



Appearance of herpes simplex keratitis on anterior segment optical coherence tomography

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Received: 20 December 2018 / Accepted: 6 July 2019 / Published online: 15 July 2019
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Abstract

Purpose To describe the anterior segment AS-OCT findings of herpetic simplex keratitis.

Methods Forty-two eyes of 42 patients with proven herpetic keratitis of varying severity were included in this prospective, observational, non-comparative case series study. All subjects underwent ophthalmologic examination and AS-OCT imaging.

Results Twenty-five of the 42 eyes (59.5%) had sub-epithelial infiltrates. In 11 of these cases, the overlying epithelium appeared intact, but in 14 cases, hydropic changes, heaping, and defects were observed. Seventeen eyes (40.5%) showed stromal involvement: six cases with scar at presentation and one case associated

with uveitis. Stromal infiltrates were also seen, in ten cases, as a diffuse or local lentiform or spindle-shaped hyper-reflective area in the stroma.

Conclusion Herpetic keratouveitis has characteristic features on AS-OCT images. This study demonstrates that herpetic keratitis also has characteristic AS-OCT features, including sub-epithelial infiltration and specific stromal hyper-reflective patterns. These features are not unique to herpetic keratitis, but AS-OCT imaging may provide useful supplementary information for diagnosing and monitoring herpetic keratitis.

Keywords Herpes simplex · Herpetic keratitis · Anterior segment optical coherence tomography

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Introduction

Herpetic keratitis is a common cause of infectious keratitis and can lead to severe visual loss [1]. In one study, 33% of patients with severe visual impairment required corneal grafts [2]. Patient diagnosis and monitoring of herpes simplex keratitis have traditionally depended upon clinical slit-lamp assessments. However, spectral-domain optical coherence tomography (OCT) can image biological tissues with an axial resolution of 5 μm and a transverse resolution of 15 μm [3, 4]. Even though this technology was designed to image posterior segment structures, many OCT systems now have anterior segment imaging

capabilities [5]. As a result, anterior segment OCT (AS-OCT) has been used to study a variety of anterior segment and ocular surface problems [6–9]. Time-domain OCT has a lower image resolution than spectral-domain OCT, but has been used to measure stromal infiltration and corneal thickness in eyes with microbial keratitis [10]. Swept-source AS-OCT has also been used to evaluate a variety of corneal conditions, including Terrien's marginal degeneration, the post-LASIK cornea, and keratoconus [11–14]. In vivo confocal microscopy was used to study corneal lesions associated with herpes simplex keratitis [15–17]. The current study used spectral-domain AS-OCT to image corneas with confirmed herpetic keratitis. This study was done to identify characteristic AS-OCT morphological features of the disease.

Materials and methods

This study was reviewed and approved by the Assiut University Institutional Review Board (Assiut, Egypt). The study adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all patients included in this study. Patients had the right to withdraw from the study without compromising regular, full clinical care.

This study included patients who presented with herpetic keratitis to the ophthalmology outpatient clinic at Assiut University or the El-Noor Eye Center (Assiut, Egypt). Herpetic keratitis was diagnosed by two cornea specialists (AKA and MAN), using slit-lamp examination, and/or a positive history for herpetic keratitis. We included only patients who previously had typical dendritic viral corneal ulcers in their hospital medical records. All cases responded to antiviral treatment. Subjects were excluded from the study if any of the following were present: age under 18 years, presence of other ocular disease, or eyes with previous ocular surgery.

Forty patients underwent AS-OCT imaging using a spectral-domain OCT system (RTVue-100, Optovue, Fremont, CA, USA). Vertical and horizontal raster scans (6.0-mm scan lines) and the add-on lens (CAM-L) scan, which provides a wider viewing angle to include the entire cornea, were obtained. Swept-source AS-OCT (Triton-DRI swept-source OCT, Topcon Co., Japan) was used in the remaining two

cases (3.0-mm scan lines). All images were analyzed by two OCT experts (WS and KA), and there was total agreement between them.

Continuous data are presented as mean \pm standard deviation. This study was a qualitative study and did not include any statistical comparisons.

Results

A total of 42 eyes of 42 patients (27 men and 15 women) with a mean age of 34.7 ± 6.5 years (range 19–46 years) were included in this study. The time between a subject's first presentation to our clinic and AS-OCT imaging was 3.4 ± 1.2 days (range 1–5 days).

The various AS-OCT findings in eyes with herpetic keratitis are summarized in Table 1. Briefly, superficial stromal keratitis was present in 11 eyes. The AS-OCT images of these eyes showed a small localized area of sub-epithelial haze and an intact overlying epithelium (Fig. 1). However, 14 eyes had more advanced disease and cystic spaces in the corneal epithelium were present. These regions coincided with hydropic degeneration, overlying diffuse sub-epithelial haze (corresponding to dendritic figures), and underlying diffuse stromal infiltrates (Fig. 2). Additionally, 10 eyes had epithelial defects with or without regenerating epithelium heaping at the ulcer edge. The underlying stroma was hyper-reflective, indicating stromal infiltration that increased with scarring progression. Some of these eyes also had an irregular endothelial plaque opposite to regions with stromal keratitis (Fig. 3). Corneal scars and infiltrates were both hyper-reflective, but were easy to differentiate from one another. Corneal infiltrates (Fig. 4b, c) had ill-defined, rounded borders with an overlying defective or intact opaque epithelial layer. In contrast, corneal scars had well-defined sharp edges with or without an overlying epithelial defect (Figs. 5, 6).

Keratic precipitates (KPs) were observed in one eye and appeared as protrusions from the corneal endothelium. Because KPs are associated with herpetic epithelial or stromal disease, they indicate the presence of keratouveitis and subsequent endothelitis (Fig. 4a, d). Additionally, floating cells were visible near the corneal endothelium (Fig. 4d) and trabeculitis, represented on AS-OCT images as a heterogeneous trabecular meshwork hyper-reflectivity, was

Table 1 Anterior segment optical coherence tomography findings in eyes with herpetic keratitis

AS-OCT finding	Clinical interpretation	Number
Stromal haze without epithelial defect (Fig. 1)	Superficial stromal keratitis	11
Sub-epithelial haze with an overlying cystic space in the corneal epithelium (Fig. 2)	Dendritic figure with underlying stromal infiltrate	14
Epithelial loss with adjacent area of epithelial heaping, and underlying area of high hyper-reflectivity (Fig. 3)	Epithelial defect overlying herpetic corneal infiltrations and scarring	10
Epithelial heaping at the edge of an epithelial defect (Fig. 3)	Healing edge of epithelial defect	
Localized stromal thickening (Fig. 4b, c)	Disciform keratitis	1
Localized endothelial thickening with protrusions (Fig. 4a, d)	Keratic precipitates caused by endothelitis in eyes with keratouveitis	
Hyper-reflectivity and thickening of the trabecular meshwork (Fig. 4e)	Trabeculitis	
Stromal condensation and thinning with an overlying epithelial defect (Fig. 5)	Post-herpetic neurotrophic ulcer	3
Stromal condensation with intact overlying epithelium (Fig. 6)	Post-herpetic scar	3

AS-OCT, anterior segment optical coherence tomography

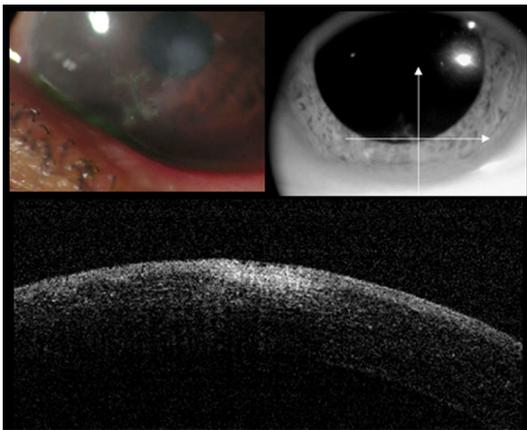


Fig. 1 Spectral domain anterior segment optical coherence tomography images showing a small localized area of sub-epithelial haze with underlying shadowing. The epithelium in the area of the dendrite appears roughened. Clinically, the subject presented with an epithelial dendritic figure and mild sub-epithelial stromal infiltration

apparent (Fig. 4e). In three other cases, a post-herpetic neurotrophic ulcer with an area of stromal condensation and thinning and an overlying epithelial defect (Fig. 5) was identified. On the other hand, the epithelium was intact over stromal condensation in three cases (Fig. 6).

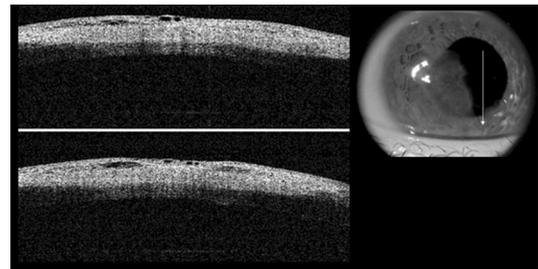


Fig. 2 Spectral-domain anterior segment optical coherence tomography images showing epithelial cystic spaces that spatially corresponded to hydropic corneal epithelium degeneration caused by the herpes simplex virus

Discussion

This study identified several AS-OCT characteristics of herpetic keratitis within various corneal layers and in the anterior chamber. Several studies have identified AS-OCT as a useful tool for examining anterior segment pathologies and corneal infections [7–11, 13]. Although Hixson et al. [18] used AS-OCT to diagnose two cases of disciform keratitis, the current study demonstrates characteristic AS-OCT findings in eyes with herpetic keratitis.

Herpetic corneal infiltrates appear on AS-OCT images as a lentiform or spindle-shaped stromal hyper-reflective area that may be localized or diffuse. Images obtained with OCT can help differentiate between active infiltrates and stromal scarring.

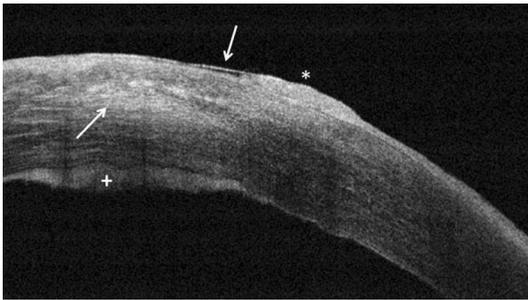


Fig. 3 Spectral-domain anterior segment optical coherence tomography image showing an epithelial defect covered by a hypo-reflective aqueous layer (tear film pooling) (arrow). Heaping regenerating epithelium is visible at the defect edge (*). The underlying area of hyper-reflectivity indicates stromal collagen condensation (scarring) (arrow). The posterior third of the cornea has a normal collagen lamellar arrangement, demonstrating a pattern similar to the peripheral cornea. Endothelial plaque is seen opposite to the region with stromal keratitis (+)

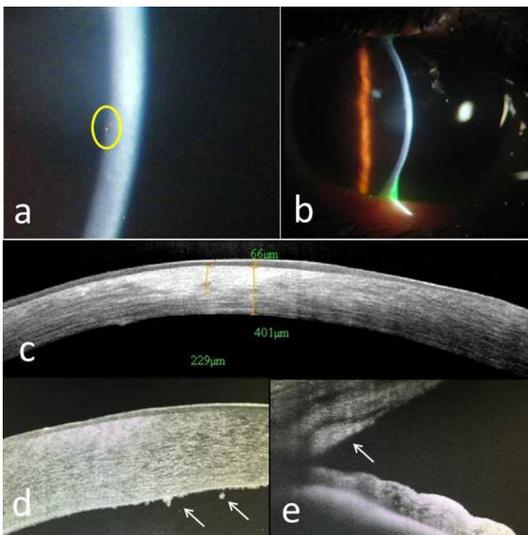


Fig. 4 Images of an eye with herpetic keratouveitis. Slit-lamp photographs showed keratic precipitates (KPs; **a**, circle) and disciform stromal thickening (**b**). Swept-source anterior segment optical coherence tomography (AS-OCT) imaging revealed irregular epithelial thickness, areas of hyper-reflectivity, and KPs (**c**). Hyper-reflective areas indicate stromal infiltration associated with disciform keratitis. A magnified view of the AS-OCT image (**d**) shows floating cells and KPs, which appear as protrusions attached to the endothelium. An irregular corneal endothelium indicates endothelitis (arrows). Imaging with AS-OCT also revealed trabecular meshwork cellular infiltration, as indicated by the presence of hyper-reflectivities (**e**)

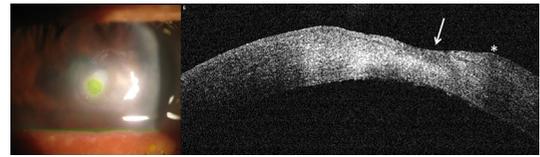


Fig. 5 Spectral domain anterior segment optical coherence tomography image of an eye with post-herpetic neurotrophic ulcer. The image shows a central area of epithelial loss (arrow) surrounded by an area of epithelial heaping (*) and an underlying area of strong hyper-reflectivity (scarring)



Fig. 6 Spectral domain anterior segment optical coherence tomography image of an eye with post-herpetic scar. The image shows a well-defined area of stromal condensation (*) with intact overlying epithelium. The color image shows a recent herpetic ulcer, stained with fluorescein, adjacent to an old post-herpetic scar (arrow)

However, this may be difficult in corneas with a combination of infiltration and scarring, as is the case during the healing process. None of the identified AS-OCT features are unique to herpetic keratitis, meaning that AS-OCT imaging can minimally help in diagnosing herpetic keratitis. However, AS-OCT imaging of a herpetic keratitis is a helpful tool to optimize the follow-up and the management of these cases. Also, this technique has been used in microbial keratitis patients to qualitatively and quantitatively determine corneal lesion extent, monitor disease progression, and evaluate treatment efficacy [10, 19].

The ability of AS-OCT to visualize small lesions (e.g., KPs) and to image the trabecular meshwork, improves its ability to diagnose uveitis in eyes with disciform keratitis particularly in eyes with an anterior chamber that is difficult to visualize because of corneal opacities. On AS-OCT images, inflammatory cells appear as hyper-reflective stromal bodies (as in disciform keratitis), hyper-reflective spots floating in the anterior chamber, or hyper-reflective aggregates on the endothelial surface (i.e., KPs). These findings are consistent with those of Konstantopoulos et al. [20], who examined AS-OCT images in eyes with microbial keratitis. Qualitative assessments can also be made with AS-OCT images, adding supplementary information to other quantitative examinations used to

follow disease progression (e.g., ultrasonic pachymetry in eyes with herpetic disciform edema [21]).

Our study had some limitations. First, it did not include an evaluation of corneal thickness measurements. Second, we only evaluated study eyes with AS-OCT one time. Therefore, further prospective, longitudinal studies are needed to examine disease progression. These studies should also examine correlations between AS-OCT and corneal histopathological findings.

In conclusion, AS-OCT imaging can visualize several characteristic morphological patterns in eyes with herpetic keratitis. Although these patterns are not specific to herpetic keratitis, AS-OCT can provide additional information that may be useful in diagnosing, managing, and treating the disease.

Acknowledgements We would like to thank Editage (www.editage.com) for English language editing.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This study was reviewed and approved by the Assiut University Institutional Review Board (Assiut, Egypt). All study conduct adhered to the tenets of the Declaration of Helsinki.

Informed consent Written informed consent was obtained from all individual participants included in this study. Patients had the right to not participate in this study and the right to withdraw from the study without compromising regular, full clinical care.

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