Management of Fuchs endothelial corneal dystrophy (FECD): a case series

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INTRODUCTION

The most prevalent type of corneal dystrophy, Fuchs endothelial corneal dystrophy (FECD), frequently causes vision loss. The corneal edema, irregular size and shape of corneal endothelial cells (CEC), Descemet's membrane (DM) thickness, and deposition of extracellular matrix in the form of guttae were its distinguishing features. The cornea expands and causes vision loss when the number of endothelial cells drops to extremely low levels. Typically, the clinical course of FECD lasts 10–20 years.1

FECD more commonly occurs bilaterally, has a slow progression, and generally occurs at 40 years and over. With a ratio of 3.5:1, the incidence is higher in women than in men. In the United States, roughly 4% of people over 40 had FECD, compared to 6.7% of Singapore's over-50 population and 3.7% of Japan's over-50 population in the Asian group.2

The etiology of FECD is multifactorial, with the important role of genetic factors and oxidative stress factors. It is inherited in an autosomal dominant manner (mutations in α2 collagen VIII (COL8A2). The clinical course of FECD is divided into four stages based on the severity. Besides being established by history taking and clinical symptoms, the diagnosis of FECD is supported by biomicroscopic examination findings. Other examination modalities used in diagnosing FECD apart from slit-lamp biomicroscopy are corneal pachymetry, OCT anterior and non-contact specular microscopy. However, these tools cannot monitor changes in the course of the disease or predict its development, especially after cataract extraction.3

Treatment of FECD is divided into medical therapy (topical hyperosmotic agents) and corneal transplantation (DMEK and PK) when visual acuity begins to be disturbed. Initial management is not specific to FECD but is used to treat all causes of edema in the corneal stroma's epithelial lining. Topical hyperosmotic agents (eye drops or ointment), which act by increasing the osmolarity of the precorneal tear film, are used to treat the corneal edema that occurs in FECD. Using a bandage contact lens aims to reduce pain from repeated erosion of the corneal epithelial layer and reduce irregular astigmatism in patients with bullous keratopathy. The use of cycloplegia and...
nonsteroidal anti-inflammatory agents are also used to treat pain that occurs due to bullous keratopathy. Using drugs that work to reduce intraocular pressure aims to reduce corneal edema in patients with FECD. Treatment of FECD using drugs aims to overcome the symptoms that occur. However, the current definitive treatment to restore visual acuity in patients with FECD is through corneal transplantation, replacing the corneal endothelial cells in damaged recipients with a layer of healthy donor endothelium. This makes FECD the most frequent indication for a corneal transplant procedure.\(^4\)\(^-\)\(^6\)

In this case series, we described three cases with FECD, but all of the cases have not undergone corneal transplantation yet due to the COVID-19 pandemic. The purpose of this case series is to discuss the etiology, pathophysiology, diagnosis, and management further so that it can be useful to increase knowledge regarding FECD.

**METHODS**

We recruited all patients with FECD visiting the eye polyclinic of Ramata Hospital from January 2020-December 2020. The diagnosis of Fuchs’ Endothelial Dystrophy was made clinically based on anamnesis and slit lamp examination by an ophthalmologist. The FECD was characterized by corneal edema, reduced density of corneal endothelial cells (CEC) with abnormal size and shape, thickening of Descement’s membrane (DM), and deposition of extracellular matrix in the form of guttae.

**CASE PRESENTATION**

Case I

A 60-year-old female came for the first time to the Eye Polyclinic, Division of Cataract and Refractive Surgery, Ramata Hospital, on July 2020. The patient complained of blurred vision in her left eye for 1 year. The blurred vision felt like seeing fog, especially in the morning, then improved afterward. For the last 4 months, the blurred vision felt like fog all day long, like sand and glare, especially when exposed to bright lights or the sun. The complaints have been getting worse for 1 month. The complaints were accompanied

**Figure 1.** Anterior segment of the right eye in Case I (courtesy of Siska); (a) corneal vascular injection (CVI) and peri corneal vascular injection (PCVI) on the conjunctiva; (b) post PK sutures; (c,d) Descemet fold on the cornea.

**Figure 2.** Anterior segment of the left eye in Case I (courtesy of Siska); (a) The cornea was edema and had thickened stroma; (b,c) guttate endothelium; (d) The lens was minimally cloudy.
by a white appearance like a blister in the middle of the clear membrane of the eye but without pain. Family history of having the same complaint in the eye and abnormalities in the lining of the eye and corneal grafts was denied. The right eye had the same complaint last year. The patient had a history of cataract surgery 1 year ago, in January 2019. The position of the lens was said to be forward, which damaged the clear membranes of the eye, then a corneal transplant was performed in June 2019. After the corneal transplant, the visual acuity was improved. History of systemic disease, drug allergies, and the use of glasses were denied.

Ophthalmological examination of the right eye revealed visual acuity 6/18; corneal vascular injection (CVI) and peri corneal vascular injection (PCVI) on the conjunctiva; and post PK sutures and Descemet fold on the cornea (Figure 1). Specular examination of the corneal endothelium revealed the central corneal thickness (CCT) was 682 µm, cell density (CD) not detected, coefficient of variation (CV) 37 %, percentage of cell hexagonality (HEX) 24 %, N 436 cells, min 113 µm, max 538 µm, AVG 226 µm, SD 83 µm.

An ophthalmological examination of the left eye revealed visual acuity on 6/12. The cornea was edema, had thickened stroma, and guttate endothelium. The lens was minimally cloudy with NO2NC3 grading (Figure 2). Intraocular pressure (IOP) was 11 mmHg. Specular examination of the corneal endothelium revealed CCT 582 µm, CD 2593 cells/mm², CV 37 % and HEX 23 %, N 193 cells, minimum 153 µm, maximum 818 µm, AVG 386 µm, SD 143 µm. The patient was diagnosed with a corneal scar on the right eye post PK and pseudophakia, FECD grade II and immature senile cataract on the left eye, and dry eye in both eyes. The patient was treated with a warm compress, lubricant eye drop (Systane® Ultra) thrice a day in the right eye, artificial eye teardrops thrice a day in both eyes and planning for phacoemulsification and DMEK in the left eye.

**Case II**

An 80-year-old female presented with a complaint of blurred vision in both eyes 6 months ago, especially in the morning.
and then improved afterward, but since 2 months ago, the complaint was felt all day long. The complaints were accompanied by a feeling of grit, pain, and glare. There was not any family history of similar complaints or corneal transplants. The patient had a history of cataract surgery in the right eye in March 2020.

Ophthalmologic examination revealed light perception visual acuity in the right eye and 1/60 in the left eye. In both eyes, the cornea was cloudy, with thickened stroma, edema in the endothelial layer to the stroma, guttate endothelium in the central part, which spread towards the periphery, and a cloudy lens (Figure 3 and Figure 4). The posterior segments were within normal limits, and the intraocular pressure was 12 mmHg for both eyes. In this patient, the specular microscopy examination was not detected. The patient was diagnosed with RLE FED grade II, LE Pseudophakia, and RE Immature Cataract. Visual acuity was light perception in the right eye and 1/60 in the left eye. She was managed with Siloxane 2x1 RLE, Oculenta gel 1x1 RLE, and DMEK in LE.

Case III

A 73-year-old male presented with a complaint of watery in both eyes. Initially, the right eye had blurred vision for 4 months, especially in the morning and then improved afterward, but since 2 weeks ago, complaints have been constant all day. The complaints were accompanied by gritty sensations, pain, and glare. Family history of similar complaints and corneal transplant were denied. The patient had a history of cataract surgery in the right eye 6 months ago and amniotic graft surgery 1 month ago. Ophthalmological examination in the right eye revealed Hand Movement (HM) vision, ciliary injection conjunctiva, a stromal scar in the cornea, bulla in the epithelium, hazy endothelium, neovascularization in the stroma, and pseudophakic lens (Figure 5). The posterior segment was within normal limits and IOP 15 mm Hg. The left eye was normal. The patient was diagnosed with pseudophakia, FED grade III, and corneal neovascularization in the right eye. He was planned for superficial keratotomy and AMT insertion and then performed PK on the right eye, Diquafosol sodium (Diquas®) eye drop twice a day, and eye fresh plus eye drop 4x1 in both eyes.

**DISCUSSION**

Loss of corneal endothelial cells, thickening of the DM, and the deposition of extracellular matrix in guttae are the hallmarks of FEDC. The cornea expands and causes vision loss when the number of endothelial cells drops to extremely low levels. Typically, the clinical course of FEDC lasts 10–20 years. More than a century ago, Professor Ernst Fuchs coined the term “Epithelial Dystrophia” to describe the condition after observing a progressive pattern of corneal opacities, mainly affecting the inferior sections of the cornea and were followed by decreased corneal sensation. Elderly patients also experience diurnal variations that affect the epithelium. Using a slit lamp biomicroscope, Koeppel saw the characteristic guttae finding described by Fuchs in the corneal endothelium of patients with corneal edema six years later.

FEDC is inherited in an autosomal dominant manner. It usually occurs bilaterally, has a slow progression, and is more common at the age of above 40. The incidence of FEDC is more common in women. In the first and second cases of our reports, the FEDC occurred in Asian women aged over 40 and occurred in both eyes. The family history of experiencing the same complaint or undergoing a corneal transplant surgery was denied in all three cases.

The clinical course of FEDC is divided into four stages based on the severity. This series’s first and second cases were diagnosed with FEDC grade II. Stage II of FEDC is marked by impaired visual acuity in patients, where patients complain of blurred vision. The corneal guttae have started to consolidate and expand outward toward the corneal periphery, which may be seen biomicroscopically. Endothelial cells thin, expand, and lose their hexagonal form as guttae develop along the DM. Because the incorporation of guttae is accompanied by an ongoing loss of endothelial cells due to edema in the epithelial lining and corneal stroma, the number of guttae is inversely correlated to the density of endothelial cells. At this stage, the patient begins to experience decreased vision and symptoms of painless glare due to increased stromal edema. The clinical signs were in accordance with the patients in our series, who complained of blurry vision, like seeing fog, sand, and glare, especially when exposed to bright lights or the sun.

In case III, both eyes are watery. Stage III of FEDC is characterized by edema in the cornea that continues into the epithelial layer and causes bullae formation in the epithelial and subepithelial layers. If the bulla was ruptured, it would cause pain in the patient and had a risk for secondary infection.

Specular microscopy is an essential diagnostic tool in the diagnosis of FEDC. The density, coefficient of variation and proportion of hexagonal cells that make up the corneal endothelium can all be calculated using specular microscopy. In individuals with FEDC, specular microscopy revealed a guttate appearance, indicated by endothelial cells with irregularly shaped and hyporeflective appearance.

On non-contact specular microscopy, it was shown that the cornea was thickening above 550 µm in all patients. The CV was increased (polymegathism) in the first and second patients but undetected in the third. The decreased hexagonal value (pleomorphism) was less than 50% in the first patient’s eye but undetected in the second and third patients.

Initial management is not specific to FEDC but is used to treat all causes of edema that occur in the epithelial layer to the corneal stroma. Topical hyperosmotic agents (eye drops or ointment), which act by increasing the osmolality of the precorneal tear film, are used to treat the corneal edema that occurs in FEDC. The use of bandage contact lenses aims to reduce pain resulting from repeated erosion of the corneal epithelial layer and reduce irregular astigmatism in patients with bullous keratopathy.

The manual dissection of the superficial corneal layers (epithelium, Bowman’s layer, and occasionally superficial stroma) is known as a superficial keratectomy (SK). Bullous keratopathy can be treated with painful superficial epithelial keratectomy.
and amniotic membrane transplantation in a less invasive way with better cosmetic outcomes. This procedure will be performed on the first patient.

Cycloplegia and nonsteroidal anti-inflammatory agents are used to treat pain that occurs as a result of bullous keratopathy. Using drugs to reduce intraocular pressure aims to reduce corneal edema in patients with FECD. This statement is in accordance with the management performed on our patients. All patients received hyperosmolar eye drops or ointment.

Treatment of FECD using drugs aims to overcome the symptoms that occur. However, the current definitive treatment to restore visual acuity in patients with FECD is a corneal transplant, replacing the damaged corneal endothelial cell layer in recipients with a healthy donor endothelial layer. This makes FECD the most frequent indication for a corneal transplant procedure.

Definitive treatment of damaged corneal endothelium was recommended before visual disturbances or discomfort occurred in the patient. Cataract formation often coexists with advanced FECD, and managing both clinical conditions to restore vision is often necessary. After Descemetorhexis, DMEK permits solely Descemet’s membrane and endothelium transplantation with grafts as thin as 10 μm into the host cornea. Compared to Descemet stripping automated endothelial keratoplasty (DSAEK), DMEK demands more advanced surgical abilities. Compared to DSAEK and PK, DMEK has the lowest risk of graft failure and the quickest visual recovery. Stages of cataract surgery in FECD patients were not significantly different from those without FECD. However, there are considerations specialized in cataract surgery to minimize intraoperative loss of corneal endothelial cells and optimize visual outcomes.

Penetrating Keratoplasty (PK) is a definitive procedure in patients with corneal decompensation caused by FECD. According to research, the percentage of FECD patients who underwent PK operations and had visual acuity of 20/40 or better at 3 months postoperatively improved to 80% after 24 months. The cornea’s healing process, the presence of sutures on the cornea, and the usage of hard contact lenses all contributed to the improvement. In research involving 908 FECD patients who received PK, graft survival rates were 97% at five years and 90% at ten years.

**CONCLUSION**

We have reported three cases of FECD. Two patients were managed with lubricant eye drops and DMEK, while the other was by penetrating keratoplasty. FECD is the most common endothelial dystrophy and the main indication for corneal transplantation when visual impairment is present. FECD is a bilateral asymmetric disease of the corneal endothelium characterized by progressive loss of endothelial cells with the formation of excretions known as guttae which can result in corneal decompensation and decreased vision. Remarkable developments in surgical and nonsurgical therapy for FECD highlight the importance of obtaining an early diagnosis for FECD before developing irreversible microstructural changes. Medical therapy in the form of topical hyperosmotic agents can be given in the initial phase and is useful for reducing corneal edema. The currently selected FECD management is Endothelial Keratoplasty (DMEK) which has shown a very good corneal clearance. Although the graft rejection rate in DMEK is low, there is still a risk of rejection with the discontinuation of topical corticosteroids.

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**CONFLICT OF INTEREST**

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**AUTHOR CONTRIBUTIONS**

All authors have contributed equally in the selection of cases and case management to this manuscript’s writing and publication.

**PATIENT’S INFORMED CONSENT**

All patients have signed a written informed consent and agreed to this study’s publication.

**REFERENCES**


