CASE REPORT

Bilateral corneal opacities and surface irregularity: role of contact lenses in a case of paraproteinemic keratopathy and multiple myeloma

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Introduction: This report features an interdisciplinary approach to diagnose and manage a case of paraproteinemic keratopathy and multiple myeloma. In addition, it suggests that rigid gas-permeable contact lenses (RGP CLs) may be a viable alternative to corneal surgery to reduce visual symptoms.

Patient and clinical findings: A 57-year-old man symptomatic for progressive blur and glare over 2 years presented with an outside diagnosis of corneal dystrophy. An examination revealed bilateral diffuse subepithelial corneal crystals in conjunction with peripheral annular deposits with demarcated ridges. Corneal topography revealed central irregular astigmatism induced by these peripheral corneal opacities.

Diagnosis, intervention, and outcomes: A hematological workup confirmed IgG Kappa monoclonal gammopathy and multiple myeloma. Visual rehabilitation for paraproteinemic keratopathy was achieved with RGP CLs, which are expected to maintain stable visual acuity while the patient undergoes systemic chemotherapy.

Conclusions: This report emphasizes the value of thoroughly investigating dystrophy-like corneal deposits of unknown etiology as monoclonal gammopathy can have adverse or even fatal systemic implications. To the authors’ knowledge, this is the first study to directly suggest RGP CL as an adaptable and economical means to improve acuity in certain cases of paraproteinemic keratopathy without resorting to surgical intervention.

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manage the visual symptoms of PPK-induced surface irregularity.

CASE REPORT

A 57-year-old man presented for gradually increasing blur and glare over 2 years. A medical history was significant for mild traumatic brain injury from an extensive history of competitive American football, recently diagnosed mild normocytic anemia, and stage 2 chronic kidney disease. The patient denied use of any medications for systemic conditions. A distant ocular history included battery acid entering both eyes and staring at a welding arc. Outside examination records 6 months ago reported a diagnosis of corneal dystrophy to be monitored routinely. However, an ocular family history was unremarkable.

Corrected distance visual acuity with spectacles was Snellen acuity 20/30 right eye and 20/50 left eye, with a refractive error in right eye of $-0.75 -0.50 \times 040$ and in left eye of $-1.75 -0.50 \times 025$. Pupils were equal, round, and reactive to light with no afferent pupillary defect. Extraocular motility and confrontation fields were full for both eyes. A slitlamp examination revealed bilateral annular anterior stromal deposits with demarcated ridges from mid-periphery to far-periphery in conjunction with diffuse subepithelial iridescent crystals (Figure 1). The stromal opacities were of greater severity in the left eye. Nonvisually significant anterior cortical and nuclear sclerotic cataracts were also noted. Intraocular pressures measured with Goldmann applanation tonometry were 14 mm Hg in both eyes. A dilated posterior segment examination was unremarkable. An anterior segment optical coherence tomography (Figure 2) examination was demonstrative of thin central corneas bilaterally. Corneal topography (Figure 3) showed peripheral steepening greater in the left eye, correlating with the peripheral and mid-peripheral location of the patient’s corneal deposits. Anterior corneal astigmatism of 2.50 diopeters (D) and 0.20 D was noted in the left and right eyes, respectively. The discrepancy between the topography measurements and the patient’s spectacle refraction for the left eye can be attributed to reducing the patient’s original cylinder refraction from 3.25 to 0.50 DC to improve visual comfort. Photographs were also taken to document corneal findings.

Given the patient’s negative ocular history of hereditary corneal dystrophy or paraproteinemia, urine and serum protein electrophoresis tests were ordered, which revealed Kappa-free light chain level of 1608.3 mg/L (reference range 3.3 to 19.4 mg/L) and a Kappa/Lambda ratio of 247.43 (reference range 0.26 to 1.65). The results were indicative of IgG kappa MG, thus confirming an ocular diagnosis of PPK. The patient was subsequently referred to hematology-oncology for further workup. Bone marrow biopsy was positive for multiple myeloma, with evidence of new lytic bone lesions on skeletal survey. Chemotherapy treatment was initiated.

The patient’s symptoms of glare were reduced with tinted glasses prescribed after a traumatic brain injury vision evaluation. Visual rehabilitation was additionally achieved with corneal RGP CLs, which improved Snellen visual acuity to 20/20 in the right eye and 20/25 in the left eye without the need for corneal surgery. A 9.2 mm diameter corneal gas-permeable lens with Optimum Comfort (Contamac) material was used on the right eye. A Rose K2 (Menicon) lens was used on the left eye as its multiple back curves would allow for improved alignment given the steeper cornea and address the patient’s secondary concern of glare and aberrations. Menicon Z material was used in the 9.0 mm diameter lens to provide oxygen permeability and comfort.

The patient endorsed no aberrations and much improved clarity in both eyes with the aforementioned lenses when compared with spectacles. Two fitting appointments were needed to make modifications before reaching good fit, visual acuity, and comfort. Visual acuity and corneal opacities remained stable at all subsequent follow-ups. The patient was expected to continue with RGP CL throughout the course of chemotherapy.

Unlike standard soft CLs, the rigid surface of a corneal RGP CL reduces optical distortion by acting as a new refractive

![Figure 1. Slitlamp photograph of the right eye (a) and left eye (b) showing diffuse iridescent corneal crystals in combination with annular opacities sparing the central axis.](image1)

![Figure 2. Anterior segment optical coherence tomography scan of the right eye (a) and left eye (b). Mid-peripheral corneal opacities can be viewed as hyperreflective areas within the anterior stroma bilaterally.](image2)
surface to mask underlying corneal surface irregularity. For the same reason, scleral lenses were considered a potential alternative if fitting with the more financially economical corneal RGP lens was unsuccessful. The scleral lens would offer an additional advantage of complete vaulting over the cornea. Referral for penetrating keratoplasty or superficial keratectomy was deferred because of the possibility of corneal deposit regression from the planned chemotherapy alone and because of literature suggesting common recurrence of these deposits after corneal surgery. The patient was in agreement to opt for minimally invasive options such as RGP CL during the course of chemotherapy treatment before resorting to surgical invention.

DISCUSSION

PPK is a rare and underdiagnosed ophthalmic finding characterized by the immunoglobulin protein deposition within the cornea because of MG. It is important to note that MG, which is present in up to 5% of the elderly population, entails a spectrum of diseases, the most common being MGUS. MGUS is a premalignant plasma cell disorder that can be a precursor to multiple myeloma, B-cell non-Hodgkin lymphoma, and chronic myeloid leukemia.6,9 This highlights the importance of serological testing in patients with suspected PPK without a history of paraproteinemia. Although the patient was recently diagnosed with anemia and kidney disease, multiple myeloma was not suspected as the underlying cause until the ocular finding of PPK. For patients with an established diagnosis of MGUS, corneal findings may remain stable, but annual hematological check is still recommended as the risk for progression of MGUS to multiple myeloma or related malignant neoplasm is approximately 1% per year.1,10 The pathophysiology for PPK remains unclear. Proposed mechanisms include immunoglobulin transport through the tear film or aqueous,3 with the diversity of patterns possibly attributed to individual differences in stromal limbal vessels and interactions with extracellular matrix, glycosaminoglycans, and keratocytes.1,3 To avoid misdiagnosis and delaying potentially critical intervention, clinicians should rule out differentials such as granular corneal dystrophy (CD), lattice CD, pre-Descemet CD, Schmody CD, gelatinous drop-like CD, corneal verticillata, cystinosis, arcus lipoides, and Salzmann nodular degeneration.1,3 A reliable mainstay treatment of PPK is yet to be determined. Visually symptomatic patients have pursued penetrating keratoplasty, superficial keratectomy, and use of topical steroids, which often provided temporary relief before recurrence of deposits.9 Treating the underlying MG, however, may improve the results of the former procedures and prevent worsening of ocular symptoms. As suggested by the patient’s corneal topography (Figure 3), PPK reduced our patient’s corrected distance visual acuity with spectacles due to peripheral corneal surface irregularity, which may induce central irregular astigmatism. The diffuse iridescent crystals did not seem to significantly affect corneal topography or visual acuity. This combination of irregular astigmatism and lack of significant central opacification made the patient an ideal candidate for corneal RGP CLs. The patient noted significant improvement in both visual acuity and glare after being fit with RGP CL. RGP CL can therefore be an economical choice in similar cases of noncentral PPK while the patient is preparing to or is in the process of receiving systemic treatment. Given that regression of corneal deposits, albeit short-lived, has been reported during systemic chemotherapy, RGP CL can be refit as needed to adjust accordingly to changes in irregular astigmatism during and after the treatment process. With the equivocal results from systemic treatment and corneal surgery, fitting a corneal or scleral RGP CL can offer more certain visual rehabilitation. In addition, it is safer, less invasive, and more likely to be effective than penetrating keratoplasty—which may eventually lead to subsequent corneal or scleral lens use anyway. In cases of MGUS in which

Figure 3. Corneal topography revealing irregular astigmatism in the right eye (a) and left eye (b) induced by paraproteinemic keratopathy.
corneal findings remain stable, RGP CL may also be ideal in achieving long-term visual rehabilitation with a minimal change to the fit.

To conclude, PPK can be an indicator of a premalignant or malignant hematological disease, and it is essential for eyecare physicians to differentiate corneal opacities of unknown etiology from benign dystrophies or degenerations. In the event of multiple myeloma, patients who undergo systemic treatment may show regression of corneal deposits and improvement in visual acuity. Surgical intervention to treat visual symptoms is relatively common but offer unpredictable success. We suggest that glare and reduced visual acuity from PPK-induced corneal surface irregularity may warrant a fitting of RGP CLs before resorting to surgical intervention.

WHAT WAS KNOWN
- Paraproteinemic keratopathy is a rare finding associated with monoclonal gammopathy, which may have severe systemic implications. Because of its highly variable appearance, differential diagnoses for paraproteinemic keratopathy (PPK) should include corneal dystrophy, degeneration, and scarring.
- There is currently no ideal management for PPK, as systemic, topical, and surgical treatment often provide only temporary visual improvement.

WHAT THIS PAPER ADDS
- RGP CLs may be a cost-effective means to manage visual symptoms in patients with PPK.
- By masking irregular astigmatism induced by surface irregularities, paraproteinemic keratopathy can delay or replace the need for surgical intervention.
- If there is a concurrent systemic therapy for paraproteinemia, adjustable lens parameters can maintain visual rehabilitation during the progression, regression, or recurrence of these subepithelial deposits.

REFERENCES
1. Lisch W, Saikia P, Pitz S, Pleyer U, Lisch C, Jaeger M, Rohrbach JM. Chameleont-like appearance of immunotactoid keratopathy. Cornea 2012;31:55–58
2. Bourne WM, Kyle RA, Brubaker RF, Greipp PR. Incidence of corneal crystals in the monoclonal gammopathies. Am J Ophthalmol 1989;107:192–193
3. Garibaldi DC, Gottsch J, de la Cruz Z, Haas M, Green WR. Immunotactoid keratopathy: A clinicopathologic case report and a review of reports of corneal involvement in systemic paraproteinemias. Surv Ophthalmol 2005; 50:61–88
4. Karakus S, Gottsch JD, Caturegli P, Eghrari AO. Monoclonal gammopathy of “ocular” significance. Am J Ophthalmol Case Rep 2019;15:100471
5. Skalicka P, Dudakova L, Palos M, Huna LJ, Evans CJ, Mahelkova G, Meliska M, Stopka T, Tuf S, Liskova P. Paraproteinemic keratopathy associated with monoclonal gammopathy of undetermined significance (MGUS): clinical findings in twelve patients including recurrence after keratoplasty. Acta Ophthalmol 2019;97:e987–e992
6. Wasielica-Poslednik J, Gericke A, Desuki A, Schlötzer-Schrehardt U, Pfeiffer N, Lisch W. Recurrence of paraproteinemic keratopathy after penetrating keratoplasty and its assessment with confocal microscopy. Am J Ophthalmol Case Rep 2018;11:87–91
7. Milman T, Kao AA, Chu D. Paraproteinemic keratopathy: the expanding diversity of clinical and pathologic manifestations. Ophthalmology 2015;122:1748–1756
8. Chiang HH, Wieland RS, Rogers TS, Gibson PC, Atweh G, McCormick G. Paraproteinemic keratopathy in monoclonal gammopathy of undetermined significance treated with primary keratoprosthesis: case report, histopathologic findings, and world literature review. Medicine (Baltimore) 2017;96:e8649
9. Tainsh LT, Coady PA, Sinard JH, Nepairdze N, Meskin SW, Adelman RA, Chow J. Asymmetric deep stromal keratopathy in a patient with multiple myeloma. Cornea 2017;36:372–374
10. Therneau TM, Kyle RA, Metlon LJ, Larson DR, Benson JT, Colby CL, Dispensieri A, Kumar S, Katzmann JA, Cerhan JR, Rajkumar SV. Incidence of monoclonal gammopathy of undetermined significance and estimation of duration before first clinical recognition. Mayo Clin Proc 2012;87:1071–1079

Disclosures: None reported

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