



Comparison of ocular surface squamous neoplasia and pterygium using anterior segment optical coherence tomography angiography

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ABSTRACT

Purpose: To compare ocular surface squamous neoplasia (OSSN) and pterygium using anterior segment optical coherence tomography angiography (AS-OCTA).

Observations: Flow patterns of conjunctival vessels in patients with OSSN and pterygium were investigated using AS-OCTA. In case 1, slit-lamp examination of a 72-year-old woman revealed an elevated lesion with increased permeability of fluorescein in the inferior nasal conjunctiva of her left eye. AS-OCTA showed markedly meandering large blood vessels in both the superficial and deep layers. Histopathological evaluation of the conjunctival biopsy indicated conjunctival intraepithelial neoplasia. Case 2 was that of a 79-year-old man with a history of three conjunctival tumor excisions. Slit-lamp examination showed an elevated lesion with hyperpermeability of fluorescein in the nasal conjunctiva of his left eye. AS-OCTA revealed increased meandering vasculature in both the superficial and deep layers. Histopathological investigation concluded that the diagnosis was squamous cell carcinoma. Case 3 involved a 61-year-old man with a pterygium. Slit-lamp examination showed typical findings of an elevated nasal lesion accompanied by a head that appeared triangular with a blunt apex. AS-OCTA revealed increased straight vasculature in the superficial layer and an avascular area in the deep layer of the pterygium head.

Conclusions and importance: AS-OCTA revealed abnormal “zigzag vessel patterns” in both the superficial and deep layers denoting meandering vessels in the patients with OSSN. In the patient with the pterygium, it showed “straight vessel patterns” signifying unbending stretched vessels in the superficial layer and an avascular zone in the deep layer of the pterygium head. These findings may be useful for the differential diagnosis of OSSN and pterygium.

1. Introduction

Optical coherence tomography angiography (OCTA) can non-invasively visualize blood flow in vessels without the use of dyes, such as a fluorescein or indocyanine green.^{1,2} The technique can be successfully applied to observe corneal neovascularization in patients with limbal stem cell deficiency^{3,4}, graft-associated neovascularization, post herpetic keratitis⁵, and the conjunctival vessels of normal subjects or patients with pterygium.⁵⁻⁷

Ocular surface squamous neoplasia (OSSN) presents as a spectrum from simple dysplasia to carcinoma *in situ*, and to invasive squamous-cell carcinoma involving the conjunctiva and the cornea. It has been reported that OSSN is uncommon, and that Caucasian populations at latitudes closer than 30° to the equator are at particular ocular risk.⁸

Thus, although there have been no reports regarding the incidence of OSSN in Japan, it is thought to be very rare. It has been reported that OSSN is often accompanied by feeding vessels typically called “cork screw vascular tufts”.⁸ In contrast, a pterygium is characterized by fibrovascular proliferation and inflammation with angiogenesis.⁹ However, OSSN is sometimes misdiagnosed as a pterygium, especially in the early stages or in patients with a history of surgery. Here, we compared OSSN and pterygiums using anterior segment OCTA (AS-OCTA).

2. Findings

2.1. Case 1

Case 1 involved a 72-year-old woman whose slit-lamp examination

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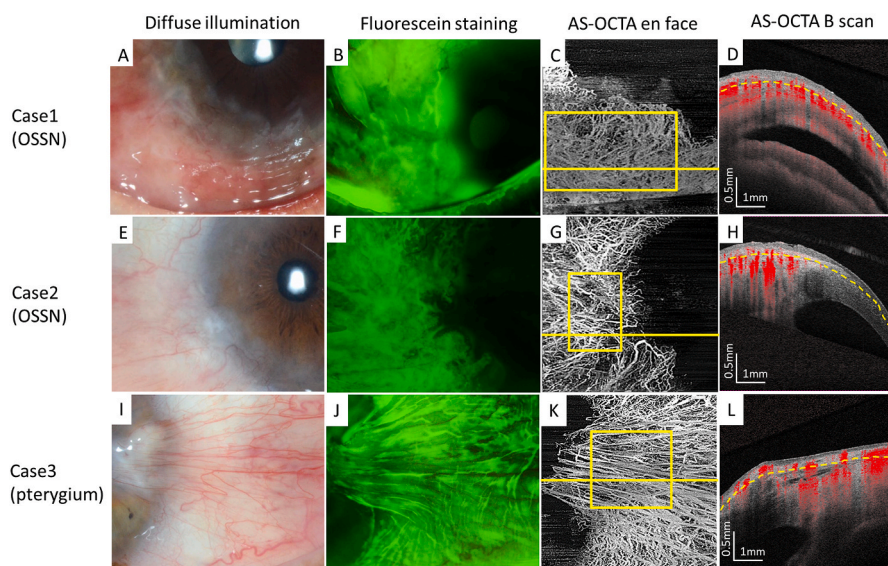


Fig. 1. Slit-lamp photography and AS-OCTA images
Diffuse illumination slit-lamp photography (A, E, I). Fluorescein staining images (B, F, J). AS-OCTA enface whole-layer images (C, G, K). The yellow square indicates the abnormal conjunctival region with high fluorescein permeability. Cross-sectional B-scan images obtained at the level shown by the yellow line in whole-layer images (D, H, L). The yellow dotted line denotes a depth of 200 μ m from the conjunctival epithelium. AS-OCTA: anterior-segment optical coherence tomography angiography. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

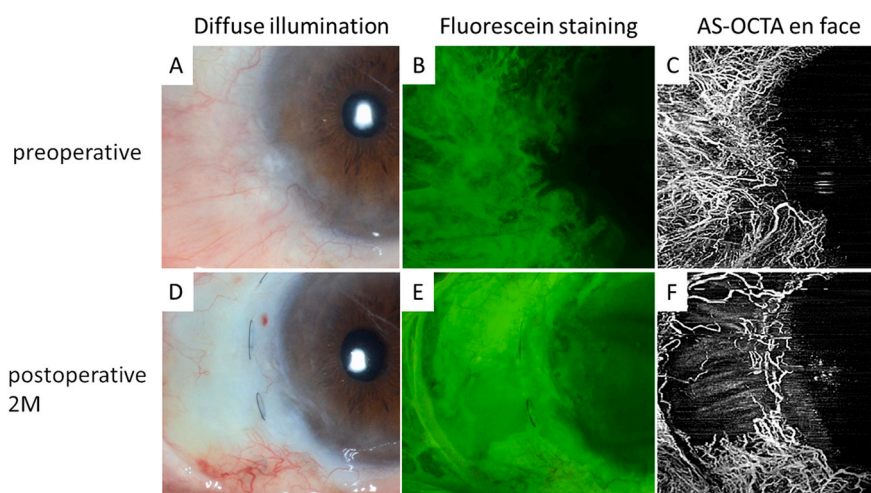


Fig. 2. Comparison of slit-lamp photography and AS-OCTA images before and after OSSN excision. Diffuse illumination slit-lamp photography (A, D). Fluorescein staining images (B, E). AS-OCTA enface whole-layer images (C, F). OSSN: ocular surface squamous neoplasia.

revealed a large elevated lesion with increased vessels and high fluorescein permeability in the inferior nasal conjunctiva of her left eye (Fig. 1A and B). AS-OCTA images were obtained, after written informed consent, using a swept-source OCT system (PLEX Elite 9000; Carl Zeiss Meditec, Dublin, CA) equipped with a 10-diopter optical adaptor lens with a 3 x 3-mm scan pattern. The enface AS-OCTA image revealed dense vasculature, and the B-scan showed both superficial and deep flows (Fig. 1C and D). Tumor excision was performed, and the pathological diagnosis was obtained as carcinoma *in situ*.

2.2. Case 2

Case 2 involved a 79-year-old man who had undergone surgery for OSSN three times. Slit-lamp examination showed an elevated lesion with hyperpermeability of fluorescein in the nasal conjunctiva of his left eye (Fig. 1E and F). The enface AS-OCTA image revealed dense vasculature (Fig. 1G and H). Tumor excision and amniotic membrane transplantation were performed, and the pathological diagnosis was squamous-cell carcinoma.

2.3. Case 3

Case 3 involved a 61-year-old man with pterygium. Slit-lamp examination showed an elevated nasal lesion accompanied by a head that appeared triangular with a blunt apex, which is typical of a pterygium (Fig. 1; I, J). AS-OCTA revealed increased vasculature (Fig. 1; K, L).

We compared preoperative and postoperative vessel structures using AS-OCTA images in Case 2 (Fig. 2). The dense vasculature observed before surgery was removed, and an avascular zone was recognized two months after OSSN excision (Fig. 2; C, F) that suggested the successful surgical removal of OSSN.

Delineation of the superficial and deep layers on AS-OCTA images was achieved after projection artifacts were removed by build-in software as previously described (Fig. 3). Superficial-layer images showed flow from the conjunctival epithelium to a depth of 200 μ m. Deep-layer images showed flow at a depth of 200–1000 μ m from the conjunctival epithelium. The AS-OCTA image flow signals of Cases 1 and 2 revealed “zigzag vessel patterns” denoting meandering vessels in both the superficial and deep layers (Fig. 3; A–F). Conversely, those of Case 3 revealed “straight vessel patterns” showing stretched vessels in the

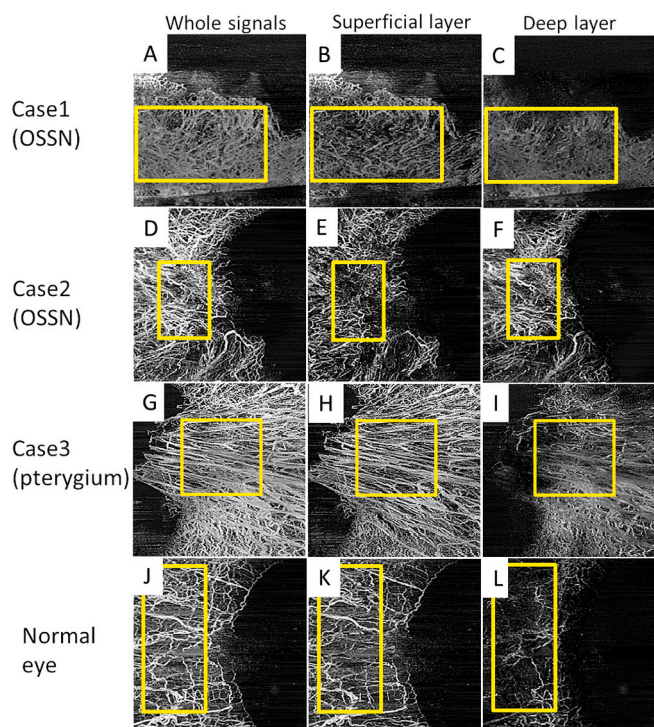


Fig. 3. Vessel patterns of the patients with OSSN and pterygium and of a normal eye as shown on AS-OCTA.

AS-OCTA enface images with whole (A, D, G, J), superficial-layer (B, E, H, K), and deep-layer (C, F, I, L) OCTA blood flow signals. The yellow quadrangle indicates the region of interest.

AS-OCTA: anterior-segment optical coherence tomography angiography, OSSN: ocular surface squamous neoplasia. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

superficial layer and an avascular zone coinciding with the head of the pterygium in the deep layer (Fig. 3; G–I).

The AS-OCTA images of the lesions were binarized with Image J (National Institutes of Health, Bethesda, MD) to calculate vessel density as previously described⁸. We considered that we should calculate the vessel density only in the affected areas. Thus, the regions of interest (ROI) for patients with OSSN and the pterygium were determined by observations using slit-lamp photography, i.e., elevated lesions with hyperpermeability by fluorescein staining for OSSN, and a nasal elevated lesion without hyperpermeability for the pterygium. Vessel density was 60.1% in Case 1, 57.1% in Case 2, and 65.3% in Case 3 in the regions of interest indicated by yellow squares in Fig. 2. We also evaluated conjunctival vessel density in eight normal eyes of eight patients at our hospital with an ROI of acquired maximum normal conjunctival areas adjacent to the limbus, and the density was 27.5%, 29.9%, 44.5%, and 44.8% in the superior, inferior, nasal, and temporal areas, respectively.

3. Discussion

AS-OCTA showed clear differences in the vascular flow pattern between OSSN and pterygium. It also clearly showed that the abnormal vessels were removed by surgical excision of the OSSN. For OSSN, Liu et al. reported that it was possible to quantitatively monitor vascular patterns within, under, and adjacent to the tumor, and that vessel patterns differed according to the clinical features of the tumor.¹⁰ Considering this report along with the results of our cases, it was suggested that AS-OCTA can be useful for the clinical evaluation of vessels for the diagnosis of OSSN and pterygiums.

Akagi et al. analyzed normal conjunctival flow patterns and compared the superficial and deep layers. The flow signals of the superficial layer showed centrifugal patterns, that is, the vessels circumferentially extended radially, whereas the flow signals of the deep-layer showed Y-shaped segmental patterns⁶. AS-OCTA revealed the breakdown of the normal conjunctival vasculature pattern in the patients with OSSN and pterygium.

We could include only two cases with OSSN in this case report because of the low incidence of the disease. Thus, future clinical studies with a larger sample size will be needed to confirm our findings regarding the differentiating features of OSSN and pterygiums on AS-OCTA.

4. Conclusions

In conclusion, AS-OCTA observation showed “zigzag vessel patterns” in OSSN in both the superficial and deep layers. Conversely, in the pterygium, it revealed “straight vessel patterns” in the superficial layer and an “avascular pattern” in the deep layer of the head. These findings may be useful for the differential diagnosis of OSSN and pterygium.

Patient consent

The patients provided written informed consent for the publication of their cases and associated images.

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Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

The patient who is the subject of this case report provided informed consent for his case to be published.

Declaration of competing interest

None.

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