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Case Report

Pressure-Induced Stromal Keratopathy after Surface Ablation Surgery

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Keywords
Surface ablation · LASIK · Stromal keratopathy · Goldmann applanation tonometry · Corneal biomechanics

Abstract
Introduction: The purpose of this clinical report was to describe an unprecedented case of bilateral pressure-induced stromal keratopathy (PISK) following corneal photorefractive keratectomy, associated with presumed herpetic keratitis, and to present tomographic and biomechanical findings before and after appropriate treatment. ***Case Presentation:*** A 33-year-old male patient was referred to our clinic with suspected delayed corneal epithelial healing 3 weeks after an uncomplicated PRK. A central layer of corneal opacity with a presumed fluid-filled interface area was observed upon slit lamp biomicroscopy. Scheimpflug images from the Pentacam® revealed a hyperreflective area beneath the central cornea. Scheimpflug-based corneal tomography, biomechanical assessment using the Pentacam® AXL Wave, and the Corvis ST® were conducted. Goldmann applanation tonometry measured 23/13 mm Hg, while noncontact tonometry intraocular pressure measured with the Corvis ST® (Corvis ST IOPnct) was 40.5/43.5 mm Hg. Treatment with oral valacyclovir, combined with ocular hypotensive therapy, led to a significant reduction in IOP and improved corneal deformation parameters after 1 month. ***Conclusion:*** Surgeons should be aware of the inaccuracy of Goldmann applanation tonometry in PISK, which can occur after LASIK or surface ablation.

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Introduction

Pressure-induced stromal keratopathy (PISK) has been reported as a rare complication after LASIK. This condition is characterized by interface haze and a fluid-filled space, typically resulting from steroid-induced elevated intraocular pressure (IOP). It does not respond to treatment with anti-inflammatory drugs (such as topical and/or oral corticosteroids or nonsteroidal anti-inflammatory drugs), and, since it is not a form of postoperative infection, topical antibiotics also have no value. In fact, PISK may even worsen with topical steroid therapy [1–5]. As most of the cases are misdiagnosed as diffuse lamellar keratitis (DLK), it does not respond to the steroid treatment commonly used for DLK. Thus, misdiagnosing this condition can lead to improper treatment, further exacerbating steroid-induced IOP elevation [1–7].

Severe glaucomatous damage can occur in cases of PISK where apparent interface fluid is absent and when excessively high IOP is not accurately measured. Severe visual loss can manifest over a few months, even in young, healthy patients with no ocular comorbidities, if a proper diagnosis is not established, IOP reduction is not initiated, and steroid use is not discontinued [2, 3, 5, 6, 8].

We present a rare case of PISK following surface ablation surgery, photorefractive keratectomy (PRK), which contrasts with the mainstream reported cases in the literature that occur after LASIK. We documented and analyzed corneal tomographic and biomechanical findings before and after treatment. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000539701).

Case Report

A 33-year-old man presented for a second opinion at a private clinic because of delayed corneal epithelial healing 3 weeks after undergoing PRK in both eyes. Preoperative refraction revealed −1.25 sph/−1.50 cyl at 150 degrees in the right eye (OD) and −1.00 sph/−1.25 cyl at 200 degrees in the left eye (OS), with a preoperative corrected distance visual acuity of 20/20 in both eyes.

At the time of the referral, the patient was using prednisolone acetate 1% four times daily in both eyes, as part of the normal treatment regimen after surface ablation procedures. The patient corrected distance visual acuity was 20/40 in the OD and 20/30 in the OS. Slit lamp examination revealed persistent epithelial defects in the OD, while no epithelial defects were observed in the OS. Both eyes displayed central corneal subepithelial and stromal haze, though no obvious fluid pocket was evident. Additionally, the OD exhibited keratic precipitates (KPs), reduced corneal sensation, and stromal infiltrates, indicating herpetic keratopathy (Fig. 1). Fundoscopy revealed a healthy optic nerve head (ONH), with a cup to disc ratio of 0.3 in both eyes, as well as no retinal abnormalities.

During this initial evaluation, high-resolution Scheimpflug imaging identified a subepithelial hyperreflective zone but no fluid accumulation in the central cornea of both eyes (Fig. 2). Goldmann applanation tonometry (GAT) recorded pressures of 23 mm Hg in the OD and 13 mm Hg in the OS. IOPs, measured with the Corvis ST® noncontact tonometer (Corvis ST IOPnct), were 40.5 mm Hg on the OD and 43.5 mm Hg on the OS (Fig. 3). Biomechanically corrected IOPs obtained with the Corvis ST® (Corvis ST bIOP) were 41.9 mm Hg in the OD and 45.7 mm Hg in the OS, with a deformation amplitude of 0.39 mm in the OD and 0.37 mm in the OS. The deformation amplitude ratio (DA ratio) was 1.6 in both eyes (Fig. 3, 4). Both biomechanical parameters are automatically compared to normative values for the patient's

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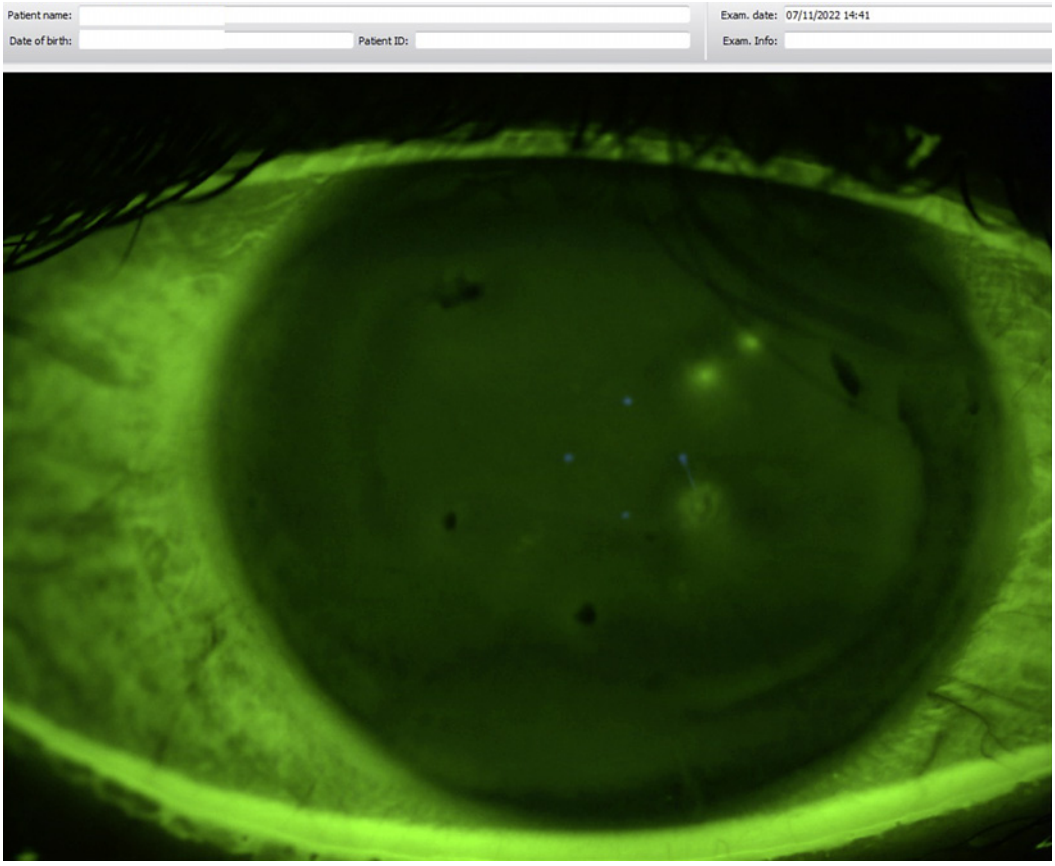

Fig. 1. Slit lamp photography of the patient's right eye (OD), demonstrating the corneal fluorescein staining lesions.

biomechanically corrected intraocular pressure (bIOP), as part of an automatic analysis made by the Corvis ST®. In Figure 4, it is evident that, initially, the DA ratio was significantly deviated from the mean (with a standard deviation of −6.26 in the OD and a standard deviation of −6.22 in the OS).

Given the patient's clinical history, slit lamp examination, bilateral OHT, and Scheimpflug imaging findings, a clinical diagnosis of bilateral PISK was established in this case. Concurrently, the patient also presented herpetic keratitis in the OD, probably due to reactivation of a latent infection. The herpetic keratitis led to the development of the stromal infiltrates, KPs, and reduced corneal sensation in the OD. The patient was prescribed oral acetazolamide 250 mg three times daily, a topical fixed combination of brimonidine and timolol maleate twice daily, and oral valacyclovir 500 mg twice daily. Topical prednisolone was reduced to twice daily. Three days after initiating this treatment regimen (oral acetazolamide and valacyclovir, topical timolol and brimonidine, and topical prednisolone with a reduced frequency of administration), uncorrected distance visual acuity improved to 20/25 in the OD and 20/20 in the OS. Slit lamp biomicroscopy revealed a substantial decrease in central corneal opacity in both eyes. Corvis ST IOPnct measured 23 mm Hg in the right eye and 13.5 mm Hg in the left eye. Corvis ST bIOP was 25 mm Hg in the right eye and 15.6 mm Hg in the left eye. The DA ratio improved to 4.50 mm in the OD and 5.30 mm in the OS (Fig. 4, 5). After 2 weeks of treatment with oral valacyclovir 500 mg twice daily, the dosage was reduced to 500 mg once daily, which was maintained for long-term prophylaxis of recurrent herpetic keratitis.

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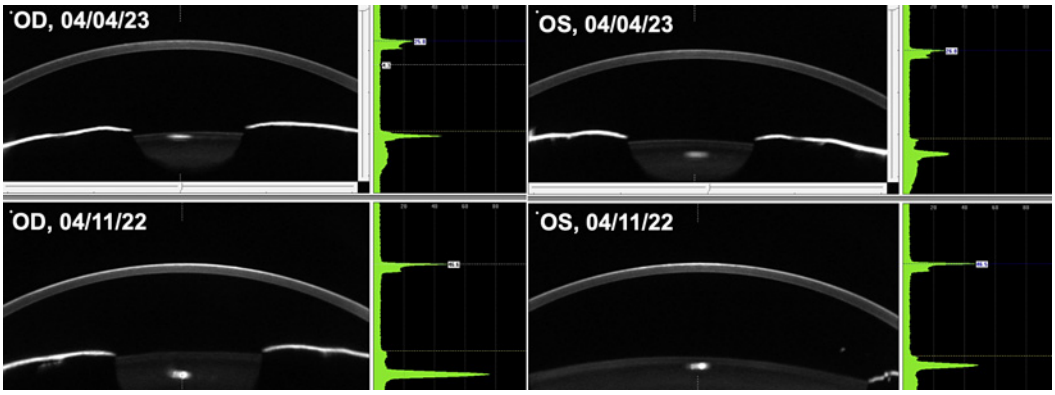

Fig. 2. Pentacam® Scheimpflug images throughout follow-up. The hyperreflective zone in the initial images is resolved in the more recent images, due to the treatment of the PISK.

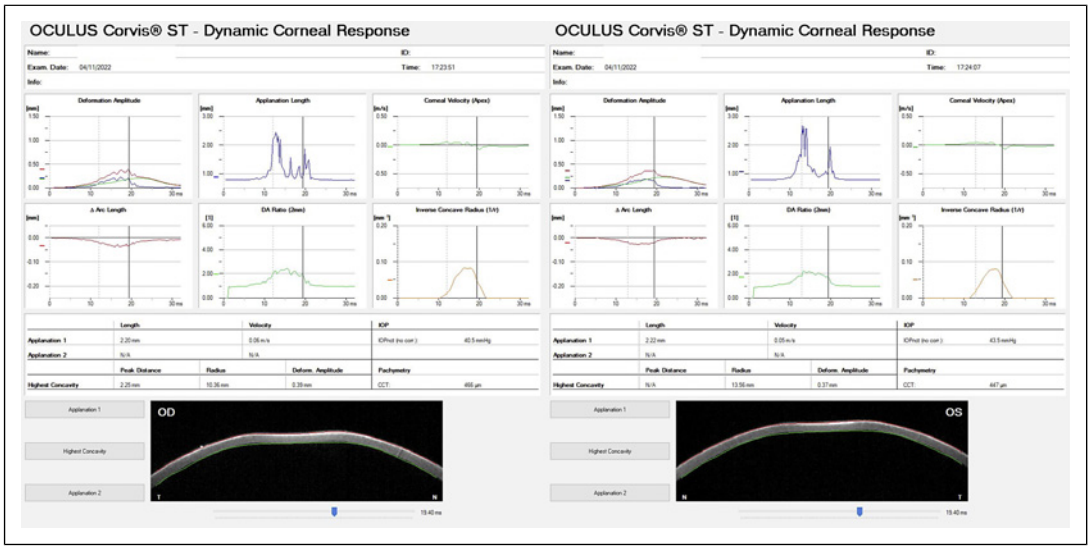

Fig. 3. Corvis® ST noncontact intraocular pressure (IOP) measurement of the patient's right eye (OD) and left eye (OS) in the initial visit to our clinic. The non-biomechanically corrected IOP (IOPnct) of the OD was 40.5 mm Hg and the IOPnct of the OS was 43.5 mm Hg.

One month after initiating oral and ocular hypotensive drugs and reducing topical corticosteroid frequency of administration, uncorrected distance visual acuity was 20/20 in both eyes. Slit lamp biomicroscopy showed no central corneal opacity. Corvis ST IOPnct measured 14.5 mm Hg in the right eye and 14 mm Hg in the left eye. Corvis bIOP was 16.6 mm Hg in the right eye and 16 mm Hg in the left eye, with a DA ratio of 1.13 mm in the right eye and 1.07 mm in the left eye.

Two months after initially presenting to our clinic, the oral acetazolamide was suspended, as well as the prednisolone acetate 1%, given the improvement in corneal transparency, complete corneal reepithelialization of the OD, and bilateral improvement of IOP. The patient remained under treatment with a topical fixed combination of brimonidine and timolol maleate twice daily and oral valacyclovir 500 mg daily.

Five months after the initial evaluation in our clinic, the patient remained stable, under treatment with topical fixed combination of brimonidine and timolol maleate twice daily and

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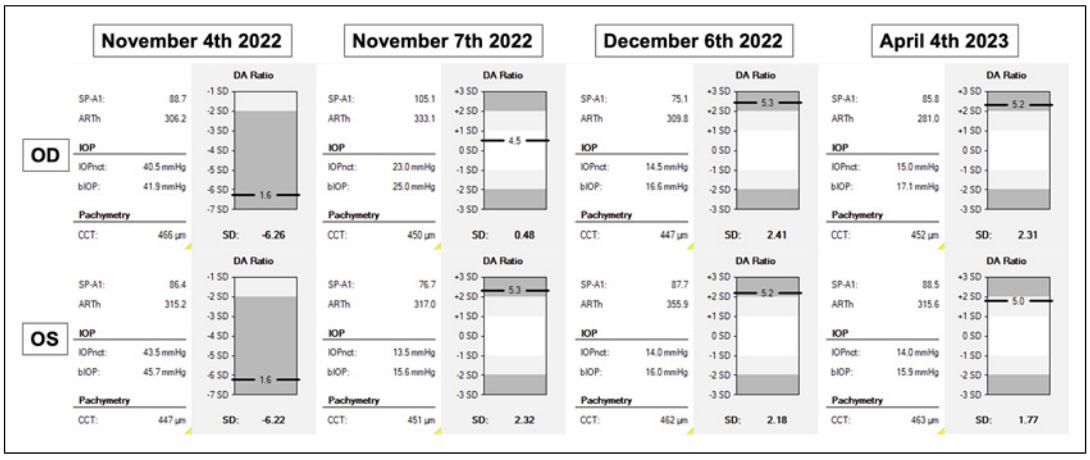

Fig. 4. Corvis® ST noncontact intraocular pressure (IOP) and deformation amplitude ratio (DA ratio) measurements of the patient's right eye (OD) and left eye (OS) throughout follow-up. Upon treatment switch to hypotensive drugs, the non-biomechanically corrected IOP (IOPnct) and the biomechanically corrected IOP decreased significantly to normal values, remaining stable, while the DA ratio significantly increased.

oral valacyclovir 500 mg daily. High-resolution Scheimpflug images showed no abnormalities (Fig. 2). Corvis ST IOPnct recorded pressures of 15 mm Hg in the right eye and 14 mm Hg in the left eye (Fig. 5). Corvis ST bIOP was 17.1 mm Hg in the right eye and 15.9 mm Hg in the left eye, with a DA ratio of 1.12 mm in the right eye and 1.17 mm in the left eye. The DA ratio was 5.2 in the OD and 5.0 in the OS (Fig. 5). There was an improvement in the DA ratio throughout follow-up, with the normalization of this ratio in the OS (1.77 standard deviation), though it remained slightly altered (in the opposite direction) in the OD (2.31 standard deviation). There are no absolute "normal" values for both DA and DA ratio, as these parameters should be evaluated simultaneously with the bIOP. In each measurement, the Corvis ST® compares the obtained value with the mean values obtained for eyes with similar bIOP and determines whether the obtained value falls within a normal range or is significantly "abnormal" (over or under the mean ± 2 standard deviations).

The ocular hypotensive agents and the oral valacyclovir were then suspended, with normal IOP and no recurrence of herpetic eye disease throughout follow-up (12 months to date). There was no increase in cup to disc ratio in both eyes and no development of fundoscopic signs of glaucoma during this period. Furthermore, there was no structural damage of the ONH, according to the multiple ONH optical coherence tomography (OCT) exams performed with the REVO60® (OPTOPOL Technology, Zawiercie, Poland).

Discussion

PISK results from elevated IOP, typically when it disrupts endothelial pump function. This disease was first described as a complication following LASIK [1]. Increased IOP seems to be essential to the pathophysiology of PISK. However, endothelial dysfunction may also contribute to its development [9]. Damage to the endothelium due to the high IOP compromises its pump function. This results in a shifting of fluid from high-pressure areas to low-pressure areas across the endothelium, causing corneal edema. In cases of LASIK, the interface space is the area of low pressure where fluid subsequently collects in patients with PISK. Classically, patients with history of uneventful LASIK surgery who have been on topical corticosteroids for a significant period of time present with blurred vision. This may develop a few days to a

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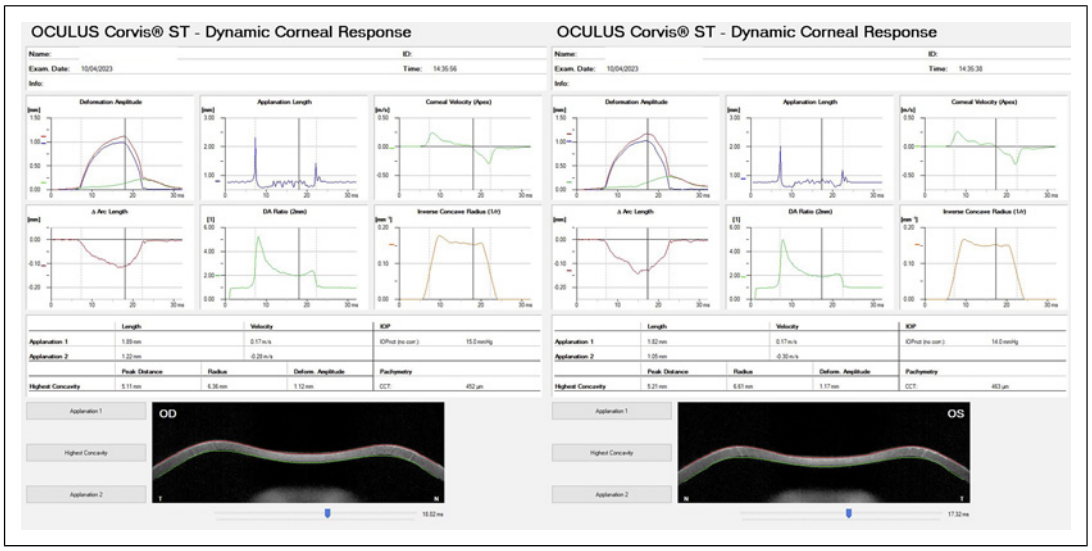

Fig. 5. Corvis® ST noncontact intraocular pressure (IOP) measurement of the patient's right eye (OD) and left eye (OS) in the last visit to our clinic. The non-biomechanically corrected IOP (IOPnct) of the OD was 15.0 mm Hg and the IOPnct of the OS was 14.0 mm Hg.

few months after uncomplicated LASIK surgery, though there are cases reported 1–16 years after the procedure [9]. Furthermore, even though IOP is increased, its measurement with applanation tonometry will yield falsely normal results, which contributes to the frequent misdiagnosis of PISK. This occurs due to the development of a fluid pocket in the lamellar interface, which is easily compressed, thus falsely decreasing IOP values determined with the GAT. Nonetheless, new tonometers that are less influenced by corneal rigidity, such as the Corvis ST®, are able to detect the true elevated IOP and thus enable the correct diagnosis of PISK, as well as prompt treatment initiation, with ocular hypotensive drugs.

In the present report, a case of steroid-induced PISK in both eyes following PRK, along with presumed herpetic keratitis in one eye, is described. This is a unique presentation of a bilateral case of PISK following PRK with concurrent presumed unilateral herpetic keratitis. There are some similarities between this case and classic cases of PISK following LASIK, such as the presence of diffuse corneal stromal opacities, the underestimation of IOP with GAT, the significantly increased bilateral IOP, in association with prolonged corticosteroid treatment, and the improvement of corneal transparency with glaucoma medications to lower IOP. Notwithstanding, some important differences are also present, such as the absence of an interface fluid cleft in both eyes, and the presence of both corneal decreased sensation and KPs in the OD, which contributed to the concurrent presumed diagnosis of herpetic keratitis. In traditional cases of PISK following LASIK, there is accumulation of fluid in the lamellar interface, created by the microkeratome or the femtosecond laser, and there is no altered corneal sensation or intraocular inflammation with KPs. It is likely that the ocular inflammation caused by the PRK procedure contributed to the reactivation of a latent herpetic infection [10]. Furthermore, the patient remained under treatment with ocular hypotensive agents for 5 months after the initial evaluation in our clinic, which is usually not necessary in most classic PISK cases. Whether this prolonged hypotensive treatment was necessary is debatable, since no trial to suspend this medication was performed; therefore, we did not assess the patient's IOP values without medication in the first 5 months of follow-up. If the patient did require prolonged hypotensive treatment, there is a possibility that the patient had undiagnosed ocular hypertension (OHT) prior to the PRK, which was discovered after the

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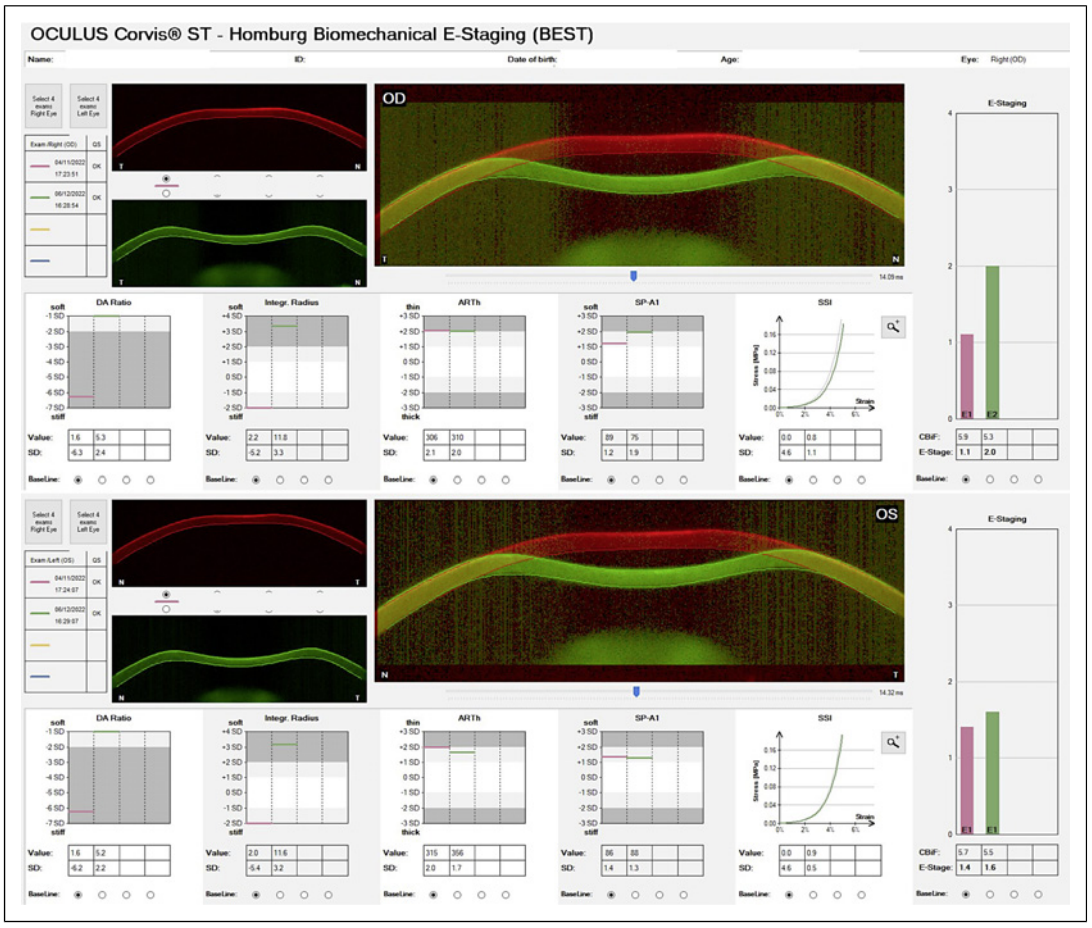

Fig. 6. Corvis® ST Homburg Biomechanical E-Staging display of the patient's right eye (OD) and left eye (OS), comparing the corneal dynamic response in the initial baseline visit (Red; November 4th, 2022) and 1 month after the initiation of treatment, with controlled and stable IOP (Green; December 6th, 2022).

surgery. However, since it was possible to suspend antiglaucoma treatment, as well as the oral valacyclovir, there is no convincing evidence that the patient presented OHT before or after the procedure.

This report also underscores the impact of IOP on corneal deformation when subjected to an air pulse. To first investigate the correlation of IOP and corneal stiffness, an experimental study examined the deformation response of three distinct contact lenses with known structural characteristics, which served as corneal models, under different chamber pressures using ultra-high-speed Scheimpflug imaging [11, 12]. Further research has consistently revealed that stiffer corneas with higher IOP exhibit lower DAs, lower DA ratios, and longer first applanation times [12, 13]. These findings align with our initial assessment, where elevated IOP correlated with corneal stiffening. Elevated IOP significantly altered the deformation response in both eyes, as depicted in Figures 3, 4, and 6. However, by reducing the pressure level, we observed a return to typical values in terms of DA and first applanation time.

Prior studies have already demonstrated the significant inaccuracy of GAT in PISK cases following LASIK, resulting in consistently lower IOP measurements than the actual values [1–5]. This case report further confirms the inadequacy of GAT in diagnosing PISK following surface ablation. Conversely, the Corvis ST IOP measurement relies on the first applanation

time. Although this measurement is influenced by corneal stiffness and thickness, it provides a more accurate assessment of IOP [8].

The bIOP, designed to be independent of corneal thickness and biomechanical properties, confirmed elevated IOP values in this case. This parameter is generally considered more precise than GAT [13]. The DA and the deflection amplitude (DfA) are two relatively new corneal biomechanical parameters which can also be measured with the Corvis ST. The DA ratio is calculated as the deformed amplitude of the central apex divided by the average deformation of two points located 1 mm (DA max 1) or 2 mm (DA max 2) on either side of the corneal apex. Similarly, the DfA is calculated as the ratio between the DfA divided by the amplitude of two points located 1 mm or 2 mm peripherally from the corneal apex. The lower the ratio, the more resistant the cornea is to deformation/deflection [13]. Regarding the case reported previously, sequential examinations revealed a progressive reduction in Corvis IOPnct and bIOP measurements. Concurrently, the DA amplitude and DA ratio returned to typical values after ocular hypotensive oral and topical drugs were initiated (Fig. 5). In Figure 6, we can appreciate the differences in corneal stiffness, with different responses to the air puff of the Corvis ST, as well as an improvement of the DA ratio, which occurred due to the normalization of the IOP in both eyes.

PISK following LASIK can mimic DLK, often leading to the incorrect administration of steroid therapy, a phenomenon documented in numerous studies. Consequently, prompt recognition and meticulous IOP monitoring are essential to prevent the risk of vision loss due to glaucomatous neuropathy [2, 3, 5, 6, 8].

To the best of our knowledge, this case report is the first to describe PISK after PRK. It emphasizes that Goldmann tonometry may erroneously indicate normal IOP levels when, in fact, they are elevated in cases of PISK, whether it occurs after LASIK or PRK [2, 3, 5, 6, 8]. Scheimpflug imaging using rotating corneal tomography and ultra-high-speed biomechanical assessments provides valuable data for accurate diagnosis and treatment planning. Several studies have already demonstrated their significance in detecting an increased susceptibility to ectasia [14–16]. This case underscores the importance of investigating ocular biomechanics for precise IOP measurement, offering insights into the actual effects of IOP fluctuations on corneal biomechanical measurements. Furthermore, while advanced technology is relevant for understanding the relevance of ocular biomechanics in the pathophysiology of glaucomatous neuropathy [17], the authors emphasize the relevance of bi-digital tonometry for detecting elevated IOP in cases with non-normal corneas.

Statement of Ethics

This study protocol was reviewed, and the need for approval was waived by the Ethics Committee of the Federal University of Rio de Janeiro (Rio De Janeiro, Brazil). The patient reported in the case report signed an informed consent form. This study is in accordance with the canons of the Declaration of Helsinki for research involving human participants. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

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The authors declare that they have no financial ties to declare. No funding or sponsorship was received for this study or publication of this article.

Conflict of Interest Statement

Renato Ambrósio Jr. is a consultant for OCULUS Optikgeräte GmbH (Wetzlar, Germany). Jaime Guedes, Rodrigo Brazuna, Alexandre Costa Neto, Denisse Josefina Mora-Paez, Rodrigo Vilares Morgado, Marcella Q. Salomão, and Fernando Faria-Correia declare that they have no competing interests. The authors have no relevant financial disclosures regarding the subject matter or materials discussed in the article.

Author Contributions

Jaime Guedes and Rodrigo Vilares Morgado: ophthalmologists who observed the subject of the case report, redacted the manuscript, and contributed to its revision and final version. Rodrigo Brazuna, Fernando Faria-Correia, and Alexandre Costa Neto: ophthalmologists who observed the subject of the case report and contributed to the revision of the manuscript. Denisse Josefina Mora-Paez: ophthalmologist who observed the subject of the case report, collected the patient's clinical data and the images of the patient's exams, and contributed to the revision of the manuscript. Marcella Q. Salomão: ophthalmologist who contributed to the multimodal corneal imaging study of the patient, oversaw the redaction of the case report, contributed to the revision process, and approved its final version. Renato Ambrósio Jr.: senior ophthalmologist who observed and followed the subject of the case report, contributed to the multimodal corneal imaging study of the patient, redacted the manuscript, and contributed to its revision and final version.

Data Availability Statement

This article is a case report. All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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