Case Report

Complicated Diabetic Keratopathy: A Case Report

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Abstract

The altered ocular surface milieu in diabetics has been a subject of research in recent times. Consequently, diabetic keratopathy is increasingly being recognized as a cause of slow and complicated wound healing of the cornea. We report a case of a young, type I diabetic male with uncontrolled blood sugars at the time of presentation. He presented to us with a 1.5 x 2 mm sterile corneal infiltrate which progressed to a large ulcer with hypopyon unresponsive to topical therapy and threatening ocular integrity. He improved only with a tight control of glycaemic status and supportive ocular therapy over a unusually long period of 4 months. We conclude that in this case of keratopathy complicated by ulceration, a tight glycaemic control was the key to healing and stabilization of the ocular surface.

Delhi J Ophthalmol 2019;30;69-71; Doi http://dx.doi.org/10.7869/djo.511

Keywords: *Diabetic Keratopathy, slow healing, tight glycaemic control*

Introduction

According to a report published by the WHO in 2016,[1] the prevalence of diabetes is steadily rising in the middle-income countries. Today the global incidence of diabetes stands at a staggering 422 million adults and diabetes alone was responsible for 1.5 million deaths in 2012. Diabetes is also an important cause of ocular morbidity. Closely following diabetic retinopathy, corneal problems are found in up to 70 % of examined diabetic patients.[2] Corneal wound healing in diabetics is frequently complicated by unusually prolonged periods of healing and ulceration leading to disastrous outcomes in some cases. However, the ocular surface in diabetics is a largely overlooked part of the eye. The various structural and functional abnormalities in the diabetic cornea have been found to contribute directly or indirectly to corneal complications such as slow epithelial healing and endothelial decompensation after procedures like cataract extraction, vitrectomy, refractive procedures and pan retinal photocoagulation.

Case History

A 34 years old male reported to our OPD with complaints of sudden onset of pain, redness and photophobia in his right eye of 3 days duration. There was no history of preceding trauma or contact lens wear. He was on insulin therapy for type 1 diabetes diagnosed 6 months from presentation. His blood sugar level at the time of presentation was 360 mg/dl (RBS). His presenting visual acuity was 6/6 in both eyes unaided. On further evaluation he was found to have a small 1.5 x 2 mm anterior stromal infiltrate in the cornea of the right eye between 9 to 10 o'clock with an overlying epithelial defect and circumcorneal congestion [Fig.1a]. Lids and adnexa were within normal limits with mildly decreased corneal sensations. Fundus evaluation showed changes of early NPDR in both eyes. A corneal scraping was performed which revealed only few gram-positive cocci (GPC) without any evidence of fungal elements. Accordingly, therapy was instituted with a broad-spectrum antibiotic (gatifloxacin 0.5% e/d- 2 hourly) and cycloplegic (homatropine 2 % e/d -3 times daily).

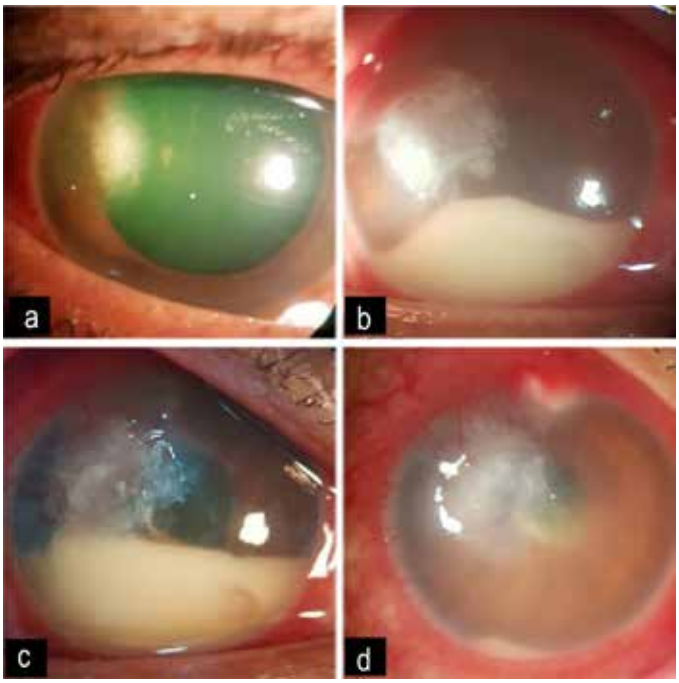

Figure 1: *(a) 1.5 x 2 mm anterior stromal infiltrate with overlying epithelial defect RBS-360 mg/dl, (b) Infiltrate increased in size and density with hypopyon at Day-11, FBS- 270 mg/dl, PPBS- 410 mg/dl , HbA1c – 10.2. (c) Progressing ulcer with a large hypopyon at Day-39, FBS- 274 mg/dl, PPBS- 384 mg/dl , (d) Paracentral infiltrate resolving but appearance of new infiltrate at 12'o clock at Day-69, FBS- 128 mg/dl, PPBS- 200 mg/dl*

However, the ulcer failed to resolve and continued progressing, alongside an escalating blood sugar level (Figure 1b and Figure 1c). We repeated scraping after stopping all antibiotics with the same result, showing a few GPCs. Continued progression prompted us to perform anterior chamber lavage due to a large hypopyon. This time the scraping showed few gram-negative bacilli on direct smear while culture for both fungus and bacteria continued to be sterile. The infiltrate showed progression with increase in the size of hypopyon. The fact that we were facing diabetic keratopathy was very clear by this time hence, we added autologous serum eye drops. Meanwhile, the treating

diabetologist modified therapy by increasing the dose of insulin. We did not consider keratoplasty as the infiltrate remained superficial but was slowly increasing in size towards the centre, the periphery of the cornea remaining clear. The blood sugar levels started to decline as a favourable response to improvisation of insulin therapy. However, a new infiltrate appeared at 12'O clock limbus (Figure 1d). But as the patient seemed to be improving overall, we continued the same therapy along with strict glycaemic control. On successive visits the ocular condition started improving with regression of hypopyon and resolution of the infiltrate with scarring and neovascularization (Figure 2a). It took 4 months and most importantly aggressive control of the blood sugar level for the ulcer to finally heal (Figure 2b).

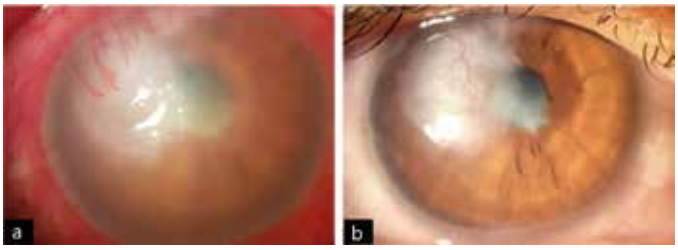

Figure 2: *(a) Resolving ulcer, Day-84, FBS- 108 mg/dl, PPBS- 196 mg/dL (b) Healed ulcer with scarring and neovascularization, Day-126, FBS- 94 mg/dl, PPBS- 161 mg/dL*

Discussion

With increasing understanding, the effects of diabetes on the ocular surface are being recognized. All layers of the cornea have manifestations of a prolonged diabetic state. Table 1 shows the abnormalities in various layers of the cornea with their pathological basis and ultrastructural changes.

Diabetic keratopathy came into recognition when patients undergoing vitrectomy for DR had corneal epithelial healing problems after removal of the epithelium.[3] It has been estimated to occur in 47–64% of diabetic patients during the course of their disease, and is the most commonly recognized corneal complication in both type 1 and type 2 diabetics.[4] Various studies and animal models have pointed towards a highly probable direct relationship between diabetic neuropathy and keratopathy.[2] However, the molecular mechanisms demonstrating the same haven't been elucidated.

Diabetic corneal neuropathy - a component of the polyneuropathy characteristic of diabetes has been found to predate the onset of diabetic retinopathy.[2] Most prominent changes occur in the sub basal nerve plexus showing a reduction in nerve fibre density.[4] Corneal neuropathy has been found to worsen after photocoagulation in PDR.[4] Advanced glycation end-products or AGEs have been implicated in various abnormalities of the diabetic cornea like increase in corneal thickness. They have been demonstrated in all layers of the cornea and are thought to induce apoptosis of cells by way of nuclear oxidative DNA damage both of the epithelium and endothelium.

The endothelial cell changes seem to be minor overall, but a few studies have pointed out that the diabetic cornea carries an increased risk of decompensation following surgery in comparison to non-diabetics.

With regards to corneal infections it has been found that diabetics are more susceptible to occurrence of infections however, the etiological differences between diabetics and non-diabetics are not significant.[5]

Table 1 : Morphological and ultrastructural changes in various layers of the cornea due to diabetes .

Layer/Structure	Abnormality	Pathophysiology	Ultrastructural changes
Epithelium	• Delayed wound healing • Persistent erosions • Epithelial fragility • Loss of epithelial barrier function • Ulceration	• Prolonged hyperglycemic states induce enhanced production and activation of MMPs leading to destruction of the BM and collagen type IV[4] • Decreased synthesis of BM components[2] • Neuropathy • Tear film abnormalities	• BM fragility • Decreased hemidesmosomes • Altered epithelial adhesion
Nerves	• Decreased sensitivity[2,4] • Delayed nerve regeneration after injury[2]	• Diabetic polyneuropathy	• Decreased sub basal nerve fiber and branch density[2] • Increased stromal nerve thickness and tortuosity
Stroma	• Increased CCT[4] • Altered stromal maintenance and remodeling[2]	• Accumulation of AGEs[6] • Upregulation of MMP-3 and MMP-10[2]	• Increased collagen crosslinking[2,4] • Abnormal collagen fibrils
Descemet's membrane and Endothelium	• Increased permeability[2,4]	• Reduced activity of Na+-K+ ATPase[4]	• Vertical lines in the DM – Waite Beetham lines[4] • Decreased hexagonality and cell density, increased coefficient of variation in cell size[4]
Tear film	• Decreased tear secretion[7] • Increased tear osmolarity[7]	• Lacrimal gland inflammation[7] • Diabetic neuropathy • Decreased mucin	• Accumulation of AGEs and hyperglycemia associated oxidative stress of the lacrimal gland[7] • Decreased density of conjunctival goblet cells

Conclusion

Given the escalating numbers of diabetics by the day, diabetic keratopathy is ready to assume CenterStage amidst cornea specialists and researchers alike. There have been a handful of case reports,[8,9,10] on the challenges in corneal wound healing in diabetics. Our case highlights the importance of a strict blood sugar level control as perhaps, the most important factor in healing of the ulcer. Other modalities of topical treatment like insulin, nerve growth factor and naltrexone,[11] are still under research. In addition, the disturbed corneal equilibrium in the diabetic patient warrants a detailed evaluation of the morphological and functional aspects of the cornea before procedures such as cataract surgery or pan retinal photocoagulation and also in contact lens users. Tear film evaluation, pachymetry, specular and confocal microscopy are invaluable in analysis and decision making in such patients.

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Cite This Article as: *Shukla P, Agarwal B, Borah E, Deori N. Complicated Diabetic Keratopathy: A Case Report.*

Acknowledgments: Nil

Conflict of interest: None declared

Source of Funding: None

Date of Submission: 25 March 2019
Date of Acceptance: 12 August 2019

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