

Unilateral Idiopathic Lipid Crystalline Keratopathy: A Clinicopathological Report

Hamidreza Hasani, Amin Zand

Eye Research Center, The Five Senses Institute, Rassoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran

Received: 17 Sep. 2020; Accepted: 16 Feb. 2021

Abstract- Lipid keratopathy refers to corneal lipid infiltrations. We report a 54-year-old female without any systemic disorder presented with a slowly progressive yellow-white infiltrate in the inferotemporal part of the left cornea for six years. Due to a visual axis involvement leading to decreased visual acuity, the patient underwent penetrating keratoplasty on the left eye. The excised corneal button specimen was sent for pathological evaluation. Anterior segment optical coherence tomography (AS-OCT) and confocal scanning microscopy showed an intra-stromal hyper-reflective material consistent with lipid crystalline keratopathy diagnosis. Histopathology revealed an excessive amount of fat droplets in corneal stroma presented as clear areas in hematoxylin and eosin (H & E) staining in keeping with Oil Red O staining. Idiopathic lipid crystalline keratopathy is a diagnosis of exclusion. For such a diagnosis, the serum lipid profile should be checked to rule out fat metabolic disorders and ocular diseases causing chronic inflammation leading to secondary corneal lipid depositions.

© 2021 Tehran University of Medical Sciences. All rights reserved.

Acta Med Iran 2021;59(4):228-231.

Keywords: Lipid keratopathy; Cornea; Crystalline keratopathy; Clinicopathological

Introduction

An unusual case of unilateral, idiopathic, lipid crystalline keratopathy is presented. Lipid deposition in the cornea occurs as a primary or secondary condition. The secondary forms are due to previous ocular traumas or associated localized or systemic pathologies. The primary form is rare and presents without any previous history of ocular trauma, systemic lipoprotein disorders, or lipid dystrophies of the cornea.

Case Report

The patient was a 54-year-old female who suffered from a yellow-white infiltrative lesion with slow progression in the inferior and temporal parts of her left cornea during the past six years. There were no other symptoms, and she did not have any history of ophthalmic disorders or trauma. She had no significant medical or family history. The best-corrected visual acuity of the right eye was 20/25, and of the left eye,

20/200. The corneal sensation of both eyes was normal. Slit-lamp biomicroscopy of the left cornea showed a yellowish-white lesion 6x7.5 mm in size involving the visual axis. Between the 4 and 7 'clock positions of the limbus, mild stromal vessels passed into the corneal infiltration deeply. Upon examination, the whole thickness of the inferior and temporal stroma was found to be involved with intact overlying epithelium. (Figure 1A). Examinations for the right eye were unremarkable, except for mild senile nuclear sclerosis cataract formation. There was no relative afferent pupillary defect (RAPD). Intraocular pressure was normal in both eyes with an I-care tonometer (Icare® ic100, Finland). Ocular ultrasonography revealed no abnormalities in the posterior segment of the affected eye. Laboratory tests of serum cholesterol and triglyceride levels, complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), antinuclear antibodies (ANA), anti-double-stranded DNA antibodies, rheumatoid factor (RF), anti-neutrophil cytoplasmic antibodies (ANCA), sarcoidosis, and tuberculosis screen were normal.

Corresponding Author: A. Zand

Eye Research Center, The Five Senses Institute, Rassoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran
Tel: +98 2166558811, Fax: +98 2164352473, E-mail address: sandpost3@gmail.com

Anterior segment optical coherence tomography (AS-OCT) imaging showed hyperreflective material with sharp tapering ends in the corneal stroma at the site of involvement. No irregularity of the Bowman layer, epithelium, or Descemet's membrane was visible (Figure 1B).

Confocal scanning revealed a dense corneal hazy zone with brilliant hyper-reflective deposits, and sharp tapering ends. Endothelium and epithelium were unremarkable. Endothelial cell density was reported as 2223.4 cell/mm² with a mean cell area of 449.8 μm². These findings suggested lipid crystalline keratopathy (Figure 1C).

An uneventful central penetrating keratoplasty was performed for the left eye. Intraoperatively, the affected part of the cornea was noted to be bulging posteriorly into the anterior chamber. Corneal donor graft diameter (7.50 mm) was punched 0.5 mm larger than the trephined recipient cornea (7.00 mm). A therapeutic contact lens was installed over the cornea at the end of surgery. During the postoperative period, topical eye drops of chloramphenicol 0.5% and betamethasone 0.1% were administered and tapered for eight weeks. The excised corneal button specimens were evaluated by an ocular pathologist for histopathological examinations.

On a postoperative day 1, the donor-recipient

interface was well-opposed, with clean sutures and minimal corneal graft edema. After 1-week, the therapeutic contact lens was removed. At the 6-week follow-up, the corneal graft was completely clear, without any staining. No complications were found postoperatively. At six months, her BCVA was 20/40, without any ocular surface disorders. No evidence of recurrence was seen during the 6-month follow-ups (Figure 2).

Histopathology

A 7-mm corneal button was prepared and bisected to two fragments. The fragments were fixed in 10% formaldehyde. They were then embedded in paraffin and sectioned. The specimens were stained with hematoxylin and eosin (H & E) and Oil Red O for fat staining. On light microscopy examination, the corneal epithelium showed mild edema with an intact Bowman layer. Increased thickness of the superficial and deep stroma was detected, with some areas of collagen fibril disorganization. Heavy infiltration of the stroma by clear spaces was present on H & E staining (Figure 1D). In this staining method, hydrophobic materials remain clear and are usually rich in fats. Descemet's membrane and endothelium appeared unremarkable. Oil Red O was used to confirm lipid deposition in the corneal stroma (Figure 1E).

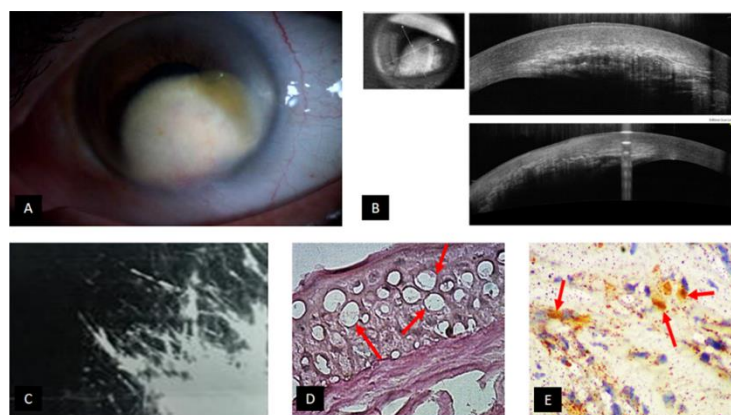


Figure 1. A: High-magnification slit-lamp biomicroscopy of the left eye exhibiting a yellowish-white lesion 6x7.5 mm in size, involving the visual axis, with an extension of deep stromal neovascularization from inferior corneoscleral limbus; B: Anterior-optical coherence tomography demonstrating hyperreflective material with sharp tapering ends in the corneal stroma at the involved site; C: Confocal scan showing hyper-reflective lipid crystals with sharp terminals at the level of deep stroma; D: Hematoxylin and eosin staining: arrows show clear spaces (hydrophobic materials);

E: Oil Red O staining: arrows demonstrate lipid-rich areas



Figure 2. One-week after central penetrating keratoplasty

Discussion

Deposition of lipid in the cornea has been observed in many disorders, including lipid keratopathy, Schnyder's corneal dystrophy, arcus senilis, and xanthogranuloma of the cornea (1,2). Secondary lipid deposition in the cornea has been found in systemic lipoprotein disorders, such as familial high-density lipoprotein deficiencies and Tangier disease (1,3).

In systemic lipoprotein disorders, usually, the corneas are involved bilaterally, without any vascularization. However, our patient had only unilateral involvement with mild peripheral deep corneal vascularization.

Arcus senilis consists of bilateral grey areas at the periphery of the cornea, which is separated from the limbus via a lucid area and maybe a physiologic aging alteration in the elderly. But, controversially, it also can develop in young patients with hyper-lipoproteinemia. In our case, central corneal involvement rendered this differential diagnosis unlikely (3).

The unilateral involvement of the cornea was against lipid dystrophies such as Schnyder's crystalline dystrophy (2).

Lipid keratopathy is one kind of corneal degeneration with a creamy or yellowish opacification appearance. Common findings in degenerative processes of the cornea are deposition of material, thinning of tissue, and neovascularization. The two main types of lipid keratopathy are the primary and secondary forms. Diagnosis of the primary type is based on the presence of lipid deposits (e.g., cholesterol and phospholipids) in the corneal stroma without any history of vascularization or inflammation with a normal serum lipid profile. To our knowledge, this type is commonly bilateral and rare. In the secondary type, corneal blood vessels are often present, which leads to chronic extravasation of cholesterol and fatty acids into the corneal stroma and subsequent opacification (4). Our patient had mild deep corneal neovascularization, especially at the inferior limbus of the affected eye, but it was not a prominent finding to be considered as the baseline etiology. Also, the patient did not mention any previous ocular trauma or particular ocular or systemic disorders, and her family history was unremarkable. In our further investigations, her lipid profile was within normal limits. Considering all these aspects, the most probable diagnosis for her condition was unilateral idiopathic lipid keratopathy.

Very few patients similar to our case with lipid deposition and without any previous ocular trauma, or systemic lipid metabolic disorders, have been reported

previously. Baum (5) presented a 72-year-old female with lipid deposition of the inferior section of the corneal stroma in one eye. Mild and deep vessels extended into this lesion. Baum's patient did not have any previous history of ocular trauma or ocular or systemic diseases. This patient underwent partial penetrating keratoplasty without any recurrence. Barishak and Stein (6) reported a 31-year-old male with unilateral idiopathic corneal lipid infiltration with vascularization of the cornea and the adjacent corneoscleral limbus. These accounts are similar to our patients. There are also some reports of bilateral idiopathic lipid deposition in the cornea. For example, Loeffler *et al.*, (7) presented a 35-year-old male with bilateral lipid depositions in the stroma and the adjacent limbal area. Their patient did not have any history of ocular or systemic diseases, including lipid metabolic disorders. Levy *et al.*, (8) presented a 44-year-old male with bilateral lipid keratopathy without corneal neovascularization. Their patient did not have any previous ocular disorders or hyperlipidemia. Ghanem *et al.*, (9) reported two cases with progressive bilateral stromal lipid depositions in the corneal peripheries. The patients' history of ocular trauma and systemic diseases was unremarkable.

The underlying pathophysiology in these idiopathic cases is not clear. A possible explanation is a mild inflammatory process at the ocular surface or at the limbal area, which was not detectable for the patient but led to vascularization of the corneal stroma and lipid infiltration. As a hypothesis, a functional disorder in the endothelial cells may be followed by the leakage of lipid materials into the neighboring tissues inducing inflammation, corneal vascularization, and further fat infiltration (10). Finally, an unknown disorder in the corneal cells may result in the release of their lipid substances into the stroma, leading to a vicious cycle of further inflammation, vascularization, and lipid deposition (7).

In conclusion, when confronting a patient with lipid keratopathy, possible underlying ocular or systemic etiologies should be ruled out before making the diagnosis of idiopathic lipid keratopathy.

References

1. Alfonso E, Arrellanes L, Boruchoff SA, Ormerod LD, Albert DM. Idiopathic bilateral lipid keratopathy. *Br J Ophthalmol* 1988;72:338-43.
2. Ghazal W, Georgeon C, Grieve K, Bouheraoua N, Borderie V. Multimodal Imaging Features of Schnyder

- Corneal Dystrophy. *J Ophthalmol* 2020;2020:6701816.
3. Lock JH, Ross CA, Flaherty M. Corneal arcus as the presenting sign of familial hypercholesterolemia in a young child. *J AAPOS* 2018;22:467-8.
 4. Pang Y, Zhan Q, Bao Y. A CARE-compliant article: ipsilateral progressive idiopathic lipid keratopathy: A case report. *Medicine (Baltimore)* 2019;98:e16589.
 5. Baum JL. Cholesterol keratopathy. *Am J Ophthalmol* 1969;67:372-5.
 6. Barishak YR, Stein R. Lipid keratopathy. *Ann Ophthalmol* 1974;6:377-80.
 7. Loeffler KU, Seifert P. Unusual idiopathic lipid keratopathy: a newly recognized entity? *Arch Ophthalmol* 2005;123:1435-8.
 8. Levy J, Benharroch D, Lifshitz T. Bilateral severe progressive idiopathic lipid keratopathy. *Int Ophthalmol* 2005;26:181-4.
 9. Ghanem RC, Ghanem VC, Victo G, Alves MR. Bilateral Progressive Idiopathic Annular Lipid Keratopathy. *Case Rep Ophthalmol Med* 2012;2012:1-4.
 10. Cogan DG, Kuwabara T. Lipid keratopathy and atheroma. *Trans Am Ophthalmol Soc* 1958;56:109-22.