Multimodal Imaging Findings in Retinopathy Associated with Facioscapulohumeral Muscular Dystrophy before and after Treatment with Intravitreal Aflibercept and Laser Photocoagulation

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**Keywords**
Facioscapulohumeral muscular dystrophy · Aflibercept · Laser photocoagulation · Optical coherence tomography · Optical coherence tomography angiography

**Abstract**
A 52-year-old man with a history of facioscapulohumeral dystrophy (FSHD) and hypertension presented with decreased vision in his left eye (OS) of several weeks' duration. The best-corrected visual acuity was 1.0 in both eyes (OU), with fundus soft exudates in the right eye (OD) and exudative maculopathy OS. Optical coherence tomography (OCT) showed macular edema and hard exudates OS, and OCT angiography (OCTA) showed nonperfusion areas and arterial tortuosity OU and a capillary aneurysm OS. After photocoagulation of the nonperfusion areas OU and intravitreal injection of aflibercept OS, the macular edema OS decreased and subjective symptoms improved. However, the nonperfusion area OS was enlarged on OCTA. We report the OCTA findings before and after antivascular endothelial growth factor treatment in a patient with FSHD.
Introduction

Facioscapulohumeral muscular dystrophy (FSHD) is a muscular dystrophy caused by expression of the DUX4 gene at the end of the long arm of chromosome 4, which is not normally expressed in adults [1]. FSHD is an autosomal dominant disorder characterized by muscle weakness and atrophy throughout the body, particularly in the face, shoulder girdle, and upper arms [2]. The common ocular complications of FSHD are retinal vascular abnormalities and rarely Coats disease-like exudative changes [3–5]; however, the details of the pathogenesis remain unclear [3–6]. In addition, no reports have been published, showing the optical coherence tomography angiography (OCTA) findings before and after antivascular endothelial growth factor (VEGF) therapy in patients with FSHD. We report the multimodal imaging findings of a patient with FSHD-related retinopathy who was treated successfully with intravitreal injections of aflibercept (IVA) (Eylea, Regeneron Pharmaceuticals, Tarrytown, NY, USA) and photocoagulation.

Case Report

A 52-year-old man presented with decreased vision in his left eye (OS) of several weeks’ duration. Since childhood, he has had alar scapula due to weakness of the proximal muscles of the upper limbs and shoulder girdle, has been unable to walk since he was 29 years old, and required artificial respiration with noninvasive positive pressure ventilation since he was 37 years old. He was able to eat on his own, but required an electric wheelchair for mobility. He had no hearing loss or mental retardation. His father has been diagnosed with FSHD. He has been diagnosed with FSHD based on the triad of clinical findings of FSHD including the autosomal dominant inheritance, typical distribution of muscle atrophy, and relatively slow progression.

The patient’s best-corrected visual acuity was 1.0 in both eyes (OU), the intraocular pressure was 16 mm Hg OU, and the anterior segments were normally OU. Fundus examination showed tortuous retinal arteries, slight cotton wool spots, and neovascularization outside the vascular arcade in his right eye (OD) (Fig. 1a) and silver-wiring arteries, capillary aneurysms, circumferential hard exudates, and neovascularization outside the vascular arcade OS (Fig. 1b). Swept-source optical coherence tomography (OCT) (DRI OCT Triton, Topcon, Japan) showed no abnormal findings OD, and cystoid macular edema and hyperreflective foci OS (Fig. 2a, b). Swept-source OCTA (DRI OCT Triton) showed arterial tortuosity OU with no significant venous abnormalities (Fig. 3a, b). A focal area of nonperfusion was seen below the macula OD (Fig. 3a). A capillary aneurysm and nonperfusion area was seen in the temporal fovea OS (Fig. 3b). Fluorescein fundus angiography was not performed due to difficulty in maintaining posture. His blood pressure remained at 150/100 mm Hg throughout the disease course; therefore, in addition to FSHD-related retinopathy, hypertensive retinopathy, retinal vein occlusion, and diabetic retinopathy were considered in the differential diagnosis. The patient took telmisartan 20 mg/day for hypertension and the blood pressure decreased to 130/90 mm Hg. There was no evidence of venous occlusion or history of diabetes mellitus. We diagnosed FSHD-related retinopathy.

Since it was presumable that the retinal changes were associated with VEGF similar to macular edema caused by retinal ischemia in diabetic retinopathy and Coats disease, IVA injection was administered twice, 1 month apart each other, and retinal photocoagulation was performed on ischemic areas outside the vascular arcade to prevent proliferative changes OS. Focal laser to aneurysmal lesions was not possible due to difficulty in accurate aiming to the aneurysms because of postural maintenance problems. Two months later, the subjective symptoms improved, and both the retinal hemorrhage and rigid exudates OS decreased (Fig. 4a). The macular edema also decreased on fundus photography and OCT (Fig. 4b). In contrast,
Fig. 1. Fundus photographs before (a, b) and after treatment (c). a Tortuous arteries and cotton wool spots (arrowheads), and neovascularization outside the arcade (arrowheads) are seen OD. b Tortuous arteries, silver-wiring arteries (arrowheads), retinal hemorrhage, circumferential hard exudates, capillary aneurysms, and neovascularization (arrowheads) are seen OS. Venous abnormalities are not obvious OU (a, b).

Fig. 2. Swept-source OCT of horizontal macular sections on the initial examination. a No abnormal findings are seen OD. b Cystic macular edema and hyperreflective foci are seen OS.
OCTA showed that arterioles were more centrally disrupted, and the nonperfusion area enlarged OS (Fig. 4c). No additional IVA injection was required; macular edema remained dry up to 6 months after the last injection.

**Discussion and Conclusion**

In 1987, it was reported that 49%–75% of patients with FSHD had retinal vascular abnormalities [3]. More recently, another group reported the OCTA findings in 33 patients with FSHD and documented that most patients had subclinical retinal vascular abnormalities.
and about 20% of patients had posterior pole vascular abnormalities [5]. However, no cases of macular abnormalities in that study lost vision. It was also reported that less than 1% of patients with FSHD developed exudative changes resembling Coats disease [4]. The current case of FSHD is a rare presentation of a fovea with Coats disease-like exudation.

Goselink et al. [5] reported that, in contrast to diabetic retinopathy and Coats disease, the large arterioles are altered, but the veins and capillaries are less impaired in patients with FSHD. Those authors speculated that this may be attributed to the presence/absence of vascular smooth muscle [5]. The OCTA finding in the current case showed not only large arteriolar abnormalities but also obvious capillary abnormalities (capillary loss and capillary aneurysm). Two possible reasons may explain this, that is, one is that the arterial abnormalities may be secondary to hypertension in addition to the arterial abnormalities caused by abnormalities of the vascular smooth muscle described previously, and the second is that a genetic abnormality directly causes capillary damage. In mice with forced expression of the DUX4 gene, vascular endothelial cells were damaged, resulting in capillary loss in muscle tissue [7]. The same mechanism may cause capillary abnormalities in the retinal vessels [7]. Although the degree of shortening of the D4Z4 repeats, which has been reported to correlate with the severity of retinopathy [5], was not investigated in this case, the presence of a severe genetic mutation was expected, in that the muscle atrophy extended to the lower limbs.

The current OCTA findings of capillary loss OU and capillary damage were similar to diabetic retinopathy and Coats disease. Therefore, IVA and photocoagulation were successful in our case, as has been reported similarly with bevacizumab (Avastin, Genentech Inc., South San Francisco, CA, USA) or ranibizumab (Genentech Inc.) and photocoagulation [8, 9]. However, in our case, the nonperfusion area was enlarged on OCTA after treatment, which may have resulted from VEGF inhibition that induced constriction of the small arteries. Increasing area of nonperfusion even with anti-VEGF therapy was reported in cases of proliferative diabetic retinopathy [10] and retinal vascular occlusion [11, 12]. Therefore, our case suggested that there is a similar reaction in retinopathy of FSHD.

As in a variety of retinopathies, multimodal imaging including OCTA is particularly useful for FSHD-related maculopathy since it allows detailed evaluation of blood vessels in a non-invasive manner. Furthermore, anti-VEGF therapy may be effective for treating cases with exudative changes.

**Statement of Ethics**

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

**Conflict of Interest Statement**

The authors have no conflict of interests for this study.

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Author Contributions

Hiroshi Shimizu, Masaki Shimizu, and Toshiya Nakano treated the subject. Hiroshi Shimizu, Kousuke Noda, and Masaki Tanito wrote the manuscript. Masaki Shimizu and Toshiya Nakano revised the manuscript. Hiroshi Shimizu, Masaki Shimizu, Toshiya Nakano, Kousuke Noda, and Masaki Tanito read and approved the final version of the manuscript.

Data Availability Statement

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

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