Epithelial hyperplasia in a patient with myopic regression after photorefractive keratectomy and utility of anterior segment optical coherence tomography in detection of epithelial changes following refractive surgery

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Case Report

CASE REPORT: Epithelial hyperplasia in a patient with myopic regression after photorefractive keratectomy and utility of anterior segment optical coherence tomography in detection of epithelial changes following refractive surgery.

Kattayoon Kate Hashemi[1] [a], David Tabibian[1], Emmanouil Blavakis[1], Myrsini Petrelli[1], Georgios Kymionis[1]

[1] Department of Ophthalmology, Jules-Gonin Eye Hospital, University of Lausanne, Fondation Asile des aveugles, Lausanne, Switzerland

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Purpose

To demonstrate the utility of anterior segment optical coherence tomography (AS-OCT) in identification of epithelial hyperplasia in a patient with myopic regression after photorefractive keratectomy (PRK).

Case Presentation

A 26-year-old woman with myopic regression after PRK for high myopia was noted to have a central epithelial hyperplasia with the aid of AS-OCT (Avanti OCT Optovue, Fremont, CA).

Conclusion

Epithelial hyperplasia can be demonstrated with the aid of AS-OCT and may correlate with myopic regression after PRK. The use of AS-OCT is not only important to elucidate the etiology of myopic regression but also to prepare accurately a retreatment strategy.

INTRODUCTION

The role of corneal epithelium in the healing process has been increasingly highlighted with the advancement in anterior segment imaging. Reinstein et al, using very high-frequency digital ultrasound, have contributed significantly to our understanding of the role of epithelium in normal, pathologic and post-surgical corneas (Reinstein et al. 1994). The emergence of anterior segment optical coherence tomography (AS-OCT) in the early 2000 enabled non-invasive and precise mapping of the epithelium. Epithelial thickness profile and remodeling have been reported in eyes with keratoconus, following myopic and hyperopic laser-assisted in situ keratomileusis (LASIK) , photorefractive keratectomy (PRK), small incision lenticule extraction (SMILE), orthokeratology, placement of cornea ring segments and corneal collage crosslinking (CXL) (Li et al. 2012; Chen et al. 2015; Rocha and Krueger 2014; Ganesh, Brar, and Relekar 2016).

Herein, we report a case of myopic regression after PRK for high myopia where epithelial hyperplasia was demonstrated with the aid of AS-OCT (Avanti OCT Optovue, Fremont, CA). All the procedures related to this case were conducted in accordance with the tenets of the Declaration of Helsinki and no identifiable information is shown in this manuscript.

CASE PRESENTATION

A 26-year-old woman, high myope, was seen in our refractive surgery department, desiring to improve her uncorrected vision. She was otherwise healthy with no known family history of keratoconus or glaucoma and her refraction was stable for two years. Corrected distance visual acuity (CDVA) was 20/16 in both eyes, with manifest and cycloplegic refraction of -8.50 -1.50 x 171° and -10.25 -0.25 x 170° in the right and left eye respectively. Slit lamp examination revealed healthy anterior and posterior segments in both eyes. Corneal tomography maps measured by Wave-Light® ALLEGRO Oculyzer (Alcon Surgical, Fort Worth, Texas) revealed in the right eye: Km 46.0 D, Kmax 49.4 D,

a **Correspondence:**
Kattayoon Kate Hashemi
Avenue de France 15, 1002 Lausanne, Switzerland
Tel +41 21 626 8111
Fax +41 21 626 8890
Email kattayoon.hashemi@fa2.ch

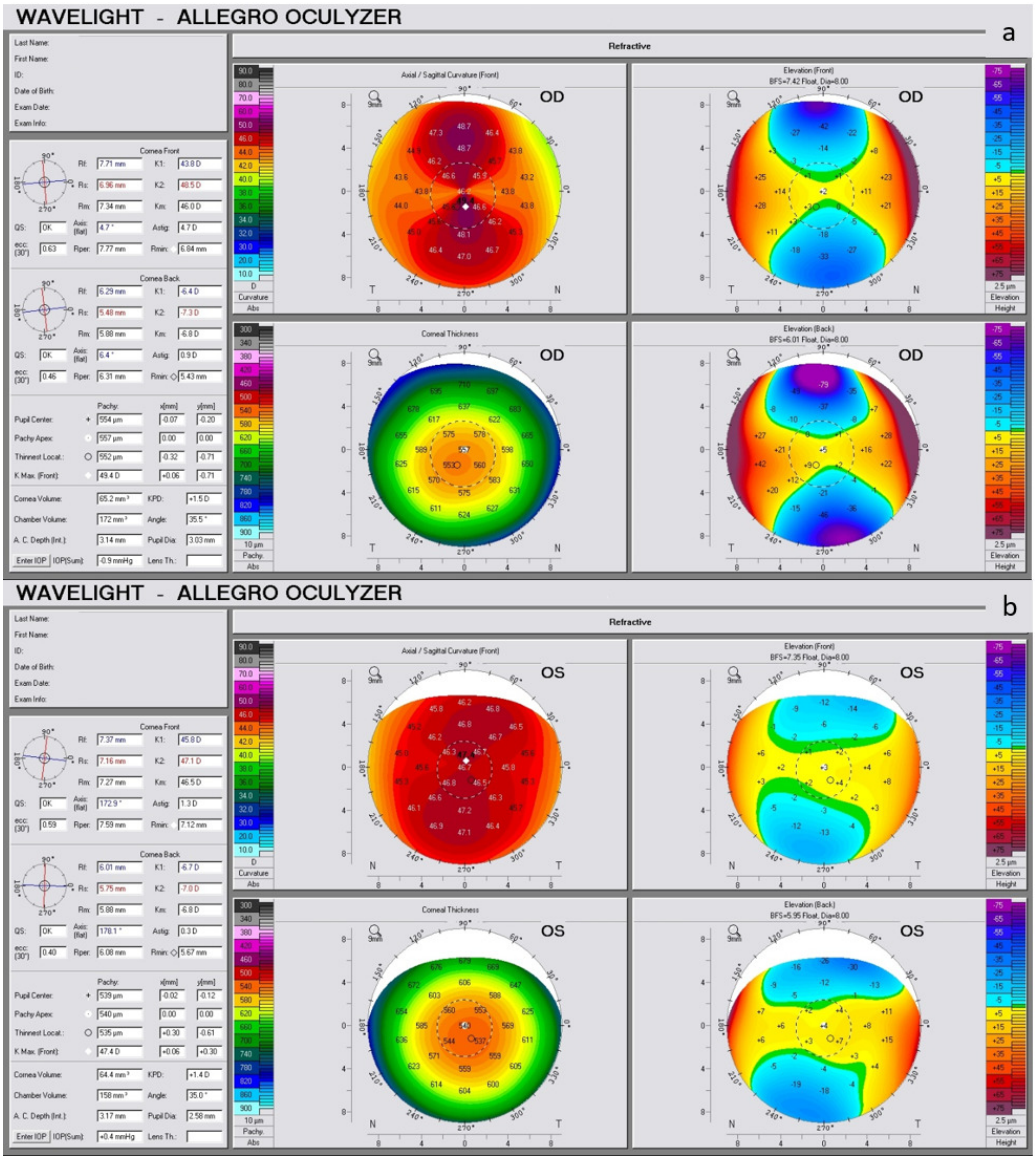

Figure 1. Pre-operative tomography of the right (a) and left (b) eye.

minimum pachymetry 552 µm and in the left eye: Km 46.5 D, Kmax 47.4 D, minimum pachymetry 535 µm (Figures 1a, 1b). As the elevated Kmax in neither eye was associated with abnormal thinning or posterior elevation, the steeper hemimeridian was superior instead of inferior and the Belin Ambrosio percentage thickness increase was within normal limits, refractive surgery was indicated in this patient. After reviewing the risks, including ectasia, and the alternatives to laser vision correction, the patient, being highly motivated, decided to undergo a PRK.

Both eyes were treated with the WaveLight® EX500 Excimer Laser (Alcon Surgical, Fort Worth, Texas) with one month interval between them and no complication was noted. The ablation depths for the right and left eye were 121.19 µm and 121.20 µm, respectively. In both eyes the optical, transition and ablation zones were 6.50 mm, 1.25 mm and 9.00 mm, respectively. A 9.0 mm electrical Amoils brush (Innovative Excimer Solutions, Toronto, ON) was used to remove the epithelium, mitomycin C (MMC) 0.02% was applied to the stromal bed during 30 seconds followed by irrigation with 60 ml chilled Balanced Salt Solution (Alcon SA, Rotkreuz, Switzerland) and after the laser treatment a bandage contact lens (Air Optix Night & Day, Speicher, Switzerland) soaked in preservative-free ofloxacin 0.3% (Floxal - Bausch & Lomb, Switzerland) was placed on the cornea. Post-operative treatment included artificial tears and ofloxacin until epithelial closure followed by fluorometholone 0.1% (FML®- Allergan Inc., Zürich, Switzerland) and ketorolac (ACULAR®, Allergan Inc., Zürich, Switzerland) three times daily for one month, two times daily for one month and once a day for one month.

In each eye the epithelium regenerated within a few days, no short-term complications were noted and three months post-operatively the spherical equivalent in both eyes was -0.5 D. However, one year later, the patient noted bilateral decrease of her vision, more pronounced in the left eye. A myopic regression was observed with spherical equivalent of -1.25 D in the right eye and -2.00 D in the left eye. Corneal tomography revealed a minimum corneal thickness of 425 µm and 406 µm in the right and left eye re-

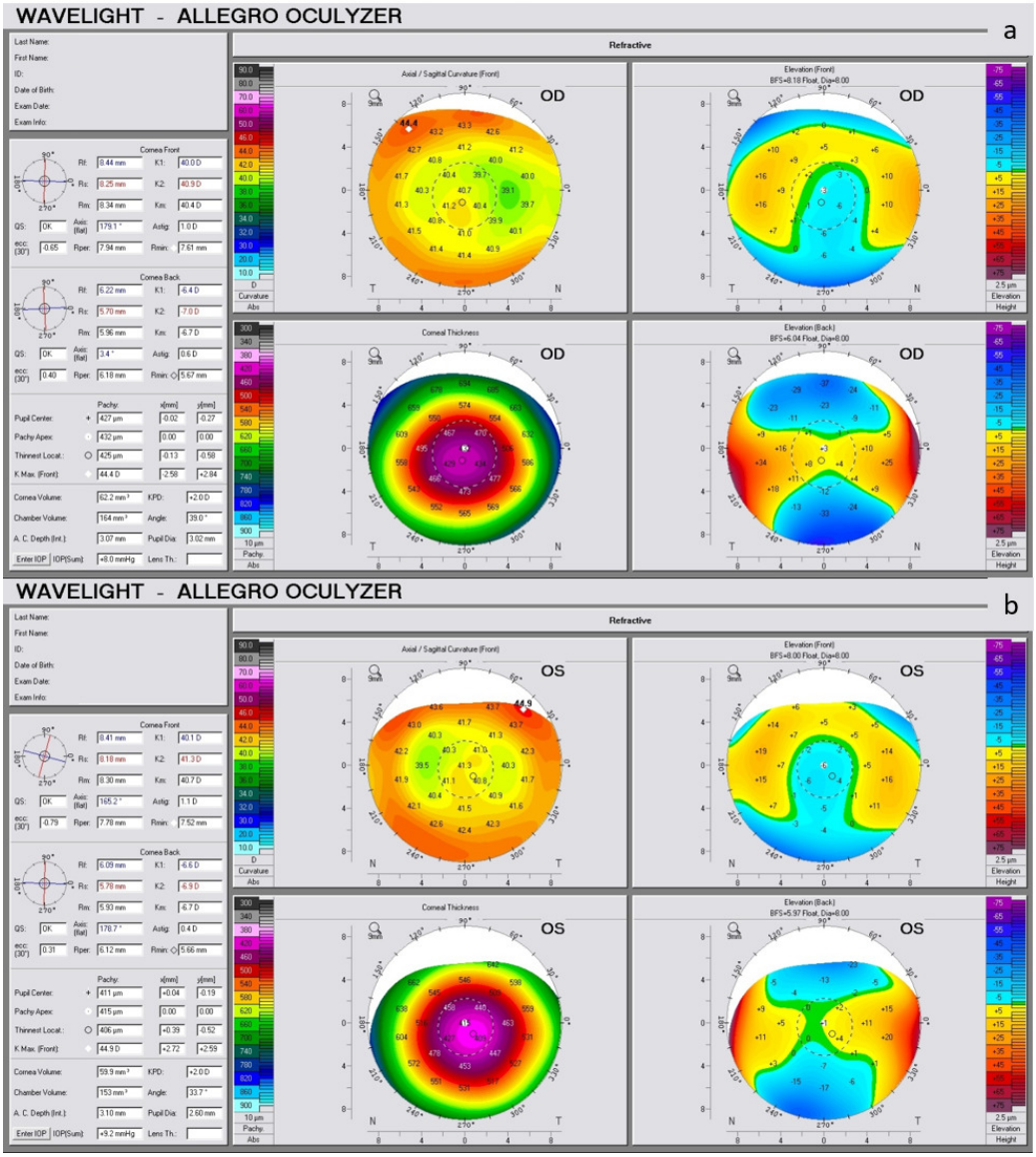

Figure 2. Tomography of the right (a) and left (b) eye 1 year postoperatively. No sign of ectasia is noted.

spectively and excluded the possibility of postoperative ectasia (Figures 2a, 2b). Epithelial maps obtained by AS-OCT revealed bilateral central epithelial thickening (Figures 3a, 3b) while other causes of myopic shift, such as increase in axial length and cataract formation, were also excluded.

In addition, a correlation was found (Figures 4a, 4b) between central epithelial thickness and the spherical equivalent of the right and left eye (R-squared 0.82 and 0.66 respectively) as well as between inferior epithelial thickness and the spherical equivalent of the right eye (R-squared =0.53). The correlation between stromal thickness and the spherical equivalent was also calculated for the right and the left eye (Figures 4c and 4d) with the R-squared values being 0.41 and 0.32 respectively.

DISCUSSION

The role of epithelial hyperplasia (EH) in regression after PRK was reported since 1996 by Gauthier et al. using a Haag-Streit optical pachymeter (Gauthier et al. 1996) while a few years later Lohmann et al. presented the case of a woman with post-PRK regression and histologically proven EH without subepithelial deposition of new collagen or proteoglycans (Lohmann, Reischl, and Marshall 1999). Following surgical treatment for myopia, corneal epithelium may thicken in the zone of ablation or take a lenticular pattern and this EH may contribute to altered refractive effect and corneal asphericity (Hou et al. 2016). Erie et al. suggested that at 1 year, every 12 µm of EH corresponds to 0.41 D of myopic regression whereas Gauthier et al. suggested that 18 µm of EH corresponds to 1 D of regression (Gauthier et al. 1996; Erie 2003). Reported stability of EH post PRK varies between three months and one year and persistent EH has been noted three to seven years after PRK using confocal microscopy (Patel et al. 2007; Ivarsen, Fledelius, and Hjortdal 2009).

The development of AS-OCT enabled the evaluation of the corneal epithelium in a non-invasive manner that provides high quality images and shows excellent repeatability (Lu et al. 2019). Following PRK and within a 6-month pe-

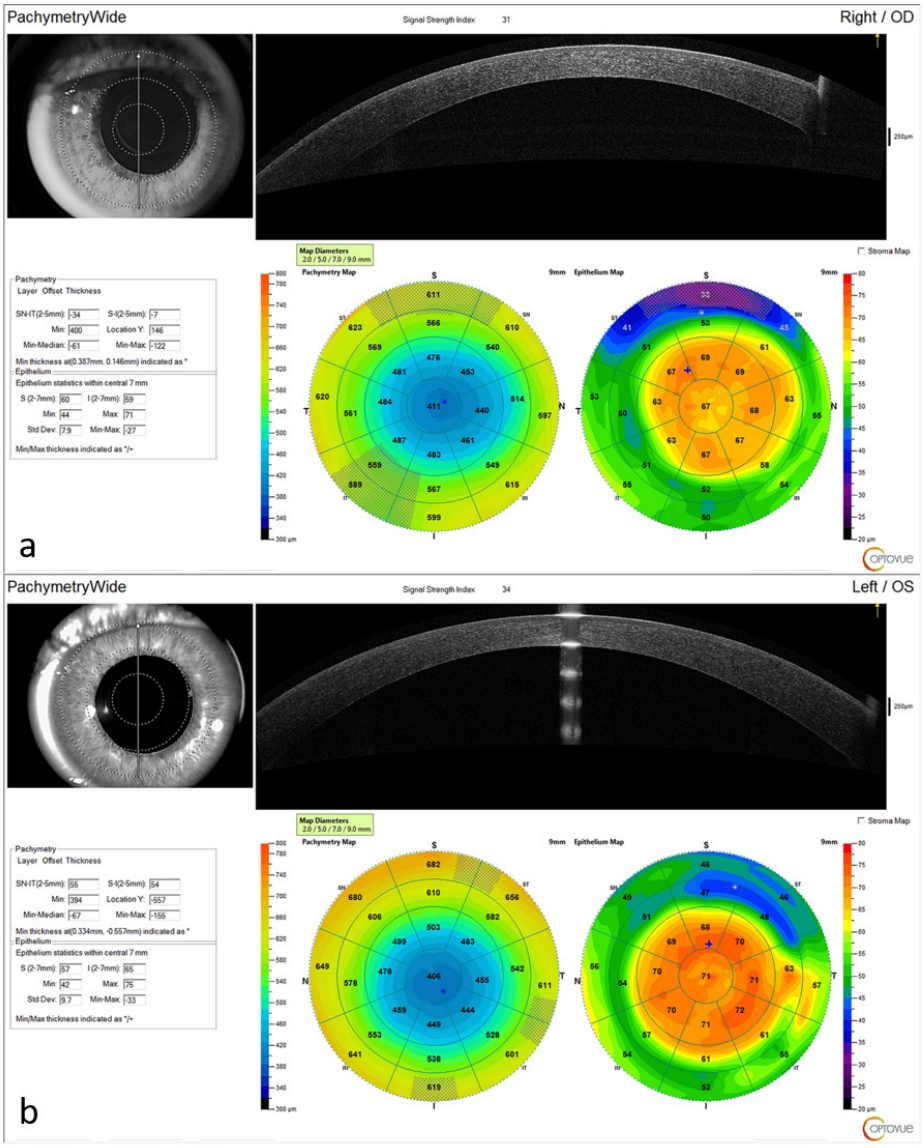

Figure 3. (a) Epithelial map as measured with AS-OCT 1 year postoperatively, right eye. Note the gradient pattern of hyperplasia with progressively thinner epithelium from center to periphery. (b) Epithelial map as measured with AS-OCT 1 year postoperatively, left eye. Note the gradient pattern of hyperplasia with progressively thinner epithelium from center to periphery and more pronounced epithelial hyperplasia than the right eye.

AS-OCT= anterior segment optical coherence tomography

riod, the thickness of the corneal epithelium gradually increases, reaching the preoperative levels in the midperipheral and peripheral zones while becoming thicker than before in the central zone (Sedaghat et al. 2019). It has also become evident that in myopic PRK, the amount of correction and the size of the treatment zone can influence the degree of epithelial thickening (Chen et al. 2015; Kang and Kim 2019). Interestingly, EH was less prominent in patients that were treated with transepithelial PRK combined with CXL than in those that underwent transepithelial PRK alone (Kang and Kim 2019).

Epithelial thickening measured with AS-OCT has also been observed following LASIK for myopia and has been positively correlated with preoperative refractive error (Kang and Kim 2019). Despite the fact that epithelial remodeling following LASIK for myopia does not seem to be related with postoperative spherical equivalent, it may affect the outcome of other refractive techniques, such as varifocal LASIK (Fan et al. 2019; Taneri et al. 2019). When SMILE is performed for the correction of myopia, EH may still occur and be correlated with the degree of preoperative myopia but remains unclear whether it affects the refractive outcome (Ganesh, Brar, and Relekar 2016; Romito et al. 2020; Luft et al. 2016). In a study that compared the epithelial thickening that was observed following LASIK and SMILE, no significant differences were observed between the two techniques, suggesting that epithelial remodelling probably results because of changes in the corneal curvature rather than in corneal denervation (Kanellopoulos 2019). Additionally, AS-OCT can also be useful for the eval-

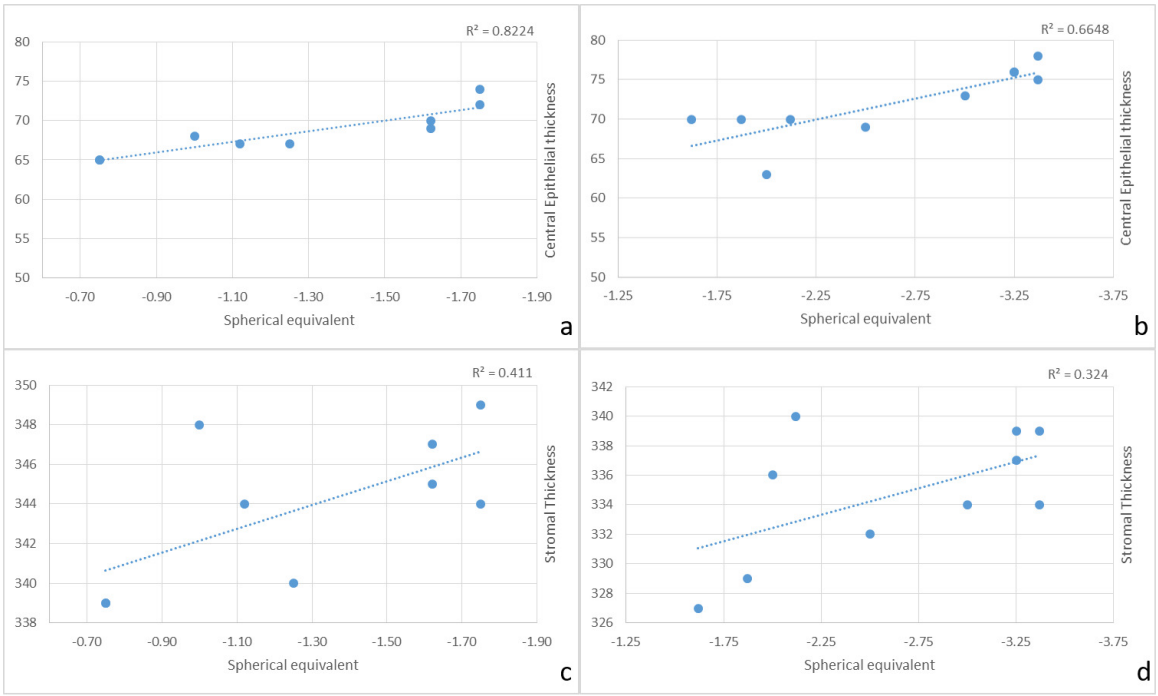

Figure 4. Graphs showing the correlation between the spherical equivalent and the central epithelial thickness in the right (a) and left (b) eye and between the spherical equivalent and the stromal thickness of the right (c) and left (d) eye.

uation of epithelial remodelling in femtosecond laser-assisted stromal lenticule addition keratoplasty (SLAK) for keratoconus, where it documents the postoperative reversal of the epithelial thinning that is observed in keratoconus (Nubile et al. 2021).

In the present case, EH was noted bilaterally for over one year after PRK. Epithelial maps of 9 mm diameter taken by AS-OCT revealed a central zone of epithelial thickening bilaterally (Figure 3), a pattern that corresponds to the laser ablation pattern and its transition zone. Interestingly, a strong correlation was observed between central epithelial thickness and spherical equivalent in both eyes, as well as between inferior epithelial thickness and spherical equivalent in the right eye. Even though the possibility of stromal remodelling as an additional contributing factor to the myopic shift cannot be excluded, the spherical equivalent in this case appears to be affected about 50% less by stromal thickness than central epithelial thickness in both eyes.

The patient is very satisfied with the results even in the presence of regression and is not interested to have any retreatment. Should she change her mind, phototherapeutic keratectomy (PTK) with mitomycine would be a management option. If there is a residual myopia despite PTK, retreatment by PRK could be considered if ectasia is consistently ruled out. Otherwise, the refractive error could be managed by placement of a phakic implant in the ciliary sulcus.

In conclusion, EH can be demonstrated with the aid of AS-OCT in a patient with myopic shift after PRK. Despite the fact that this shift could not be totally explained by the EH observed, this case serves as a reminder of the importance of AS-OCT in the detection of EH in patients who present with regression after laser refractive surgery.

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