SAMPLE CASE REPORT

Title: Cornea Case Report

Map-Dot-Fingerprint Dystrophy/Recurrent Corneal Erosions

Candidate’s Name:

Word Count:

Practitioner:

Location:
Abstract:

This case report reviews the history of a 56-year-old man with EBMD presenting with corneal erosion in one eye after cataract surgery. Suddenly, a couple of weeks after the erosion resolves, he presents with similar defect in the un-operated eye. The un-operated eye goes through one more episode a couple of weeks after first one healed. His symptoms (worst shortly after awakening) were irritation, tearing, blurry vision, redness, and photophobia. Main risk factors for corneal erosion in this patient were corneal dystrophy and cataract surgery. It is known corneal erosions leave poor adhesions of the basement epithelial membrane, which increases chances of future re-occurrence. Epithelial debridement, bandage contact lens, antibiotic, and lubrication coverage aided in the healing of the presenting erosions. Steroid coverage was added to reduce future re-occurrences and prevent corneal scar formation. This case report also reviews the pathophysiology of EBMD and corneal erosions, along with other treatment modalities. It is suggested (due to patient’s risk factors, presenting signs, and mechanism of action of different treatment modalities) this patient may benefit better and have a better prognosis if other treatment modalities are added to this patient’s management plan.

Introduction:

Majority of Recurrent Corneal Erosion cases are related to history of trauma. 46% of cases are caused by corneal dystrophies, mainly Map-Dot-Fingerprint Dystrophy or EBMD (most common cornea dystrophy). EBMD is known for having poor epithelial basement membranes with an autosomal dominant inheritance component. The poor adhesion complexes in EBMD are thought to predispose the epithelium to corneal erosions. Corneal erosions are painful epithelial defects seen with fluorescein pooling. Treatment is targeted to eliminating patient’s symptoms by prescribing an NSAID and placing a bandage contact lens, preventing infection by prescribing an antibiotic, and preventing future re-occurrence and aiding the formation of stronger adhesion complexes by debriding the epithelium, prescribing lubrication, mild steroid drops, doxycycline, and surgical intervention in severe cases.
Case Summary:

15/06/17

LE Cataract surgery follow up: 56-year-old male complains of mild irritation. Negative discharge. Positive FBS, redness, and mild discomfort. Medical history: Arthritis, taking Prednisone 8 mg/day. History of ARMD in both eyes. Current drops: Ocuflox 0.3% QD LE, Acular 0.4% QD LE, and Pred Forte 1% QD LE.


Pupils and EOM’s: normal.

RE: Blepharitis, pannus, cornea epithelium cysts and refractile lines. Cornea guttata. Quiet anterior chamber. Grade 3- NS. IOP 12 mmhg.

LE: Blepharitis. 3-9 O’clock inferior epithelial erosion. Cornea epithelium cysts and refractile lines. Cornea guttata. Quiet anterior chamber. IOL clear and centered. IOP deferred.

Retina: Mild macula drusen both eyes.

Diagnosis/Management: Epithelial erosion LE. Map-dot-fingerprint dystrophy both eyes. Epithelium debrided LE. Bandage CL placed. Discontinue Acular 0.4%, switch Pred Forte 1% to Pred minims 0.5% TID LE. Continue Ocuflox 0.3% QD in LE. Return 2 weeks.

05/07/17


Pupils and EOM’s: normal.

RE: Unchanged.


Retina: Unchanged.
Diagnosis/Management: Improved epithelial erosion LE. Map-dot-fingerprint dystrophy both eyes. Bandage CL taken out. Continue Pred minims 0.5% TID LE. Ocuflox 0.3% BID LE. Add Hylo Forte 0.2% every two hours LE. Return 1 month.

07/08/17

Emergency: Severe irritation and redness in RE. Negative discharge.


Pupils and EOM’s: normal.


LE: Unchanged.

Retina: Unchanged.

Diagnosis/Management: Epithelial erosion RE. Map-dot-fingerprint dystrophy both eyes. Loose epithelium debrided. Bandage CL placed. Chloramphenicol 0.5% QID RE, Hylo Forte 0.2% every two hours RE. Return 2 weeks.

21/08/17

Healed Cornea. Bandage CL out. Chloramphenicol 0.5% TID RE, Hylo Forte every hour RE. Return 2 weeks.

31/08/17


Pupils and EOM’s: Normal.


LE: Unchanged.
Retina: Unchanged.

Diagnosis/Management: Recurrent epithelial erosion RE. Map-dot-fingerprint dystrophy both eyes. Bandage CL placed. Chloramphenicol 0.5% QID in RE. Hylo Forte 0.2% every hour RE. Return 1 week.

04/09/17


Pupils and EOM’s: Normal.


LE: Unchanged.

Retina: Unchanged.

Diagnosis/Management: Improving recurrent epithelial erosion RE. Map-dot-fingerprint dystrophy both eyes. Bandage CL taken out. Chloramphenicol 0.5% TID in RE. Hylo Forte 0.2% every hour RE. Add Pred minims 0.5% TID RE. Return 1 week.

Diagnosis:

Map-Dot-Fingerprint is the most common corneal dystrophy presenting with diffused gray patches, white cysts, and/or refractile lines in epithelium. It’s associated with recurrent corneal erosions, and may cause reduced BCVA.\(^1\) Erosions can be painful and acute (most likely presenting after awakening) and are seen as epithelial defects/abrasions with fluorescein pooling. They are caused by corneal dystrophies, trauma, cornea and/or cataract surgery.\(^2\)

Karpecki and Shechtman\(^3\) concluded 42% of individuals present with EBMD and 33% of those patients experience recurrent corneal erosions. 76% of individuals, over 50, experience the condition.

EBMD can have epithelial cells trapped in debris or cysts seen with a negative fluorescein staining pattern. Dr. Bass\(^4\) describes the opacities as “small continents on a map, fingerprint
swirls, small dot opacities and bleb or milky-white opacities [...] created of abnormal basement membrane material. The deposits can occur within the epithelial layers (maps), between the epithelial cells (fingerprint swirls) or within the epithelial cells (dots).”

Condition is seen bilaterally and with irregular keratometry mires. The opacities are slow progressive found centrally in younger patients, and spread to the periphery becoming denser with age. VA will be affected if opacities are big and on visual axis.

A study proved 46% of patients with recurrent corneal erosions had Map-Dot-Fingerprint dystrophy. Another study proved 90% of patients with EBMD and recurrent corneal erosion involved the inferior third of the cornea.

Erosions leave poor basement epithelial membrane adhesions, increasing chances for future recurrence. Symptoms (first happening upon awakening) include irritation, significant pain, tearing, blurry vision, redness, photophobia, and discomfort. Signs range from epithelium full-thickness defects to superficial punctate keratitis. Condition is common in females and in those aged 40-50 years old.

This patient’s first erosion happened upon awakening after cataract surgery in LE. All episodes had a big epithelial defect (with fluorescein pooling) and healed into SPK. Main erosion risk factors for this patient were age, map-dot-fingerprint dystrophy, blepharitis, and cataract surgery. Refractive surgery and cataract surgery can result in erosions in patients with EBMD.

Kabat reports 60% of patients with recurrent corneal erosion had trauma. 17% of them had other predisposing factors like incisional ocular surgery, which is the case for this patient in the LE, but not the RE. Making up that other 17% are corneal dystrophies, which we know is the case in this patient (EBMD). Other dystrophies which can also contribute to corneal erosions, are: Reis-Bucklers dystrophy seen as central sub-epithelial reticular gray opacities. Lattice and granular dystrophies present in the central stroma not in the epithelium like this patient.

Fuchs endothelial dystrophy can also contribute to corneal erosions. This patient presenting with endothelial corneal guttate can be a confounding factor. Fuchs dystrophy can be eliminated as he didn’t present with stromal corneal edema, endothelium pigment dusting, descemet folds, or sub-epithelial scar tissue.
Pseudophakic Bullous Keratopathy\textsuperscript{10} can cause corneal erosions. This condition presents with reduced BCVA, tearing, pain, photophobia, red eye and history of cataract surgery. All these signs were present in this patient, but we can eliminate it as the patient didn’t present with corneal edema, corneal bullae, descemet folds, nor cornea neovascularization. Also, the patient presented with similar condition in the RE, which was an un-operated eye.

\textbf{Pathophysiology:}

Karpecki and Shechtman,\textsuperscript{3} explain various studies have shown an autosomal dominant inheritance component in EBMD. Boutbol and others,\textsuperscript{11} studied two families with EBMD, proving a two-point mutation in genes TGFBI and BIGH3 (also present in other cornea dystrophies). Bass\textsuperscript{4} states the mutations are localized to TGFBI gene (keratoepithelin gene) on chromosome 5. TGFBI/BIGH3 are found in the extracellular matrix. They bind to collagen and fibrinogen, which support cell spreading, cell adhesion, corneal development and healing. The mutation affects the gene and its function. The part of the cornea that is affected is determined by which phenotype it presents with. In the case of EBMD, the mutation affects the corneal epithelium and Bowman’s membrane.\textsuperscript{11}

EBMD has poor basement membranes. It is characterized for having thickened, redundant, and misdirected basement membranes originating from the basal epithelial cells, and extending superficially into the corneal epithelium. The epithelial cells produce finger-like projections or redundant white opacities that protrude from a poor thickened basement membrane.\textsuperscript{3,11} “The extra sheets of basement membrane grow into the epithelium [and] as the epithelium matures, it traps the membrane to create the cysts and lines [seen in EBMD].”\textsuperscript{5}

EBMD causes 20\% to 30\% of recurrent corneal erosions.\textsuperscript{6} These erosions are smaller than the ones caused by trauma. McNulty \textsuperscript{6} explains, adhesion complexes (hemidesmosomes and type VII collagen-anchoring fibrils) anchor the corneal epithelium to the basement membrane and bowman’s layer. These adhesion complexes get disrupted in corneal dystrophies, which predisposes the epithelium to erosions.

Repetitive erosions cause repetitive elevation of the epithelium, which leads to further abnormalities in the basement membrane. The repetitive erosions diminish the role of the adhesion complexes by increasing matrix metalloproteinases (MMP)-2 and -9 which affect
fibrils and basement membranes. Bronner states when an erosion removes the basement membrane, it can take up to eight weeks for the adherence to take place again. This leaves an immature or absent adhesion complex before that, leaving the patient with a higher risk for the epithelium to slough off again. This usually happens at night when the ocular surface is dry and the epithelium adheres to the eyelid. When the patient opens his eyes in the morning, the adhesion is disrupted and an erosion occurs, explaining why most patients complain of it upon awakening.

Patient had blepharitis which has been shown to be in high rates in patients with non-traumatic corneal erosions. The epithelial healing is affected by the fatty acids (produced by the meibum in response to the increased bacterial lipase) caused by the high number of Staphylococcus epidermidis (present in blepharitis), predisposing the patient to recurrent erosions.

Recurrent corneal erosions, if overlooked or not treated properly, can lead to debilitating symptoms. Patients can suffer from photophobia, moderate to severe eye pain, and worst-case scenario corneal scarring leading to visual changes. Watson SL, and others stated the repeated episodes of breakdown of the corneal surface can predispose the cornea to infections, and if not treated properly, it can cause cornea scarring and subsequent vision loss.

Management:

The practitioner discontinued Acular 0.4%, and switched Pred Forte 1% to Pred minims 0.5% (drops given after cataract surgery). Acular 0.4% is an NSAID with anti-inflammatory and pain relief properties, but it was discontinued because it diminishes epithelial healing. Pred Forte 1% was switched to Pred minims 0.5% because steroids reduce epithelial healing and reduce immunity against infection (not beneficial in this case with a corneal “open wound’). It was switched to a milder steroid as the patient still needed anti-inflammatory coverage to avoid post-operative complications.

McNulty states topical antibiotics should be prescribed in corneal erosion cases to decrease the risk of microbial keratitis. Ocuflox 0.3% QID LE was prescribed. It is a broad spectrum, bactericidal, second-generation fluoroquinolone. It blocks bacterial DNA synthesis
by inhibiting the topoisomerase enzymes (DNA gyrase/DNA enzyme topoisomerase IV). This stops the duplication, transcription, and repair of bacterial DNA, eliminating bacterial load.\textsuperscript{14} Contraindications include reactions to medication, and it’s not recommended in pregnant women. A concern with this class is bacterial resistance. It has been suggested four generation fluoroquinolones may provide superior coverage.\textsuperscript{16}

Non-therapeutic treatment included epithelium debridement and bandage CL. “Mechanical debridement of loosely adhered or nonadherent epithelium provides a smooth basement membrane to which healthy epithelium may re-adhere.” Bandage CL helps protect the epithelium from the shearing force of the eyelids. Bronner\textsuperscript{7} states there is a long-term benefit using bandage CLs as these aids the epithelial adhesion complex to mature and prevent future epithelial erosions. Kabat,\textsuperscript{8} advices on good antibiotic coverage with bandage CLs to prevent microbial infection.

Hypertonic agents serve to lubricate and to reduce nocturnal corneal edema in corneal erosions, promoting adhesions between epithelial layer and basement membrane.\textsuperscript{7,8}

Hylo Forte 0.2\% every two hours was also prescribed. It is a hypotonic sodium hyaluronate based preservative free eye drop, which “aids in a gradual release of water molecules, which increases the duration of wettability [. and also] seems to have protective effects on the corneal epithelium.” McNulty,\textsuperscript{6} states frequent use of non-preserved artificial tears helps with re-epithelialization, but it hasn’t been proven to prevent recurrences. They also prevent irritation and symptoms in EBMD. It’s preservative free property aids patients with previous reactions to preservatives.

Epithelium was debrided and bandage CL was placed in RE after presenting with erosion. Hylo Forte 0.2\%, and Chloramphenicol 0.5\% QID RE was prescribed. Chloramphenicol 0.5\% is a bacteriostatic antibiotic. It binds to the bacterial ribosomes (A2451/A2452 residues in the 23S rRNA of the 50S ribosomal subunit)\textsuperscript{18}, and it prevents bacterial protein synthesis by inhibiting the peptidyl transferase activity.\textsuperscript{18} It’s a broad spectrum antibiotic, except Pseudomonas coverage, and penetrates the cornea well. It’s used to prevent microbial keratitis in corneal erosion cases. Melton and Thomas,\textsuperscript{15} warn against its use as its been implicated with aplastic anemia deaths. It may also trigger bone marrow aplasia in patients with a genetic predisposition.
Karpecki, and Shechtman³ suggest a steroid and doxycycline combination help corneal erosion cases secondary to EBMD. “The mechanism of action occurs through suppression of the enzyme matrix metalloproteinase-9 (MMP-9), which is widely responsible for catalyzing corneal erosion [...] Patients treated with a combination of these medications demonstrated rapid resolution and experienced no recurrences of corneal erosion.”³ Once abrasion healed, Pred minims 0.5% TID RE was prescribed. It’s a corticosteroid, which suppresses MMP activity and expression. Bronner⁷ states Matrix metalloproteinases are enzymes that remodel the degradation of connective tissue. MMP-2 and MMP-9 play a key role in corneal erosions because they break down the components of the epithelial adhesion complex. The tear film of patients with corneal erosions show an increase MMP-2 and MMP-9, which leads to unstable epithelial basement membranes, and increase the chances of recurrent corneal erosions. Steroids can reduce these proteins and the chances of future corneal erosions. Bronner⁷ states suppression of MMPs should be carried out for a long time, but because of the known side effects of corticosteroids, carefully monitoring should be established. Side effects include IOP increase, posterior subcapsular cataracts, and reduced healing. It’s important to assure the epithelial erosion is healed/closed before a corticosteroid is introduced as this will delay it’s healing.⁷ Wang L and others,¹⁹ suggested combination therapy of Doxycycline and corticosteroid worked better in relieving symptoms and future re-occurrence of corneal erosions than either treatment alone.

Non-therapeutic treatments include anterior stromal puncture and amniotic membranes transplantation. McNulty⁶ describes the first consisting of multiple stroma penetrations through the epithelium, forming scar attachments and improving epithelial adhesions. Side effects include decreased acuity and glare. The second consists of transplanting an amniotic membrane that serves as bandage. It has anti-inflammatory and anti-scarring effects on the cornea as it contains MMP-9 inhibitors. It reduces vascularization, inflammatory mediators, and scar response. It provides an artificial basement membrane for re-epithelialization, antimicrobial effects, and promotes appropriate innervation.⁷
**Prognosis:**

This patient with EBMD presented with a corneal erosion after cataract surgery. The fellow eye presented with similar condition and similar risks factors (Age, Blepharitis, and EBMD). These risk factors, except for the cataract surgery, can be managed but can’t be eliminated or avoided. I suspect he will suffer from this condition in the future as well. The occurrences are happening too close to each other, which are not allowing for the epithelium to heal properly and re-built the adhesion complex.

Epithelium debridement, bandage CLs, antibiotic drops, and lubricating drops will help heal these episodes and will help with symptoms, but it will not prevent future re-occurrences. “Although debridement aids the resolution of the acute erosive episode, evidence that debridement alone can prevent additional episodes is lacking.”

Once lesion healed, a steroid was prescribed which may help to prevent future re-occurrences. However, it will work best if prescribed in combination with Doxycycline.

I believe this patient is a right candidate for anterior stromal puncture or amniotic membrane transplantation. Both have been shown to help patients with recurrent erosions and EBMD. These will give the cornea the tools to heal properly and prevent future re-occurrences. These will prevent future episodes and lower the chances of corneal scarring and vision loss, which is of great aid to this patient with ARMD. McNulty, supports this by describing the results of a small study examining long-term effects of patients with history of recurrent corneal erosions treated with amniotic membrane who had failure with previous conservative treatment. The study concluded only 1/10 subjects reported re-occurrence after amniotic membrane treatment. He concludes “Recurrent corneal erosion is relatively common, and may not be adequately managed with medications. Surgical intervention may enhance outcomes and reduce recurrences.”

I believe because of the patient’s risk factors and presentations; his prognosis is fair (with high chances of reoccurrence and possible cornea scars). His future prognosis can be improved if these last treatment options are explored.
References:

11. Sandrine Boutboul, Graeme Black, John Moore, Janet Sinton, Maurice Menasche, Francis L Munier, Laurent Lauroche, Marc Abitbol, and Daniel Schorderet. ‘A subset of Patients with Epithelial Basement Membrane Corneal Dystrophy has Mutation in TGFBI/BlIGH3’ Human Genome Variation Society Journal 27(6). Available at: http://onlinelibrary.wiley.com/doi/10.1002/humu.20331/epdf?referrer_access_token=xGmuLoyfDLjWUe6vRkahFo4keas67K9QMdWULTWMo8NpsgUd4G17L-00QXTSTx8gsVlh MizW2jf3UzHovWk5BDCM5P3NcJj8igqwgQ0LnaUCL9des6Mvep_yhvZMUQjeOeSceZwvEkMJNkW9EAML74aF3Ug2xwZ19e5qGjROF0fy8r9mv1Cen8hQHWTLuU. [2006]. Pgs. 553-557


