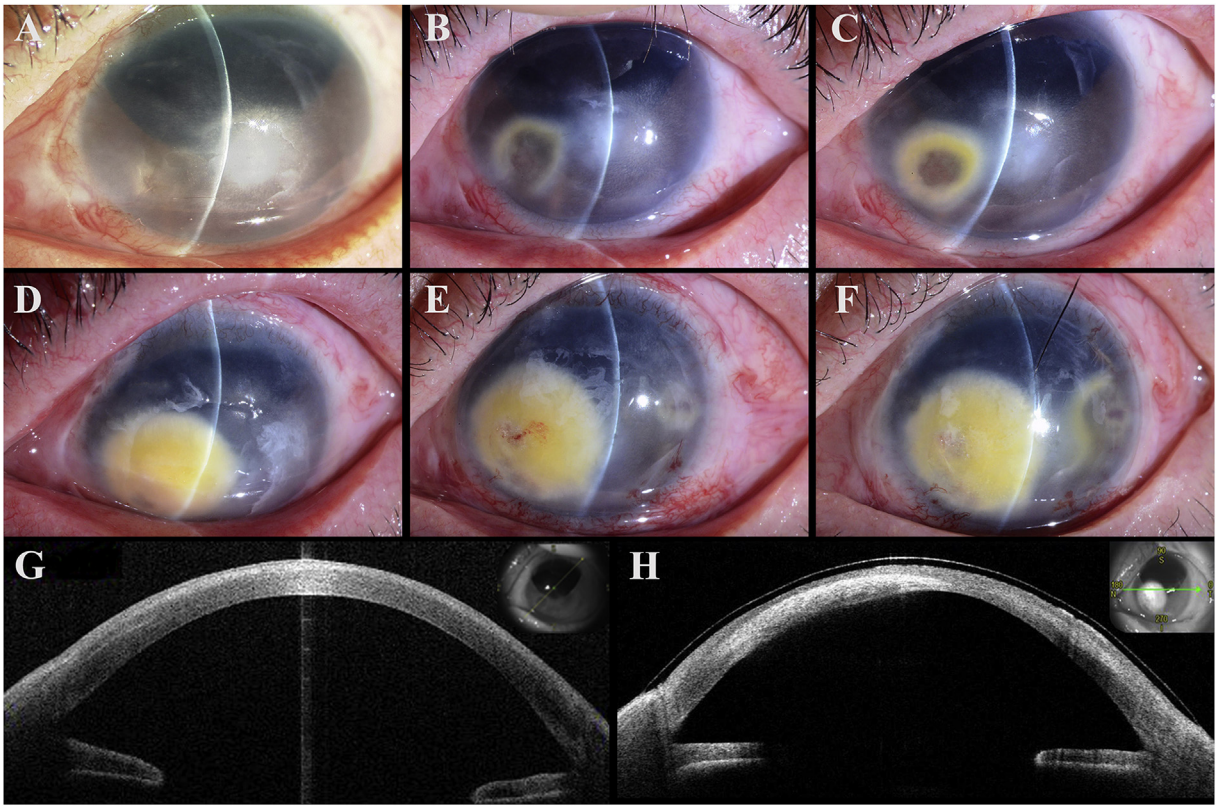

Fig. 2. One-year slit lamp and anterior segment optical coherence tomography (ASOCT) findings Slit lamp images (2 month interval) at presentation reveals a yellow, rapidly forming, ring-like mass in the inferior nasal left cornea in the presence of a corneal epithelial defect (A–C). Conjunctival vessels are seen crossing the limbus and forming a central vascular lesion, which is gradually surrounded by yellow, xanthomatous material. Appearance of a second lesion in the temporal left cornea one year after presentation of the initial lesion (3 month interval) (D–F). A common characteristic growth pattern between lesions was noted: conjunctival vessel infiltration of the cornea, followed by vascular lesion formation and accumulation of yellow material around the lesion. ASOCT at initial presentation reveals a thin line of hyper reflective material in the corneal stroma (G). ASOCT at the appearance of a second lesion one year later reveals a considerably expanded hyper reflective area associated with the initial lesion and a new hyper reflective stromal area corresponding to the new lesion (H). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Patient consent

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Ethics and consent to participate

The Institutional Review Board of the Osaka University Medical School approved the research protocol, and the procedures conformed to the tenets of the Declaration of Helsinki.

Conflicts of interest

The all authors have no financial disclosures.

Funding

No funding or grant support.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ajoc.2018.06.008.

References

1. Diamandidou E, Cohen PR, Kurzrock R. Mycosis fungoides and Sezary syndrome. *Blood.* 1996;88(7):2385–2409.
2. Criscione VD, Weinstock MA. Incidence of cutaneous T-cell lymphoma in the United States, 1973-2002. *Arch Dermatol.* 2007;143(7):854–859.
3. Stenson S, Ramsay DL. Ocular findings in mycosis fungoides. *Arch Ophthalmol.* 1981;99(2):272–277.
4. Cook Jr BE, Bartley GB, Pittelkow MR. Ophthalmic abnormalities in patients with cutaneous T-cell lymphoma. *Ophthalmology.* 1999;106(7):1339–1344.
5. Jusufbegovic D, Char DH. Clinical variability of ocular involvement in mycosis fungoides. *JAMA Ophthalmol.* 2015;133(3):341–343.
6. O'Day J, Rotstein H, Weiner JM. Conjunctival involvement with mycosis fungoides in a patient receiving PUVA therapy. *Ophthalmology.* 1985;92(1):109–113.
7. Rubegni P, Flori ML, Mittica V, Tosi GM, Fimiani M. A case of conjunctival involvement with mycosis fungoides successfully treated by surgery. *Eye.* 1997;11:565–566.
8. Svendsen FH, Rasmussen PK, Coupland SE, et al. Lymphoma of the eyelid - an international multicenter retrospective study. *Am J Ophthalmol.* 2017;177(5):58–68.
9. Ito T, Tokura Y, Yoshinari Y, Furukawa F, Takigawa M. Normolipaemic plane xanthomatosis associated with mycosis fungoides. *Br J Dermatol.* 2000;142(6):1235–1236.
10. Cogan DG, Kuwabara T. Lipid keratopathy and atheroma. *Trans Am Ophthalmol Soc.* 1958;56:109–122.
11. Alfonso E, Arrellanes L, Boruchoff SA, Ormerod LD, Albert DM. Idiopathic bilateral lipid keratopathy. *Br J Ophthalmol.* 1988;72(5):338–343.
12. Crispin S. Ocular lipid deposition and hyperlipoproteinaemia. *Prog Retin Eye Res.* 2002;21:169–224.