

CASE REPORT

**AN ATYPICAL CASE OF BILATERAL CORNEAL OPACITY:
WHAT ARE THE POSSIBLE DIAGNOSIS?**

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ABSTRACT

Introduction: Corneal opacity can be divided into inflammatory and noninflammatory entities. The clinical presentation and characteristics of a corneal opacity can often help reach a diagnosis. However, atypical cases are more challenging to diagnose. This report aims to explore an atypical case of corneal opacity and the diagnostic approach through its clinical presentation.

Case Report: A thirty-seven-year-old female patient had a chief complaint of gradual blurry vision in both eyes and slowly growing whitish lesions one year prior. The patient recalled a history of bilateral eye redness two years ago. The anterior segment examination and AS-OCT revealed bilateral, smooth, oedematous pearly-white elevated opacity with well-demarcated margins at the center of the cornea, with epithelial depth. The diagnosis of corneal keloid was favored, with GDLD and SND as the differential diagnosis. In local anesthesia, the patient underwent superficial keratectomy and amniotic membrane transplantation of the right eye. On one month follow-up, the patient felt an improvement in her subjective complaints with a normal appearance of the cornea.

Discussion: The atypical characteristics found in our case didn't fit a single mold, as it shared features of post-injury hypertrophic scar, degenerative, and dystrophy. We diagnosed the patient with corneal keloid caused by suspicion of subclinical infection. Although GDLD and SND were still possible, the working diagnosis was enough to warrant a therapeutic surgical removal.

Conclusion: Atypical presentations make diagnosis more challenging. However, despite improvements in diagnostic modalities, signs, and symptoms remain very helpful in reaching a working diagnosis.

Keywords: corneal keloid, subclinical infection, rare disease

INTRODUCTION

When encountering corneal opacity, one of the ways to reach a diagnosis is by dividing between noninflammatory and inflammatory entities. Noninflammatory cases can be divided into six groups: dystrophy, degeneration, deposition, developmental, ectasia, and scarring. Each disease's characteristics can help reach a working diagnosis before invasive diagnostic tests such as pathological exams. However, diagnosis can be more challenging to reach when it comes to atypical cases as the clinical presentation of the disease does not fit the mold of any common findings. Therefore, this report aims to discuss the natural course and diagnostic approach of an atypical corneal opacity.^{1,2,3}

CASE ILLUSTRATION

A 37-year-old female patient came to Cipto Mangunkusumo Kirana Hospital with a chief complaint of gradual blurry visions in both eyes for one year before admission. Aside from blurry visions, she had subjective complaints of eye discomfort, glare, and cosmetic considerations due to noticeable whitish lesions on both eyes. Her complaints were alleviated at night and got worse in the morning. She denied any history of direct trauma to the eye. The patient had a history of redness and eye washing with betel leaf water two years ago, followed by blurry visions of both eyes since. After the incident, the patient went to primary health care and was given steroid eye drops. She denied any history of keloids in any part of the body, contact lens wear, spectacles, or eye surgery. She also refused a history of prolonged consumption of any drugs. There was no history of similar complaints in her family.

At first admission, the patient's uncorrected visual acuity was 6/15 F in both eyes. The right eye's best corrected visual acuity was 6/6F2 on C-1,00 x 900, and the left was 6/7.5F2 on C-1,00 x 750. Although the visual acuity was relatively good, her condition significantly bothered the patient. The intraocular pressure of both eyes was normal. The anterior segment examination revealed bilateral, smooth, edematous pearly-white elevated opacity with well-demarcated margins at the center of the cornea and epithelial depth on both eyes. The only difference was the lesion size, which was 3.1 mm x 4.4 mm on the right eye, and 3.4 mm x 4.9 mm on the left eye. There was no infiltrate or neovascularization. The staining was negative on both eyes (Figure 1).

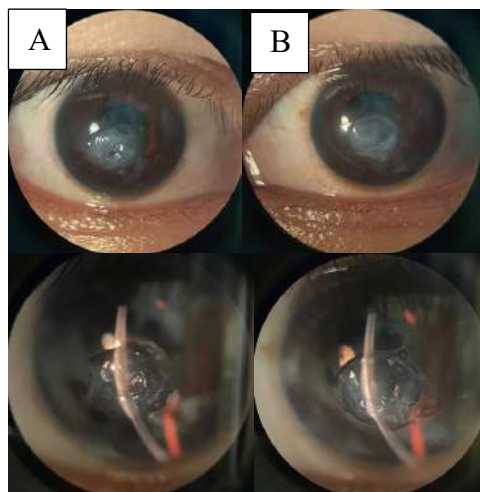


Figure 1. Ophthalmology examinations of (a) right and (b) left eye at first admission.

We performed anterior segment optical coherence tomography (AS-OCT), which revealed highly echogenic anterior lesions with intact epithelium and was well demarcated from the normal corneal stroma. Subepithelial fibrosis can also be seen (Figure 2).

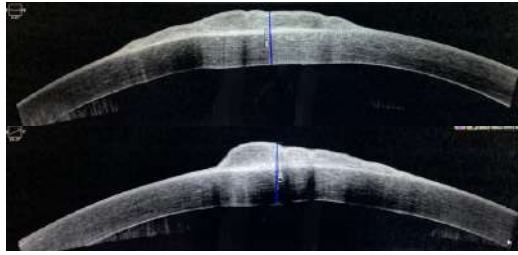


Figure 2. AS-OCT of the (a) right and (b) left eye at the first admission.

Initially, we assessed this patient with corneal keloids in both eyes. The diagnosis of corneal keloid was favored because of the characteristics of clinical appearance. The differential diagnosis thought in our case are gelatinous drop-like corneal dystrophy (GDL) and Salzmann Nodular Degeneration (SND). The patient was given hyperosmotic agent eye drops six times and artificial tears six times in both eyes. We planned for superficial keratectomy and amniotic membrane transplantation of both eyes in local anesthesia (Figure 3).

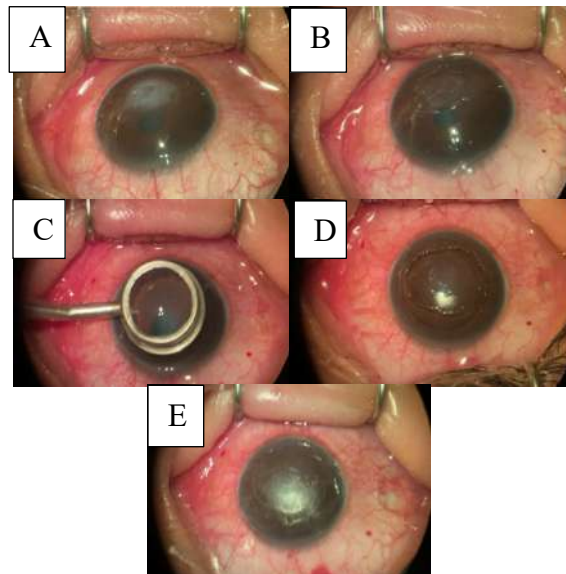


Figure 3. Intraoperative pictures. (a) Corneal keloid at the paracentral inferior of the right eye, (b) local excision and superficial keratectomy using forceps and, (c), (d) alcohol delamination with 20% alcohol for 40 seconds and keratectomy, and (e) amniotic membrane transplantation and fixation suture at 4 spots using nylon suture.

The surgery was done successfully on the right eye. Unfortunately, a histopathological examination was not performed. The patient was given a bandage contact lens after the procedure. Postoperatively, she was treated with levofloxacin eye drops 6x and prednisolone acetate 4x of the right eye. On follow-up day 1, the visual acuity was decreased to 6/24. The cornea's surface was regular with a partially dissolved amniotic membrane transplant. Over

time, the amniotic membrane transplant dissolved, and the cornea became clearer, leaving corneal cicatrix at the paracentral inferior cornea (Figure 4).

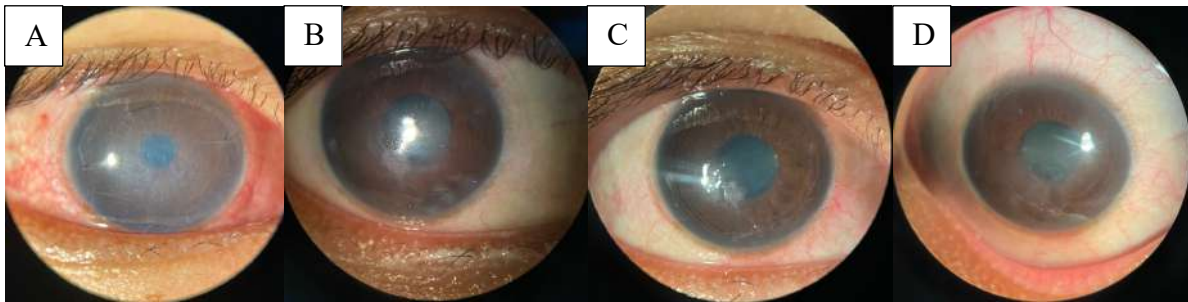


Figure 4. Post-operative pictures. (a) day one, (b) day 7, (c) day 14, and (d) day 30.

On the 1-month follow-up, the patient's final uncorrected visual acuity was 6/15 with the clear cornea, and the best corrected visual acuity was 6/6F2, the same as pre-operative [Figure 5]. AS-OCT also showed subepithelial fibrosis, but there was no sign of recurrence. Cosmetically, our patient was satisfied with the result. The same procedure was planned for the left eye, with an additional histopathology examination to further establish the diagnosis. On 3rd month follow-up, the patient exhibits no signs of recurrence.

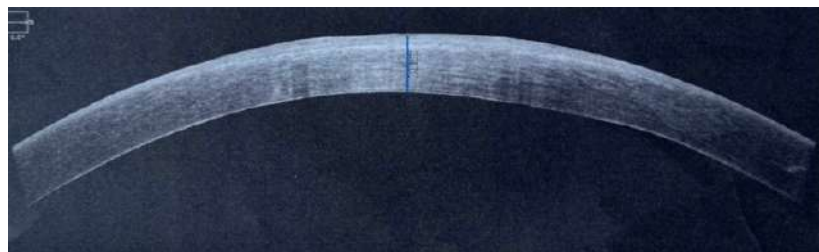


Figure 5. Post-operative 1 month AS-OCT of the right eye.

DISCUSSION

Corneal opacity is part of the external eye entities which can usually be seen upon a patient's entry. During the patient examination, assessing the patient's general appearance is essential to mark any signs of systemic involvement as a clue for diagnosis. Our 37-year-old female patient reported blurry visions, eye discomfort, glare, and cosmetic complaints of both eyes. She denied any systemic complaints and no signs of ophthalmic inflammation. She also didn't have a history of prolonged drug consumption. The patient reported a history of bilateral eye redness two years prior, which she treated with betel leaf water, suggesting the possibility of subclinical infection or unknown eye trauma. She reported no similar complaints in her family. When encountering noninflammatory corneal opacity, there are six big groups to

consider: dystrophy, degeneration, deposition, developmental, ectasia, and scarring. Corneal deposition was excluded because the lesions in deposition are commonly bilateral, located mostly peripheral, and usually drug-induced. Developmental diseases were excluded because they are primarily present at birth. Ectasia was excluded because the clinical manifestation showed no corneal thinning.³

The ruling out of deposition, developmental, and ectasia leaves us with dystrophy, degenerative, and scarring. Dystrophies are usually familial, bilateral, present early in life, primarily affect one layer, and are not associated with systemic disease. Degenerations can be both unilateral or bilateral, primary or secondary, present later in life, and mostly with typical appearances. Meanwhile, corneal keloid is typically a single growing smooth pearly-like lesion mostly found in patients with a history of injury or infection of the cornea. Some cases of corneal keloid can be related to congenital conditions or even idiopathic.³ The anterior segment examination of our patient showed bilateral, smooth, and edematous elevated opacity with well-demarcated margins located at the center of the cornea. Both opacities had epithelial depth and were almost symmetrical, with a slight difference in size. AS-OCT showed intact epithelium and clear borders from the healthy corneal stroma. There was also subepithelial fibrosis.

Atypical presentations make diagnosis more challenging. The centrally located bilateral and almost symmetrical opacity with slow progression and no systemic association supported the characteristics of dystrophy. However, the age of our patient and no history of similar disease in the patient's family were characteristics of degeneration. The patient also had a history of bilateral eye redness and eye washing with betel leaf water two years ago, followed by blurry visions of both eyes since, which could support the diagnosis of a corneal keloid. We initially assessed the patient with corneal keloids. Corneal keloid is a rare disease with a characteristic of a single growing smooth pearly-like lesion, often found in patients with a history of injury to the cornea. Although rare, it can occur spontaneously without any known injury. The lesion in a corneal keloid does not regress over time and is likely to grow outside of its initial borders. It can appear months or even years after trauma and can happen to any age ranging from 2 months old to 72 years old, more likely in the first 20 to 30 years. However, corneal keloids are more likely to appear unilaterally, although bilateral cases have been reported.^{1,4,5}

In our case, the patient had no history of direct eye trauma or surgery, but it was reported that two years before the patient's first admission, the patient had a case of bilateral eye redness. This information suggested the possibility of infections as the etiology of keloids. Any infection could lead to the formation of keloids, be it viral, bacterial, or fungal. One theory suggests that

subclinical corneal infections could stimulate excessive repair by leaving intrastromal antigens as persistent stimuli, eventually forming a corneal keloid. Corneal keloids can appear months to years after injury to the eye, explaining how the suspected infection in our patient had happened two years ago, followed by corneal opacity appearance one year later, a year before the patient's first admission to our care. It is important to note that in adults, grey-white, elevated, and localized lesion with glistening and smooth surface after a history of trauma or inflammation (in this case, infection) is almost pathognomonic for corneal keloid.^{1,4,6}

From the clinical presentation, we determined two other differential diagnoses. The first one is gelatinous drop-like corneal dystrophy (GDL), also known as amyloidosis or primary familial amyloidosis. GDL usually appears in the first to second decade of life. The clinical signs are a significant decrease in visual acuity, foreign body sensation, and photophobia. On slit-lamp, the opacity appears subepithelial, drop-like, with a positive fluorescein test. Usually, they appear like small nodules, frequently with superficial vascularization. AS-OCT shows dense, hyperreflective, and nodular formations with basal epithelial depth. The epithelium is often disrupted with an intact basement membrane. Some characteristics that didn't support this diagnosis were the age of onset, a less significant decrease in our patient's vision, negative staining results, no family history, and no drop-like appearance nor vascularization.^{3,7}

The third differential diagnosis is Salzmann nodular degeneration (SND). SND is an idiopathic noninflammatory disease. It typically appears as a bilateral subepithelial elevated nodules with gray-white or blue-white color at the central or paracentral of the cornea. They are primarily seen in middle-aged and older women. SND can be associated with dry eye, exposure, and long-standing keratitis, even appearing years after keratitis has subsided. Although appearance is atypical to SND, the central bilateral and almost symmetrical appearance still supports this diagnosis. As a superficial entity, SND is also more likely to cause a non-significant decrease in visual acuity, such as observed in our patient. Moreover, our patient's age and gender also match this diagnosis.³

AS-OCT is very useful for exploring the anterior segment of the eyes. It can help detect the depth, extent, and distribution of materials in corneal layers, which are useful for detecting corneal dystrophies. GDL typically shows dense, hyperreflective nodular formations at the basal epithelial layer, and unlike in our case, the epithelium is sometimes disrupted.⁸ AS-OCT in SND usually shows bright, hyperreflective, subepithelial deposits above the Bowman layer covered by a thin epithelium layer.⁹ Another diagnostic tool that can be used is ultrasound biomicroscopy (UBM). AS-OCT and UBM can be used to evaluate the anterior segment. However, AS-OCT provides better imaging of superficial lesions, while UBM has deeper penetration into

ocular structures. AS-OCT's advantages are that it's less invasive, simpler, faster, and has higher resolution. However, UBM proves superior in cases where the disease impacts light penetration, i.e., the thickening of corneal epithelium or scarring of the stromal layer.¹⁰ In cases with difficult penetration, such as in corneal keloids with thickened keratinized epithelium, UBM can be the modality of choice. Histopathological examination remains the gold standard for diagnosis. However, clinical findings are often sufficient to warrant a working diagnosis and therapeutic surgical removal.^{2,4,11}

Although the patient's visual acuity before surgery was relatively good, surgical removal of the lesion was opted for due to subjective complaints of eye discomfort, glare, and the patient's cosmetic considerations. In corneal keloids, some indications for surgery include visual impairment, symptoms of tear film disturbance, eyelid closure interference, and cosmetic reasons. There are various treatment options for managing keloids, such as superficial lamellar keratectomy (SLK), lamellar keratoplasty, and penetrating keratoplasty. Considering the size and the epithelial depth of our patient's lesion and clear from any concurrent structural abnormalities, local excision with SLK was chosen. Alcohol was also used to smoothen the corneal surface. Various adjuncts can also be used to improve surgical outcomes. To reduce the likeliness of recurrence, we used an amniotic membrane as the adjunctive for its anti-inflammatory and antifibrotic properties. It is worth noting that surgical removal is also the definitive therapy for both GDLD and SND.¹⁻³

After surgery, the patient reported improvement in symptoms of glare and eye discomfort; she was also cosmetically satisfied. Subepithelial fibrosis remained, but the fibrosis had already existed before surgery, as seen on the patient's pre-operative AS-OCT. Should treatment of the remaining fibrosis be considered, phototherapeutic keratectomy could be an effective and beneficial procedure to manage superficial corneal diseases.¹² Several recurrences have been reported after treatment, and the use of amniotic membranes in preventing recurrence showed varying results. Lee et al. reported some recurrences of corneal keloid after SLK with the amniotic membrane in 4 patients, with all recurrences occurring within ten months post-surgery. However, surgical results in corneal keloids differ widely, with some patients exhibiting no recurrence after the SLK procedure. Recurrence could occur due to activities by the remaining fibroblast unremoved during superficial keratectomy.^{2,13,14} Three months post-surgery, the patient exhibits no signs of recurrence, but further follow-up is required.

CONCLUSION

Atypical presentations make diagnosis more challenging. A more accessible approach to corneal opacity is dividing between inflammatory and noninflammatory entities. Despite improvements in technology and diagnostic modalities, signs and symptoms remain very helpful in diagnosing. From the clinical presentation, we ruled corneal keloid, GDL, and SND as the three differential diagnosis. Although the definitive diagnosis required histopathological examination, a working diagnosis through the clinical presentation was enough to warrant therapeutic surgical removal, especially in our case, where surgical removal was the definitive treatment for all three differential diagnosis.

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