ORIGINAL ARTICLE

OCT angiography of acute non-arteritic anterior ischemic optic neuropathy

OCT angiographie des neuropathies optiques ischémiques antérieures aiguës non artéritiques

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KEYWORDS
OCT angiography; Acute anterior ischemic optic neuropathy; Optic neuropathy; Optic nerve; Optic nerve imaging

Summary
Purpose. — To describe changes of the retinal peripapillary microvasculature on optical coherence tomography angiography (OCT-A) in non-arteritic anterior ischemic optic (NAION) neuropathy.

Methods. — Observational study of 10 patients at the acute phase of NAION. OCT-A was performed using a 3 mm × 3 mm square centered on the optic disc (Cirrus HD-OCT with Angioplex, Carl Zeiss Meditec, Dublin, CA). A qualitative comparison was made with the healthy fellow eye of each patient. All patients had a fluorescein angiography (HRA2, Heidelberg, Germany) and a visual field examination (Octopus 101, Haag-Streit, USA).

Results. — In the affected eyes, OCT-A showed clear modifications in the radial peripapillary network. In all these eyes, a focal disappearance of the superficial capillary radial pattern was present, twisted and irregular. In 8 eyes, there was also a lack of vascularization in some focal areas, appearing as dark areas. No correlation was found between the topography of the vascular alteration shown on OCT-A and visual field pattern defects.

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Introduction

Non-arteritic anterior ischemic optic neuropathy (NAION) results from an acute ischemic insult to the proximal portion of the optic nerve (ON). The etiology is still controversial, but small ON is admitted to be the main risk factor. The diagnosis relies on clinical examination (sudden visual loss, optic nerve head edema) and further investigations as visual field and fluorescein angiography (FA). The latter demonstrates a delayed early filling of the optic nerve head, followed by a fluorescein leakage at the late phase of the FA.

OCT angiography (OCT-A) is a new technology allowing the imaging of retinal microvascular flow without the injection of an intravenous dye. So far, it has been used mainly for the visualization of retina vessels in diabetic retinopathy, of choroidal new vessels in exudative age-related macular degeneration. But OCT-A also visualizes the peripapillary vascularization, and studies have already demonstrated a peripapillary decreased perfusion in glaucoma [1]. We propose to describe the modifications of the peripapillary vascularization at the acute stage of NAION using OCT-A.

Methods

Study patients

This prospective observational study was performed from April 30, 2015 to December 24, 2015 at the Ophthalmology Department of the University Hospital of Bordeaux. The protocol was approved by the ethic committee of the French Society of Ophthalmology and performed in accord with the tenets of the Declaration of Helsinki. Written informed consent was obtained from each participant. All patients were consecutively enrolled because of a sudden and recent vision loss (less than 10 days) related to NAION. In order to confirm the diagnosis of NAION, all patients underwent a complete visual examination, including best-corrected visual acuity, fundus examination, and fluorescein angiography. A visual field test was performed on all patients, except 4 due to a poor visual acuity. The diagnosis of NAION was done on the clinical symptoms and the angiographic features as described above. None of the patients presented any inflammatory features, and erythrocyte sedimentation rate and C-reactive protein were normal. None of

Résumé
But. — Décrire les modifications de la microcirculation péripapillaire sur l’OCT angiographie (OCT-A) à la phase aiguë des neuropathies optiques ischémiques antérieures non artéritiques (NOIA).

Méthodes. — Étude observationnelle portant sur 10 patients à la phase aiguë d’une NOIA. L’acquisition des images était faite à l’aide de l’OCT angiographie AngioPlex de Zeiss Meditec (Dublin, CA) sur des cubes de 3 mm × 3 mm. Pour chaque patient, une analyse comparative avec l’œil Adelphé était réalisée. Tous les patients avaient par ailleurs une angiographie à la fluorescéine (HRA2, Heidelberg, Allemagne) et un champ visuel (Octopus 101°, Haag-Streit, États-Unis).

Résultats. — Au niveau des yeux atteints, le réseau vasculaire péripapillaire est nettement modifié sur l’OCT-A. Chez tous les patients, une désorganisation focale de la disposition radi- aire des vaisseaux péripapillaires était retrouvée, associée à une déformation des capillaires. Chez 8 patients existait aussi une disparition focale du réseau vasculaire, les zones apparaissant noires. Aucune corrélation n’a été mise en évidence entre la topographie de l’atteinte vasculaire sur l’OCT-A et les déficits du champ visuel.

Conclusion. — L’OCT-A est une nouvelle technique d’imagerie, facile et sans danger, permettant la visualisation de modifications du réseau capillaire péripapillaire à la phase aiguë des NOIA. Ces modifications sont probablement liées à une altération du flux sanguin prélaminaire. L’absence de corrélation entre la topographie des altérations vasculaires sur l’OCT-A et celle des déficits du champ visuel laisse supposer que ces dernières sont plutôt secondaires aux perturbations du flux sanguin de l’artère ciliaire postérieure.

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the patients presented any evidence of glaucoma disease, nor optic disc drusen. The non-included eye was normal, except one eye with an optic disc drusen. Besides, none of them declared any amiodarone treatment.

OCT angiography

We used the Cirrus HD-OCT with AngioPlex™ (Carl Zeiss Meditec, Dublin, CA, USA) to image the vascular flow. Each B-Scan in the scan pattern is repeated 4 times consecutively. Comparisons of signal intensity on consecutive B-scans in the same location will reveal some areas with signal intensity change over time, and some areas with constant signal. These differences induce a temporal contrast change in a specific location is thought to be due to erythrocyte motion, and hence indicates a location of a vessel. The central wavelength was 840 nm, and the acquisition speed was 68,000 A-Scan/s. Optical micro-angiography (OMAG) algorithm was used to extract the OCT-A information. A real-time retinal tracking system, FastTrac™, which corrects eye motion, improves the image quality.

The OCT angiography was performed at the acute phase of the NOinan. Scans were acquired on a 3 × 3 mm square basis centered on the optic nerve head. The automatic segmentation provided by the software allowed to obtain the visualization of different vascularization layers, respectively from the inner to the outer retina:

- the radial peripapillary capillary network, at the level of the nerve fiber layer;
- the inner vascular plexus, at the level of the complex ganglion cell layer to the outer nuclear layer;
- the deep vascular plexus, at the level of the outer nuclear layer;
- the choriocapillaris;
- choroidal networks.

The normal vascularization has been already described [2,3]. In summary, a dense microvascular network is arranged around the disc in a radial pattern, the superficial capillaries being tangled with the retinal nerve fibers. The radial peripapillary capillary network appeared bright and well visible, while the inner vascularplexus was less identified underneath, twisted and darker (Fig. 1). Because of the mask effect of the pigment epithelium, the choriocapillaris and choroidal networks are not analyzable.

Besides, in case of ON edema, the automatic segmentation remained hazardous as the retinal nerve fiber layer is hardly differentiated from the complex ganglion cell-outernuclear layer. The analysis was performed on a semi-automatically segmented slab, including the whole inner retina from the internal limiting membrane to the outer retinal nucleary layer (Fig. 2a). Thus, the radial capillary network and the inner vascular plexus were layered on the same image (Fig. 2b). Another consequence of the presence of optic nerve edema was the absence of the disc excavation, allowing the visualization of the disc and the peripapillary vascularization on the same level.

Visual field testing

A visual field examination (Octopus 101®, Haag-Streit, USA) was done. The system was set for the glaucoma 30° test.

\[ \text{Figure 1. OCT-A in the right eye of patient 9 displaying a normal peripapillary network. The superficial capillaries appeared well identified with a radial pattern. The inner plexus is less identified underneath, with twisted and darker vessels.} \]

size III white stimulus, with the Tendency Oriented Perimetry algorithm. The pattern deficit and the standard indices (mean deviation, loss variance) were analyzed.

Fluorescein angiography

A fluorescein angiography centered on the optic nerve head was performed (HRA2, Heidelberg, Germany).

Analysis

A qualitative comparison was made between both eyes of each patient. This comparison was based on the difference in the capillary network layout and the vascular density around the optic nerve head. As little is known about the peripapillary network in elderly patients, we decided to compare the NAION eye with the healthy eye of each patient. Besides, in case of vascular risk factors, the latter would have modified the vascular network of both eyes in the same way. Finally, we tried to find out an anatomic-functional correlation between the vascular disorganization visualized on the OCT-A, and the visual field pattern and severity deficit. No comparison with fluorescein angiograms was attempted, as the analysis of the peripapillary vascularization is hardly feasible at the early stage and impossible at the late stage of FA because of the fluorescein leakage.

Results

Patient demographics

Ten eyes of ten patients were consecutively included, 5 men and 5 women. The patients age ranged from 59 to 88 years, with a mean age of 70.9 (± 9.02) years.
Figure 2. OCT B-scan of a NAION optic nerve head of patient 3 showing the segmentation from the internal limiting membrane to the outer retinal layer (a); OCT-A of the same eye displaying the radial peripapillary capillary network and the inner vascular plexus, on the same layer. Because of the optic disc edema, the excavation has disappeared (b).

Visual field testing

Visual data are detailed in Table 1. Six patients underwent a static 30° visual field. The other four patients had a too low visual acuity to perform the visual field testing.

Fluorescein angiography

In all patients, a delayed optic nerve head filling was present in the NAION eye, followed by a papillary leakage on the late phase.

OCT angiograms qualitative analysis

All patients demonstrated at least a loss of the radial aspect of the peripapillary network associated with a reduction of the vascular density. Furthermore, 8 patients over 10 presented a severe loss of the peripapillary vascularization. This severe damage consisted of black areas in which no vessels were visible (Fig. 3). And among these 8 patients, 7 displayed these black areas in a global pattern around the optic nerve (Table 1).

Anatomo-functional correlation

For one patient (patient 4), there was a strong correlation because of a severe nasal loss on the OCT-A associated with a temporal defect in the visual field (Fig. 4 and Table 1).

For 6 patients (patients 2, 6, 7, 8, 9 and 10), we considered the correlation as weak. A severe global loss of the peripapillary network was observed on OCT-A, with a large visual deficit in the visual field, but the pattern of the

<table>
<thead>
<tr>
<th>Patients</th>
<th>OCT-A peripapillary vascularization</th>
<th>Visual field pattern</th>
<th>Visual field indices (dB)</th>
<th>Correlation</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>MD</td>
<td>LV</td>
</tr>
<tr>
<td>1</td>
<td>Severe global loss</td>
<td>Concentric loss</td>
<td>7.9</td>
<td>29.6</td>
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<tr>
<td>2</td>
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<td>Marked central and nasal loss</td>
<td>25.2</td>
<td>10.9</td>
</tr>
<tr>
<td>3</td>
<td>Mean global loss</td>
<td>Marked inferior defect</td>
<td>9.8</td>
<td>59.4</td>
</tr>
<tr>
<td>4</td>
<td>Severe nasal loss</td>
<td>Infero- and superotemporal arcuate defect + central scotoma</td>
<td>8.6</td>
<td>19.9</td>
</tr>
<tr>
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<td>Marked central and peripheral loss</td>
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<td>39.2</td>
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<td>103.7</td>
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<td>Non-registrable</td>
<td>—</td>
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<td>10</td>
<td>Severe global loss</td>
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</table>

MD: mean deviation; LV: loss variance; dB: decibel.
**Figure 3.** Patient 10 was a 82-year-old female with a NAION on the left eye. Right OCT-A eye showed a regular radial peripapillary network (a); on the left eye, the vascular density is very low, with large black areas, giving a darker image (b).

**Figure 4.** Patient 4 was a 62-year-old man complaining of an acute visual loss in his right eye since 24 hours. On the left OCT-A, the peripapillary network appeared normal (a), but the disc vascularization was apparent because of the presence of an optic disc drusen. Right eye OCT-A (b) demonstrated a restricted nasal peripapillary vascular network, with a large arcuate dark appearance around the optic nerve head (orange arrows). The visual field (c) demonstrated an infero- and superotemporal defect, with a central scotoma.
visual field defect was not correlated with the loss on OCT-A (Fig. 5).

For 3 patients, there was no correlation at all, either because of a severe peripapillary damage associated with a mild visual field deficit (patient 1) or because of a mean global loss on the OCT-A associated with a marked deficit (patients 3, 5) (Fig. 6).

**Discussion**

Because histologic studies are rarely reported, the pathophysiologic processes involved in the NAION are not firmly established. Vascular supply to the anterior optic nerve (prelaminar, laminar and retrolaminar regions) comes from three sources which interconnect each other: the choroid, the pial vessels which perforate the optic nerve surface, and capillaries derived from retinal circulation. Even if the most significant contribution to the vascularization of the optic nerve comes from the choroidal blood flow, the peripapillary capillaries, which derive from the central retinal artery branches, also contribute to the vascularization of the prelaminar portion of the optic nerve [4]. The analysis of the peripapillary vascularization on OCT angiography at the acute phase of an ischemic neuropathy is of prime interest to improve our understanding of the pathogenesis of the disease. Furthermore, as the superficial capillaries are arranged along the nerve fibers, one may observe a potential modification of the regular layout of the capillaries during and after the ischemic death of the retinal nerve fibers [5].

To our knowledge, this is the first case series of OCT-A in NAION eyes with anatomo-functional correlation study. In our case series of NAION, peripapillary vascular network was imaged with the SD-OCT angioplex. The imaging of the vessel density and layout was good, better than has been previously visualized with fluorescein angiography.

In our cases, because of the optic disc edema at the acute phase of NAION, the inner retinal layers around the optic nerve head were poorly differentiated. The inner retina appeared overall thickened from the internal limiting membrane to the outer nuclear layer. It was therefore not possible to use the automatic segmentation for our
analyses. However, the semi-automatic segmentation allowed us to analyze properly the whole inner retina. The images obtained through this method overlaid the radial peripapillary capillary network and the inner vascular plexus.

In the affected eyes, OCT-A showed clear modifications in the radial peripapillary network. In all these eyes, a decrease of the vascular density was at least demonstrated and capillaries were found to be twisted and irregular. In 8 eyes, the alteration was more severe, with a lack of vascularization in some focal areas, appearing as dark zones (patient 9, Fig. 1). For 7 patients, the damages affected the entire peripapillary area. For 1 patient, only the nasal half was involved.

We found a strict correlation between OCT-A and visual field pattern deficit only for 1 patient in which a nasal vascular alteration was associated with a consistent temporal visual field deficit (patient 4). In 3 cases, there was no correlation at all: a moderate vascular alteration on OCT-A can be associated with a marked visual field deficit, or on the opposite a severe global loss can be associated with no central visual loss. In the 6 remaining patients, we considered that the correlation was mild: in patients 2 and 6, the vascular alteration was severe and associated with a visual field defect, but without any consistent pattern. In patients 7 to 10, the visual loss was so severe that they could not perform the visual field testing. In these latter cases, one can assume the presence of a large central scotoma, which has been considered as a mild correlation. These results suggest that the visual field deficits may be due more to posterior ciliary artery blood flow disturbance than to the peripapillary one.

Decreased papillary capillary blood flow in NAION patients has already been described with laser Doppler [6]. As OCT-A identifies vascular structures by detecting erythrocyte movement in blood vessels, non-visible capillaries may correspond to flow velocities below the OCT-A threshold, or to ischemic areas.

A recent study conducted on 4 patients with NAION reported a peripapillary network less visible [7]. Vascular density and perfusion in peripapillary area have already been described in glaucoma patients [1,3,8] and in response to hyperoxia [9]. A decreased of peripapillary blood flow has been shown in glaucoma patients, even before retinal nerve fiber layer thinning. Similar results were described after

Figure 6. Patient 1 was a 59-year-old male with a NAION on the left eye. On the right OCT-A, the radial pattern appeared bright and well visible (a). On the left OCT-A, the superficial capillaries appeared fewer and twisted, delineating numerous black areas (b). The visual field showed a concentric deficit with no central scotoma (c).
hyperoxia without changes in the peripapillary vascular
layout.
Concerning the vascular rearrangement in our series, two
hypotheses can be raised. First, as the retinal nerve fibers
are tangled with the superficial capillaries, the death of the
first could influence the distribution of the seconds. A second
hypothesis could also be proposed: the scarcity of normal
blood vessels might reshape the regular radial pattern.
This study has some limitations. The limited number of
patients weakens the anatomo-clinic conclusions. The
absence of quantified data does not permit to measure the
blood flow and the vascular density reduction. But the
qualitative analysis is very contributive, showing the
involvement of the prelaminar vascularization in the NAION,
and the severity of the capillary damage. Furthermore, it
is not the presence of an optic nerve edema itself that
induces these modifications. Some unpublished data related
to papilledema [10] have shown patchy areas of decreased
capillary density on the optic nerve head but not in the
peripapillary area.

Conclusion
In our series, OCT-A appears as a safe and easy imaging
modality able to demonstrate changes in the superficial
peripapillary vascular network distribution during the acute
phase of NAION. More studies are required to state whether
it could be routinely used for the diagnosis of ischemic
neuropathy or for the differential diagnosis of optic nerve
edema and, in turn, replace fluorescein angiography in these
indications.

Funding
No funding was received for this research.

Ethical approval
All procedures performed were in accordance with the ethi-
cal standards of the National Research Committee and with
the 1964 Helsinki declaration and its later amendments.

Informed consent
Informed consent was obtained from all individual
participants included in the study.

Disclosure of interest
Rougier: Allergan, Bausch&Lomb, Bayer, Novartis, Thea,
Zeiss, Horus Pharma.
Delyfer: Allergan, Bausch&Lomb, Bayer, Novartis, Thea,
Zeiss.
Korobelnik: Allergan, Bausch&Lomb, Bayer, Novartis,
Thea, Zeiss.

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