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Original article

Anterior amorphous corneal opacity and corneal thinning

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ABSTRACT

Purpose: To present the clinical features of four cases with bilateral anterior amorphous corneal opacity.
Methods: A retrospective study in four patients with bilateral anterior amorphous corneal opacity was conducted. Examinations included visual acuity, keratometry, slit-lamp biomicroscopy, confocal microscopy, anterior segment optical coherence topography, and histology.
Results: Three female and one male patients (mean age, 52.3 ± 8.9 years) showed bilaterally oval, amorphous sheetlike corneal opacities with central depression and thinning. Superior limbal opacities were observed in two of these patients. The best-corrected visual acuity ranged from 20/50 to 20/400, and the mean of the keratometry was 39.81 ± 3.97 D (diopters). They had mild dry eyes. The anterior segment optical coherence topography demonstrated hyporeflective abnormalities in the anterior depressed stroma in these four patients. Confocal microscopy revealed large round cells at the epithelial layer in one patient, and amorphous opacities with some strand-shaped opacities in the anterior stroma in all four patients. The mean of the corneal endothelial cells density in the eight eyes was 1521 ± 402 cells/mm^2. Central corneal stromalysis occurred in three patients, and descemetocele developed in two eyes. One patient received penetrating keratoplasty and two underwent lamellar keratoplasty. The histology of the corneal specimen revealed edematous basal epithelial cells, focal collagen disorganization in the thin stroma, and wartlike excrescences in a thickened Descemet's membrane.
Conclusion: Anterior amorphous corneal opacity is a rare keratopathy and may be one kind of rare corneal degeneration or dystrophy. Corneal stromalysis may occur in hyporefrective amorphous opacities and progress to descemetocele.

1. Introduction

A flat and thin central cornea is a rare keratopathy that may be caused by long-term contact lens use,[1] dellen,[2] or posterior amorphous corneal dystrophy (PACD).[3] Corneal dellen are localized depressions in the periphery of the cornea that are usually adjacent to the elevated surface. Poor wetting of the tear film causes corneal dehydration and thinning.[4] PACD is characterized by bilaterally thin and flat central corneas with a deep, stromal sheetlike opacity. The epithelium, Bowman's layer, and anterior stroma are usually normal. Here, we report four sporadic cases that had bilaterally anterior oval amorphous corneal opacities, which is different from the typical presentation of PACD. Corneal stromalysis occurred in three cases, and two cases progressed to descemetocele.

2. Methods

A retrospective study in a case series of four patients with bilateral anterior amorphous corneal opacity was conducted at the National Taiwan University Hospital, Taipei, Taiwan from 2006 to 2013. They were all sporadic without a family history of corneal opacity. Examinations included visual acuity, keratometry, slit-lamp biomicroscopy, confocal microscopy, anterior segment optical coherence topography (AS-OCT), and histology. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of the National Taiwan University Hospital.

Conflicts of interest: The authors have no proprietary or financial interests in any material discussed in this article.

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3. Results

3.1. Case 1

A 43-year-old woman had a history of wearing soft contact lenses for 10 years and slowly progressive blurred vision. In 1993, bilateral, oval opacities were noted at the central cornea in the clinic of the National Taiwan University Hospital. The best-corrected visual acuity (BCVA) was 20/30 in both eyes. Specular microscopy (Keeler Konan, SP5500; Keeler Instruments, Broomall, PA, USA) revealed bilateral decreased endothelial cell density (ECD) of 860 cells/mm^2 and 1700 cells/mm^2 in the right and left eyes, respectively. Basal tear secretion test was measured using Schirmer's test after topical anesthesia with 0.5% proparacaine and demonstrated 1 mm and 5 mm per 5 minutes in the right and left eyes, respectively. Then the patient stopped wearing soft contact lens and received artificial tears treatment. Although superficial punctate erosions were minimal during the regular follow-up, the central oval opacities and superior arcus opacities slowly increased. In 2004, the central cornea began to thin and flatten. The BCVA decreased to 20/200 × +5.0/−3.75 diopters (D) with a keratometry (*K*) value of 38.25 D × 59°/42.25 D × 149° in the right eye and to 20/60 × +5.0/−4.0 D with a *K* of 36.62 D × 45°/40.37 D × 135° in the left eye. Confocal microscopy (ConfoScan 3; Nike Inc., Fremont, CA, USA) revealed that the ECD had decreased to 920 cells/mm^2 in the right eye and 1469 cells/mm^2 in the left eye. In March 2006, she felt a foreign body sensation and experienced redness in the right eye for 1 week. Biomicroscopy revealed central corneal melting and descemetocele with a 2 mm × 3 mm epithelial defect in the right eye (Fig. 1A), and an oval and depressed opacity in the left eye (Fig. 1B). Despite pannus at the superior limbus, no active infiltrate or anterior chamber reaction was noted in the right eye. The left eye was silent without any punctate corneal erosion. Bacterial and viral cultures yielded negative results. A 7.5-mm penetrating keratoplasty was performed uneventfully. Postoperatively, artificial tears and topical betamethasone 0.1% were given four times daily. The corneal graft has remained clear and the vision is 20/40 at 7 postoperative years.

3.2. Case 2

A 56-year-old woman had mild eye pain and foreign body sensation in the left eye for 2 weeks in May 2010. Herpetic keratitis was suspected, and she was treated with 5% acyclovir ointment elsewhere. After 1 week, her symptoms did not improve, and she was referred to our clinic because of corneal melting and impending corneal perforation in the left eye. Her BCVA was 20/100 × +5.0/−3.0 D with a *K* of 36.25 D × 130°/43.25 D × 40° in the right eye and 20/400 in the left eye. The right eye showed an oval, depressed, and sheetlike opacity in the anterior stroma (Fig. 1C). The left eye demonstrated a large descemetocele without infiltrate or anterior chamber reaction (Fig. 1D). A 2 mm × 4 mm epithelial defect corresponds to the area of the descemetocele. Superior limbal opacities were present in both eyes. Bacterial and viral cultures showed negative results. Schirmer's test indicated 5 mm and 3 mm per 5 minutes in the right and left eyes, respectively. Artificial tears were given, and a lamellar keratoplasty was performed in the left eye. The postoperative vision remained at 20/100.

3.3. Case 3

A 45-year-old woman had bilateral blurred vision for many years. She visited our clinic with a BCVA of 20/400 × +0.75/−8.0 D in the right eye and of 20/50 × −1.50/−2.25 D in the left eye in May 2010. Keratometry showed a *K* of 39.00 D × 160°/47.12 D × 70° in the right eye and 41.12 D × 118°/42.37 D × 28° in the left eye. Her biomicroscopy revealed superior limbal opacities and oval, translucent corneal opacities in the anterior stroma in both eyes (Fig. 1E and F). Some brownish pigment deposits were noted in the central depression area. Although Schirmer's test was 0 mm per 5 minutes in both eyes, only little punctate corneal erosion was found. Artificial tears were given, and both eyes were stationary at the 3-year follow-up.

3.4. Case 4

A 65-year-old man had a history of bilateral corneal opacities with central flattening for 14 years. His initial vision was 20/100 × +3.25/−5.0 D in the right eye and 20/100 × +2.50/−2.75 D in the left eye in 1999. The corneal *K* was 36.62 D × 117/38.50 D × 27° in the right eye and 41.37 D × 118°/43.50 D × 28° in the left eye. In June 2013, he felt irritation in the right eye for 1 month. The BCVA was 20/100 in both eyes with a *K* of 31.86 D × 120°/37.34 *D* × 30° in the right eye and 37.00 D × 54°/44.5 D × 144° in the left eye. A paracentral dellen (2 mm × 1 mm) was found in the central amorphous opacity area of the right eye (Fig. 1G). The left eye demonstrated some iron pigment deposits on the anterior stroma opacity with Descemet folds (Fig. 1H). Schirmer's test showed 2 mm per 5 minutes in both eyes. Because the dellen became large with a 2 mm × 2 mm epithelial defect later, a lamellar keratoplasty was performed with a corneal patch graft in August 2013. Postoperatively, artificial tears four times daily and autologous serum 20% every 2 hours daily were given. The cornea was stationary at 2 months postoperatively. However, it spontaneously melted with a 3 mm × 4 mm epithelial defect, again in the central amorphous area later (Fig. 1I). No corneal infiltrate or anterior chamber reaction was found. Results of bacterial and viral cultures were negative. A lamellar keratoplasty with a larger corneal graft was done uneventfully. Postoperatively, the cornea remained stationary with artificial tears and autologous serum 20%.

Although tear secretion decreased in all four patients, they did not have severe dry eye symptoms or superficial punctate keratitis, which might cause corneal melting. Their eyelids were normal without meibomitis or lagophthalmos. Their conjunctivas were unremarkable without papillary or follicular inflammatory reaction. Corneal esthesiometry using the Cochet–Bonnet esthesiometer showed longer than 55 mm in all eyes of these four patients. The mean of the *K* in the seven eyes was 39.81 ± 3.97 D. Corneal topography (TMS-4; Tomey Corporation, Nagoya, Japan) in the seven eyes demonstrated flat and irregular corneal surfaces with a mean of the minimal *K* (36.57 ± 2.91 D).

AS-OCT (Visante; Carl Zeiss Meditec, Dublin, CA, USA) showed anterior hyporeflective abnormalities and some deep hyperreflective opacities in the thin and depressed corneas in the left eye of Case 1 (Fig. 2A), in the right eye of Case 2 (Fig. 2B), in both eyes of Case 3 (Fig. 2C), and in both eyes of Case 4 (Fig. 2D).

Confocal microscopy demonstrated numerous large round cells at the basal epithelial layer in the left cornea of Case 1 (Fig. 3A), and amorphous opacities with strand-shaped opacities in the anterior corneal stroma (Fig. 3B) as well as some granular hyperreflective opacities at the layer of Descemet's membrane (Fig. 3C) in all four cases. The endothelial cells revealed mild polymegathism and pleomorphism, and did not have appearance of cornea guttata. The mean of the central ECD in the eight eyes of our four cases was 1521 ± 402 cells/mm^2 (range 920–2176 cells/mm^2). Nerve fibers slightly decreased in the amorphous areas of the corneal stroma, but other areas were normal.

Histopathology of the corneal button in Case 1 showed focal epithelial cells with intracellular edema at the basal layer, thickening of the basal layer of epithelium with focal vaguely irregular

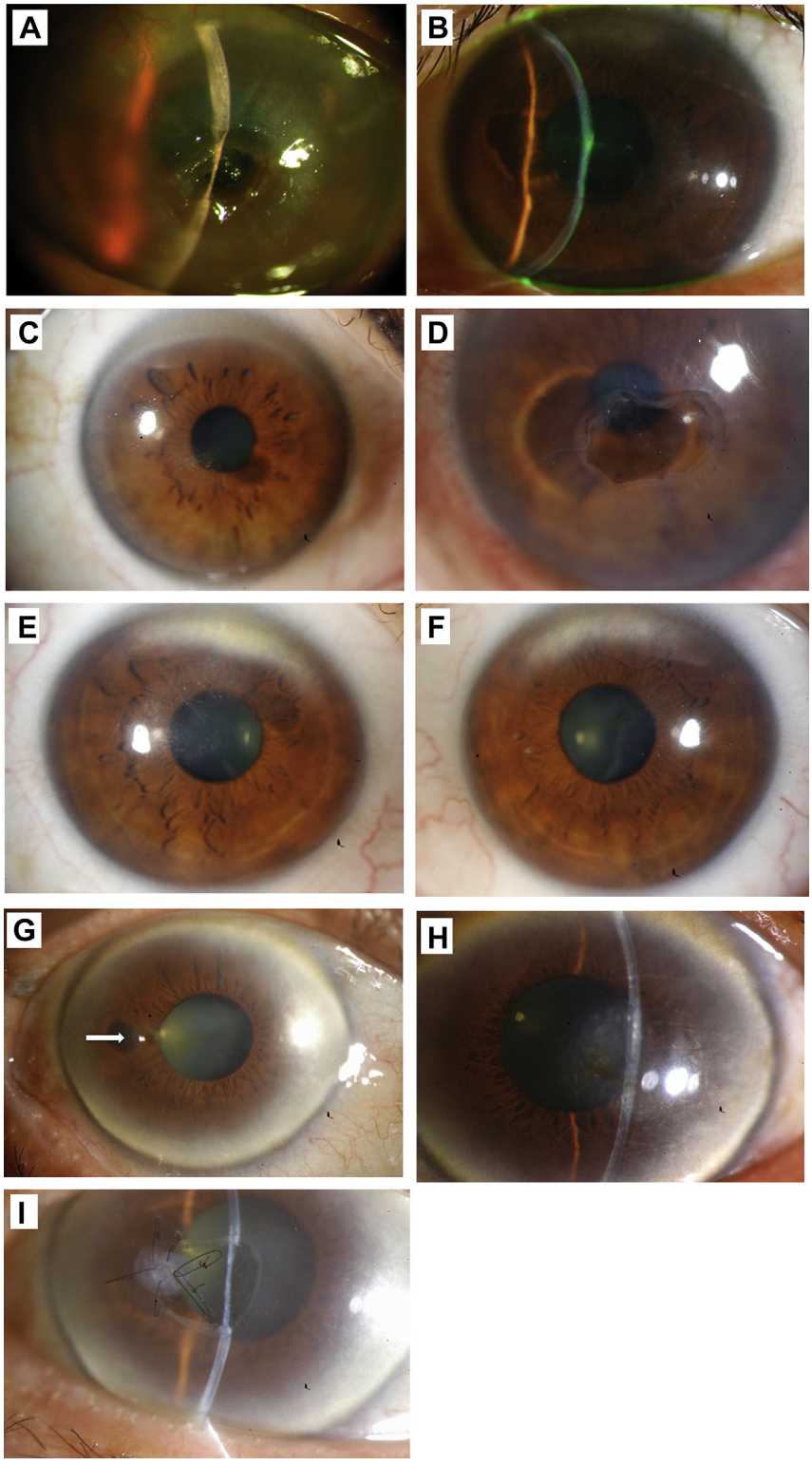

Fig. 1. Slit-lamp biomicroscopy. Case 1 shows (A) central corneal melting and superior pannus with Descemet folds in the right eye and (B) central thin depressed corneal opacity in the left eye. Case 2 shows (C) an oval sheetlike opacity in the central, thin, and flat cornea in the right eye, and (D) a large descemetocele without infiltration in the left eye. Case 3 demonstrates (E) central amorphous corneal opacity in the central thin and depressed area of the right eye and (F) a relatively smaller opacity in the left eye. Case 4 has (G) a paracentral dellen (arrow) in the anterior amorphous opacity area of the right eye and (H) a paracentral whitish opacity with some brownish pigment deposits and Descemet folds in the left eye. (I) Corneal melting occurred in the central anterior amorphous opacities adjacent to the patch graft. Superior limbal opacities are observed in Cases 1 and 3.

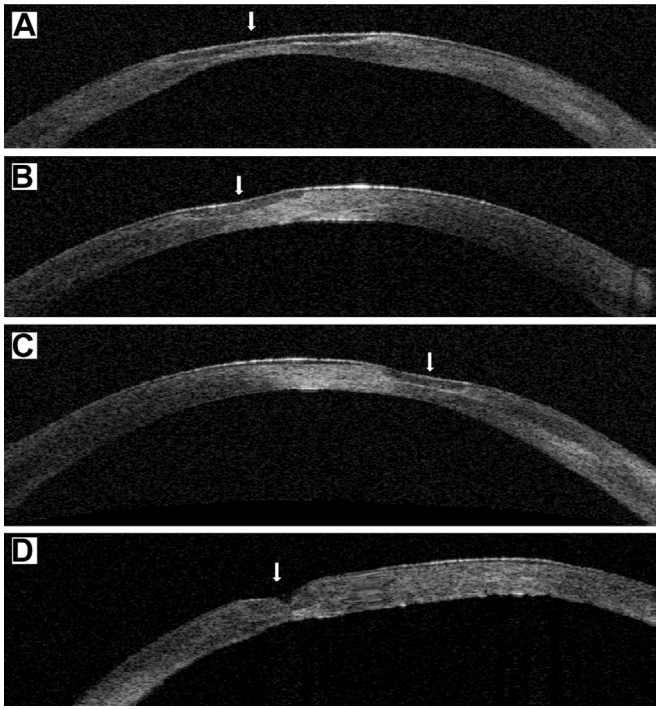

Fig. 2. Anterior segment optical coherence topography. Hyporeflective abnormalities (arrows) are found in the anterior corneal stroma of (A) the left eye of Case 1, (B) the right eye of Case 2, and (C) the right eye of Case 3. (D) The right eye of Case 4 presents a focal dellen (arrow) in the anterior hyporeflective area and some deep hyperreflective opacities with an irregular thick Descemet's membrane.

subepithelial ingrowth, focal absence of Bowman's layer, disorganized collagen in the thin stroma, and wartlike excrescences in the thickened Descemet's membrane. The endothelium was unremarkable owing to attenuation in processes (Fig. 4A and B). These edematous cells were highlighted by cytokeratin immunostain, which indicated that they were edematous basal epithelial cells (Fig. 4C). These histologic results corresponded to the findings of confocal microscopy and AS-OCT.

4. Discussion

The common features of these four sporadic cases were oval amorphous opacities in the thin and depressed area of the central cornea, and decreased ECD. These anterior amorphous opacities were relatively transparent. They were not associated with systemic diseases or autoimmune diseases. Keratometry and corneal topography revealed a flat *K* in the central cornea. AS-OCT showed anterior hyporeflective abnormalities in the amorphous opacities and some deep hyperreflective opacities. Confocal microscopy demonstrated amorphous opacities and strand-shaped opacities in the superficial stroma and some hyperreflective opacity at the layer of the Descemet's membrane. The corneal findings in PACD may be similar to some of our cases. However, PACD is an autosomal dominant disorder characterized by bilateral thin and flat corneas with deep, stromal amorphous sheetlike opacity, whereas the four cases in our study were sporadic and their oval opacities were located more anteriorly in the stroma than would be expected with PACD. The histology in our case was not the same as that in a typical PACD, which has fracture and disruption of the stromal lamella adjacent to Descemet's membrane, disorganization of collagen fibrils, and focal attenuation of endothelial cells.[5] Later, Roth et al[6] found more generalized abnormalities in a variant PACD case with subepithelial deposits and a thick collagenous layer posterior to Descemet's membrane. Although we cannot rule out the possibility of variants of PACD, the location and microscopic structures of anterior amorphous opacities in our four cases did not resemble this variant case.

Climatic proteoglycan stroma keratopathy is another similar corneal disorder.[7] Its corneal characteristics include a central, horizontally oval, and translucent stromal haze in the anterior stroma, central corneal flattening, and excess intracellular and extracellular stromal proteoglycan deposits. Climatic factors were postulated to

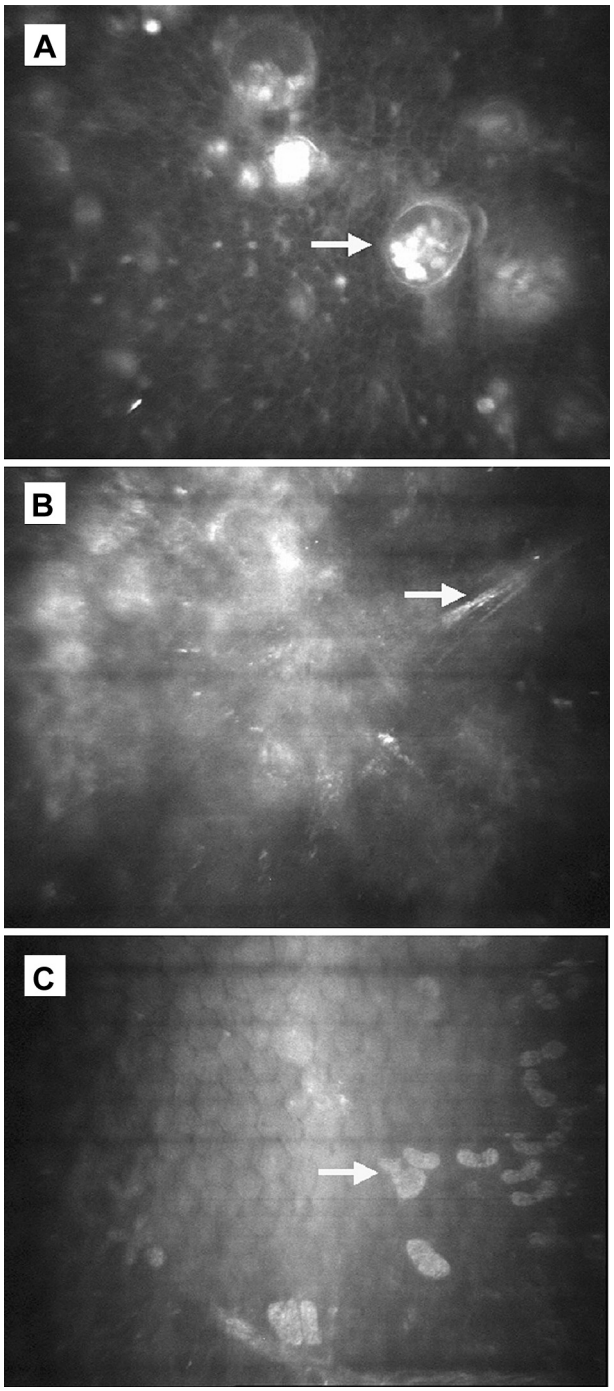

Fig. 3. Confocal microscopy. (A) Some large round cells (arrow) with dot opacities inside are found at the basal epithelial layer in the left eye of Case 1. (B) Amorphous opacities with strand-shaped opacities (arrow) in the anterior stroma and (C) some granular opacities (arrow) at Descemet's layer are observed in all four cases.

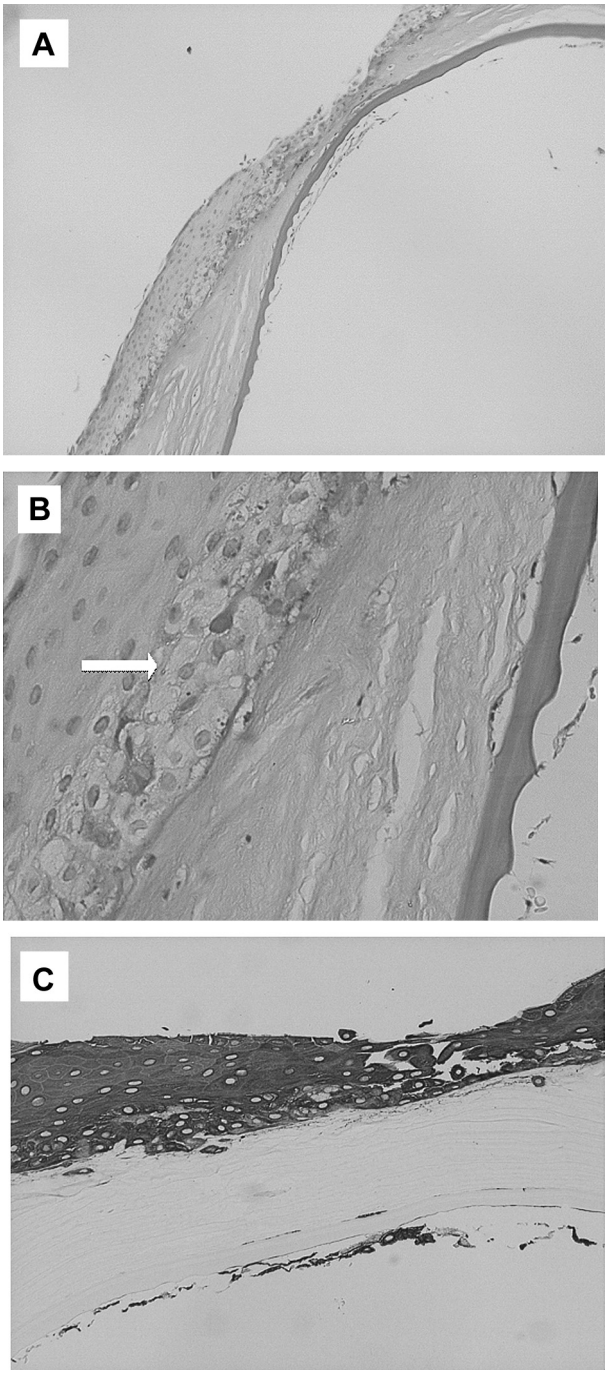

Fig. 4. Histopathology. (A) The right eye of Case 1 demonstrates a focal thinning of the epithelium and stroma surrounded by epithelial hyperplasia (PAS, original magnification, ×40). (B) Higher magnification reveals large edematous epithelial cells (arrow) at the basal epithelial layer, focal disorganized collagen in the thin stroma, and bumplike excrescences in the thickened Descemet's membrane (PAS stain, original magnification ×400). (C) Superficial epithelial cells and these large edematous cells are highlighted by cytokeratin immunostain (40×). PAS = periodic acid-Schiff stain.

play a pathogenic role in this disorder because of exposure to a sunny and dusty environment in the Middle East, and a lack of family history. Our four patients lived in the city of Taipei and had no history of long-term exposure to a sunny or windy environment. Their opacities were more transparent than the presentation of climatic proteoglycan stroma keratopathy, and the microscopic changes in the epithelial and endothelial layers were also different.

Corneal dellen is a localized thin and depressed area that is usually adjacent to an elevated area secondary to conjunctival chemosis or pinguecula. It often occurs in the peripheral cornea and may be associated with a previous corneoconjunctival surgery. These structural abnormalities alter the uniform spreading of tears in the corneal surface and cause corneal thinning. However, our four cases had no pinguecula or history of ocular surgery, and the thin and flat area was located at the central area instead of the periphery. Herpes stromal keratitis may cause stromal melting and descemetocele,[8] but our three corneal stromalysis cases did not have stromal infiltrates or positive herpes culture results. Although negative culture results cannot exclude the possibility of herpes keratitis, most cases of herpes keratitis occur unilaterally and cause more opaque opacities than the amorphous opacities in our cases.

Other external eye diseases may cause corneal ulceration including dry eye, neurotrophic keratopathy, exposure keratitis, blepharitis, rosacea, or vernal keratoconjunctivitis. Our four cases did not have such kinds of presentation except dry eyes. Although confocal microscopy showed slightly decreased nerve fibers, their corneal sensation was within the normal limit. However, we could not rule out the possibility of neurotrophic effect to cause dry eyes. Our patients' eyelids and conjunctiva were normal without inflammation. Although they had mild dry eyes, severe superficial punctate keratopathy or an inflamed eye did not occur. Although dry eyes may not play a major role in the corneal flattening and thinning, they may contribute to the exacerbation of corneal stromalysis in our cases. At any rate, anterior oval amorphous opacities were rarely observed in cases with mild dry eyes. Old interstitial keratitis might be associated with stromal haze, thinning, and the thick Descemet's membrane. However, most cases of old interstitial keratitis were unilateral, and their opacities might be multifocal and usually denser than those found in our cases.

Schnyder's corneal dystrophy is an autosomal dominant disorder of a bilateral central anterior stromal opacity and arcus, associated with abnormal deposits of cholesterol and phospholipids.[9] The four cases in our study were sporadic and did not have typical crystalline deposits. Corneal flattening and thinning usually do not occur in Schnyder's corneal dystrophy. Thick Descemet's membrane and decreased endothelial cells in our cases did not coincide with the histologic findings in Schnyder's corneal dystrophy.

The anterior amorphous opacities in the four cases were relatively transparent and seem to have a vesicle-like appearance, which is different from the presentation in most common corneal opacities. The localized flattening and thinning of the corneas became a corneal dellen and contributed to the brownish iron pigment deposits. The hyporeflective amorphous vesicle-like abnormalities may be vulnerable to a minor trauma. In particular, these patients had mild dry eyes. Once a corneal epithelium defect occurs at the amorphous vesicle, these hyporeflective opacities may melt easily and progress to descemetocele within a short period. To our knowledge, anterior amorphous opacities with superior limbal opacities have not been previously reported in the literature, especially with spontaneous corneal stromalysis and descemetocele. These four cases may be variants of PACD or other types of rare amorphous corneal dystrophy/degeneration. However, it is difficult to make a conclusion with only four cases; further study with more cases is needed to clarify this rare keratopathy.

Acknowledgments

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