Noninvasive Imaging of a Vasoproliferative Retinal Tumor Treated with Cryopexy

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Abstract
Optical coherence tomographic angiography (OCTA) has emerged as a rapid, noninvasive imaging modality to visualize the vascular networks in the retina and choroid. Here, we report the clinical findings in a case of primary vasoproliferative retinal tumor (VPRT) observed by the wide-field swept-source OCTA. A 74-year-old male patient with central vision loss and metamorphopsia in his left eye was referred to our hospital. At the first visit, the best-corrected visual acuity was 20/20 OD and 20/40 OS. Fundus examination revealed the presence of the epiretinal membrane and inferotemporal reddish retinal tumor in the left eye. Fluorescein angiography and indocyanine green angiography (ICGA) showed leaky characteristics and sharply defined structure of vessels in the retinal tumor, respectively. The patient was diagnosed with the VPRT with secondary epiretinal membrane and underwent pars plana vitrectomy with internal limiting membrane peeling, retinal photocoagulation, and triple freeze and thaw procedure using cryopexy. Whereas wide-field swept-source OCTA preoperatively depicted the flow signals as distinctive vascular structures similar to ICGA, the tumor color turned out to be ischemic white, and the flow signals detected by wide-field OCTA disappeared after the surgery, indicating that the freezing effect of transscleral cryopexy sufficiently reached the surface of the tumor. In sum, wide-field swept-source OCTA is a useful imaging modality that can be noninvasively and repetitively performed to determine the treatment effect in cases of peripheral retinal tumors such as VPRT.
Introduction

Vasoproliferative retinal tumor (VPRT) is a yellow-reddish tumor commonly located in the inferotemporal quadrant of the retina and is frequently associated with subretinal fluid, retinal exudation, and epiretinal membrane [1]. VPRT has been classified into two types, i.e., primary and secondary VPRTs, and secondary VPRT is accompanied by other ocular diseases, such as retinitis pigmentosa, uveitis, chronic retinal detachment, and others [1]. Histological examination demonstrated that VPRT consists largely of glial cells; however, the tumor is also interlaced with a fine capillary network and small-hyalinized vessels [2]. Fluorescein angiography (FA) displayed hyperfluorescence in the arteriovenous passages and dye leakage from tumor vessels in the late phase [1, 3], and in contrast with typical findings in retinal hemangioblastoma, the retinal feeder vessels were not or only mildly dilated in cases of VPRT [3, 4]. It was also described that indocyanine green angiography (ICGA) was useful to show the abnormal vessels on VPRT [5]. The previous findings emphasized that both FA and ICGA are crucial for the clinical follow-up of VPRT. However, because of the invasiveness and risk of the angiograms, it is difficult to frequently perform angiograms for patients with VPRT, most of which exhibit a good clinical course without surgical intervention.

Recently, optical coherence tomographic angiography (OCTA) has emerged as a rapid, noninvasive imaging modality to visualize the vascular networks in the retina and choroid. A new generation of OCTA devices enables us to capture wide-field images of the peripheral fundus in a single scan. Here, we report the clinical findings in a case of primary VPRT observed by the wide-field swept-source OCTA.

Case Presentation

A 74-year-old male patient with central vision loss and metamorphopsia in his left eye for the previous 3 months was referred to our hospital for further evaluation. He had neither familial history nor medical history other than dyslipidemia. At the first visit, the best-corrected visual acuity was 20/20 and 20/40 in the right and left eyes, respectively. Anterior-segment slit-lamp examination was unremarkable except for mild cataract OU, and intraocular pressure was within the normal range. Fundus examination and OCT C-scan revealed the presence of an epiretinal membrane, retinal fold, and inferotemporal reddish retinal tumor without obvious feeder or draining vessels in the left eye (Fig. 1). FA displayed hyperfluorescence in the early phase and leakage in the late phase (Fig. 2). ICGA showed sharply defined vessels in
the retinal tumor in the early phase, and tissue staining in the late phase, presumably corresponding to blood vessels inside the tumor (Fig. 2). For OCTA imaging, wide-field swept-source OCTA (Xephilio OCT-S1, Canon Lifecare Solutions Inc., Japan) was used. Xephilio has a feature to narrow the angle of shooting frame and enables the frame to move to the peripheral retina. Using the functions, a high-resolution OCTA image of the superficial layer of the tumor (11 mm × 11 mm) was obtained, and the images depicted the distinctive vascular structures, similar to ICGA, on the tumor surface (Fig. 3a, b). In the fellow eye, the anterior segment and retinal examination including peripheral retinal examination were all normal. Based on the location, tumor color, and angiographic findings, the patient was diagnosed with the VPRT with a secondary epiretinal membrane. The patient underwent pars plana vitrectomy with internal limiting membrane peeling, retinal photocoagulation, and triple freeze and thaw procedure using cryopexy (Fig. 3c). Postoperatively, flow signals of the tumor vessel disappeared in the

Fig. 2. Fluorescein angiography (FA) and indocyanine green angiography (ICGA) in the present case of VPRT. FA displayed the inferotemporal retinal tumor showing hyperfluorescence in the early phase and leakage in the late phase. No obvious dilated feeder vessel was noted. ICGA showed sharply defined vessels in the retinal tumor in the early phase, and tissue staining in the late phase.
wide-field OCTA image (Fig. 3d, e), and the tumor color turned out to be ischemic white (Fig. 3f). The retinal structure was distinctly improved by the removal of the epiretinal membrane, and the best-corrected visual acuity was 20/20 vision after 6 months. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

**Discussion**

Here, we report a case of VPRT in which we noninvasively observed the disappearance of flow signals in the tumor after a cryopexy treatment using wide-field swept-source OCTA. Evaluation of the vascular structure is crucial for the assessment of the disease status in patients with VPRT, and in general, we evaluate the vascular structure in retinal tumors including VPRT by fundus angiography, i.e., FA and ICGA, both of which are relatively invasive. To the best of our knowledge, this is the first report of noninvasive clinical observation of VPRT using an OCTA device.

So far, FA and ICGA have been widely used to follow up the clinical course of VPRT. Since leakage of fluorescein sodium increases at a rate proportional to the number of immature...
vessels of tumor vasculature, FA is useful in evaluating and monitoring the superficial vascular structure of VPRT. However, due to the fluorescence leakage and tissue staining [4], it is difficult to depict the fine vascular structure in the tumor by FA. By contrast, indocyanine green dye solution mostly binds to plasma proteins including albumin in the blood and normally remains within the blood vessel [6]. Therefore, ICGA has the advantage to observe the fine vascular structure in VPRT, compared with FA. Using ICGA, it was previously reported that the blood vessels showed hypofluorescence when the activity of VPRT declined [5]. These reports demonstrated that FA and ICGA are valuable and even indispensable examination methods for the clinical follow-up of VPRT. However, FA and ICGA require venipuncture and long examination times. In addition, anaphylactoid manifestations to intravenous injection of the dyes, particularly fluorescein sodium, are occasionally experienced in clinical settings [7]. For the inconvenience and risk, repetitive FA and ICGA for patients with VPRT is challenging in actual clinical practice. In this respect, OCTA is extremely useful for the observation of VPRT. However, conventional OCTA has been unsuitable for the purpose because of the angle of view and the examination time for image averaging.

Recently, a new generation of OCTA devices, Xephilio OCT-S1, has emerged in the clinical arena of fundus imaging. The state-of-the-art OCTA, which captures wide-field images of up to 23 × 20 mm, enables us to observe peripheral retinal tumors such as VPRT. In fact, the preoperative OCTA images in the present case revealed the vascular structure in VPRT similar to the ICGA images. Rather, the vascular structure was more unequivocally visualized by OCTA in comparison with ICGA. This could be explained by the absence of any leakage or tissue staining in the OCTA images. Whereas previous histological studies demonstrated that VPRT contains vascular structure inside the tumor [8, 9], considering the optical depth penetration of OCTA, it is presumable that the vascular structure depicted by OCTA, in this case, was the superficial tumor vessels of VPRT. Notably, the color of VPRT turned out to be ischemic white after a cryopexy treatment, and postoperative OCTA images showed the disappearance of blood flow signals at the tumor in the present case. These changes indicate that the freezing effect of transscleral cryopexy sufficiently reached the surface of the tumor, while OCTA may not evaluate vascular structures inside the tumor unlike fundus angiography, i.e., FA and ICGA. Further studies are warranted to validate the usefulness of wide-field swept-source OCTA as a noninvasive examination for clinical observation of vascular tumors in the peripheral fundus.

In summary, wide-field swept-source OCTA is a noninvasive examination that can be repetitively performed in cases of peripheral retinal tumors such as VPRT. With advances in OCT technology, OCTA has the potential to become not only the first choice of examination for retinal tumors but also a device for determining the treatment effect for peripheral retinal tumors.

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**Statement of Ethics**

The patient was treated in accordance with the tenets of the Declaration of Helsinki. Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Ethical approval is not required for this study in accordance with local or national guidelines.
Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Tetsuya Tanimukai took primary care of the patient and mainly contributed to the writing of the manuscript. Kousuke Noda supervised and revised the work. Kiriko Hirooka examined the patient and collected the data/images. Satoru Kase and Susumu Ishida provided critical manuscript revisions.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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