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Case Report

Management of Coats-Like Disease in a Forty-Four-Year-Old Patient with FSHD Type I

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Keywords

Coats disease · Facioscapulohumeral dystrophy · Facioscapulohumeral dystrophy type I · Management · Case report

Abstract

A forty-four-year-old female patient known for FSHD type I, with unremarkable past ocular history, complained of progressive visual acuity deterioration during a routine ophthalmological visit. Best-corrected visual acuity (BCVA) was 1.0 decimal Snellen equivalent bilaterally. Dilated fundus examination showed evidence of retinal Coats-like disease in the left eye, while the right eye showed significant retinal vascular tortuosity. Multimodal examinations (OCT scans and FA-fluorescein angiography) revealed large areas of retinal ischemia, thus confirming a retinal vascular disorder compatible with the diagnosis of Coats-like disease. Left eye laser photocoagulation of the ischemic areas was performed to avoid neovascular complications that had not been detected during follow-up visits (12 months), and BCVA in the left eye remained stable at 1.0 decimals Snellen equivalent. Coats-like disease in a patient affected by FSHD type I should always be screened even in the absence of any prior ocular diseases. Guidelines concerning the ophthalmological management of adults affected by FSHD are lacking. Based on this case, we recommend performing a yearly complete ophthalmological checkup with dilated fundus examination and retinal imaging. Patients should, furthermore, be encouraged to seek medical attention when noticing deterioration of visual acuity or other visual symptoms in order to avoid missing potential sight-threatening ocular complications.

This study was conducted at the Ophthalmology Department of the Ospedale Regionale di Lugano, Ente Ospedaliero Cantonale (EOC), Lugano, Switzerland.

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Introduction

Facioscapulohumeral dystrophy (FSHD) is the third most common muscular dystrophy after Duchenne's and myotonic dystrophy. It is inherited in an autosomal dominant fashion, with an age-dependent penetrance [1]. Molecular genetics of FSHD type I feature a loss of a critical number of microsatellite repeats (D4Z4) in the subtelomeric region of chromosome 4q35 [2, 3]. In healthy individuals, both copies of 4q35 contain between 11 and 100 D4Z4 repeats [4]. Interestingly, reports found that DNA methylation levels in this region are comparable to those observed in transcriptionally silent heterochromatin regions [1, 5]. FSHD1 patients, on the contrary, exhibit a heterozygous contraction in the number of repeats (1–10) in the 4q35 region, which in turn leads to a reduction in DNA methylation. The loss of the heavy methylation status of this array ushers to a chromatin restructuration into a more relaxed and transcriptionally permissive conformation [2]. This new chromatin structure favors, in permissive haplotypes, the transcription of the *DUX4* gene, which is present in the last D4Z4 repeat and codes for a germline transcription factor usually repressed in somatic cells [4]. Ectopic expression of *DUX4* in skeletal muscle cells is finally thought to be the cause of cellular damage and hence of clinical manifestations [4]. Several molecular mechanisms have been ascribed to the toxic effect of *DUX4*, but none so far has shed light on the *DUX4* ectopic expression-related vascular complications. *DUX4* could also be present in muscle tissue of genetically diagnosed asymptomatic FSHD subjects and at low levels in genetically unaffected subjects, leading to the concept that epigenetic modifiers could play a role in how *DUX4* expression influences the disease [4].

The clinical findings are mainly centered on the weakness of the muscles of the facial and scapulohumeral regions. However, extra-muscular manifestations include high-frequency hearing loss and, ophthalmologically, retinal vascular aberrations that rarely result in exudative retinopathy, also known as Coats-like disease [6].

Coats disease is an idiopathic retinal telangiectasia, commonly unilateral (95%), more prevalent in males (75%) than females, and the onset of the manifestations usually present in the first decade of life [7]. Vascular ocular fundus signs include telangiectasias and fusiform aneurysmal arteriolar dilatations, most often in the temporal retina, associated with intra- and subretinal exudates. Visual acuity is affected only in the case of foveal involvement, such as in the case of cystoid macular edema formation. Potential complications are exudative retinal detachment, neovascular glaucoma, uveitis, cataract, and phthisis bulbi [7].

Case Presentation

A forty-four-year-old female patient affected by FSHD type I, genotype unknown, also affected by endometriosis treated with progesterone, arterial hypertension under pharmacological control, and obstructive sleep apnea under continuous positive airway pressure device control, complained of augmented bilateral lacrimation and burning sensation for several months. She also noticed a bilateral deterioration of visual acuity, more pronounced in the left eye. Her past ocular history was unremarkable, and her last ophthalmologic checkup had been 12 months prior to this visit. CARE Checklist guidelines, attached as supplementary material (for all online suppl. material, see https://doi.org/10.1159/000531007), were followed for the presentation of this case report.

Ophthalmic Findings

Bilateral best-corrected visual acuity was 1.0 decimal Snellen equivalent, with a spherical equivalent of +0.625 and +0.5 diopters in the right and left eye, respectively. Slit-lamp examination showed significant bilateral lagophthalmos of 4 mm with signs of early band

keratopathy, probably related to keratoconjunctivitis sicca due to increased tear evaporation or exposition keratopathy due to lagophthalmos. The anterior chamber was without flare or cells. The pupil reaction was physiologic to both light and accommodation.

Dilated ophthalmoscopy of the right eye revealed pronounced retinal vessel tortuosity without other pathological findings (Fig. 1a). Dilated ophthalmoscopy of the left eye showed telangiectasias in the parafoveal temporal macula associated with macular edema, focal dot-blot hemorrhages, and hard exudates. Various ghost vessels and retinal hemorrhages were observed in the retinal periphery (Fig. 1b). Optical coherence tomography (OCT) examination of the right eye was within normal parameters. In contrast, in the left eye, it proved the presence of intraretinal fluid juxtafoveally associated with numerous intraretinal hyper-reflective spots (Fig. 1c–d). Fluorescein angiography (FA) of the left eye confirmed the clinical appearance of a peripheral occlusive vascular retinal disease, with large areas of retinal ischemia (Fig. 2). Altogether, the findings were compatible with the diagnosis of Coats-like disease in the left eye. A second FA performed 6 months after the initial presentation revealed novel retinal ischemic areas that required further laser therapy.

Management

We performed panretinal laser photocoagulation of the ischemic retinal areas in the left eye in order to prevent retinal neovascular complications (Fig. 3). At the 12-month follow-up visit, best-corrected visual acuity in the left eye remained stable at 1.0 decimal Snellen equivalent, no neovascular complications were detected, dilated fundoscopy and OCT imaging did not reveal any signs of macular edema, nor novel retinal ischemic changes. Right eye ocular examination remained within normal parameters. Yearly follow-up visits were recommended to monitor for potential new disease manifestations.

Discussion

Coats-like disease is a rare but well-documented ocular complication of FSHD type I and manifests predominantly in male patients with a mean age of onset between the two first decades of life [8, 9]. Coats disease, as an isolated disease, also affects predominantly male than female patients [10]. FSHD, on the contrary, in most cases, is inherited in an autosomal dominant pattern with about 10% of de novo mutations with a high frequency of somatic mosaicism and does not exhibit sex differences [11].

Retinal abnormalities are frequently subclinical in patients with FSHD and mainly consist of increased arterial tortuosity, telangiectasias, hemorrhages, exudates, or posterior pole anomalies [12]. In rare cases, however, ischemic peripheral retinal areas may develop; these zones are best evidenced upon FA examinations and require prompt laser photocoagulation treatment to prevent neovascular complications.

Typical Coats-like retinal vasculopathy in FSHD type I may be addressed successfully with the well-established retinal laser therapy to prevent neovascular sequelae. Macular and retinal exudation seems to be inferior to “real” Coats disease.

The role of ophthalmologists in the follow-up of FSHD patients is pivotal for screening potential retinal manifestations of the disease. Interestingly, we found reports where routine ophthalmologic examination led to the diagnosis of subclinical FSHD based on initial retinal findings [13].

Recently, a panel of experts concertedly proposed opinion-based management guidelines for FSHD patients, including an ophthalmologic screening. Tawil and colleagues recommended ophthalmological follow-up for adult-onset FSHD only if a vascular disease is present or

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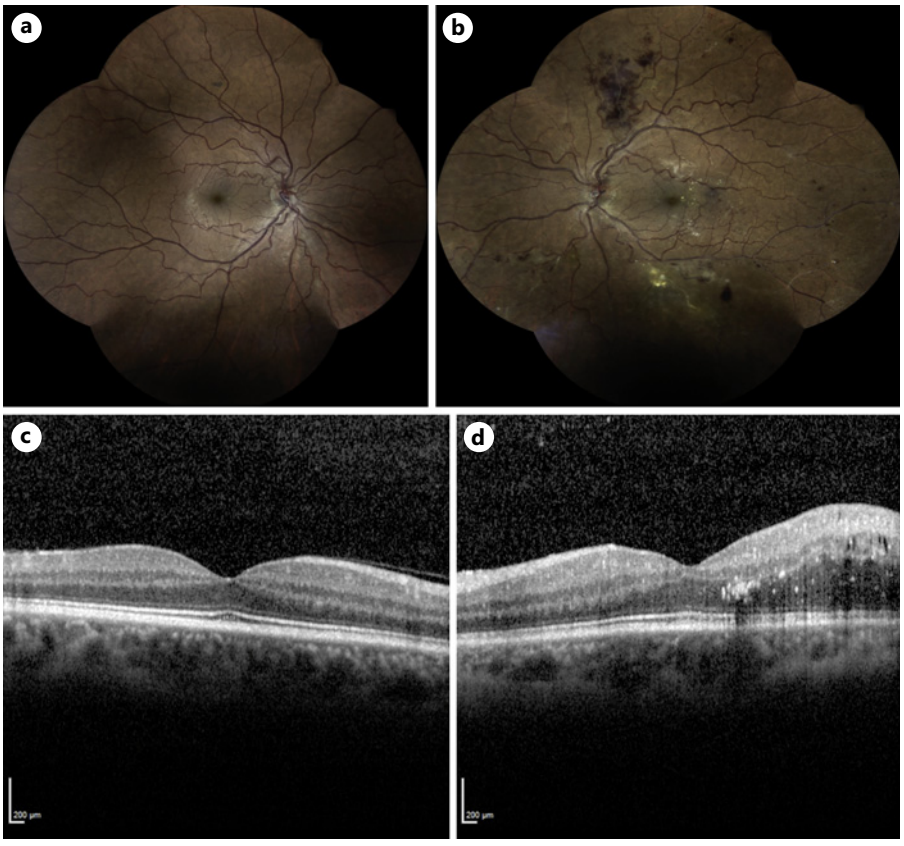

Fig. 1. Multimodal imaging of the 44-year-old female patient affected by FSHD type I. **a** Panoramic color fundus photography (Eidon®, 160° with auto montage) of the right eye showing increased retinal vessel tortuosity at the posterior pole and in the periphery. **b** Panoramic color fundus photography (Eidon®, 160° with auto montage) of the left eye with macular edema in the temporal aspect of the macula as evidenced by the presence of telangiectatic vessels, hard exudates, and dot-blot hemorrhages. The retinal periphery shows increased retinal vessel tortuosity, various ghost vessels in all quadrants, dot-blot and flame-shaped hemorrhages. The vascular exudative and ischemic changes are more pronounced superior and inferior. **c**, **d** Heidelberg Spectralis® OCT images of the right eye, and left eye, respectively. Normal neuroretinal morphology with absence of macular edema can be appreciated in the right eye, while the left shows consistently with the fundus photography intraretinal cystoid edema in the temporal aspect of the fovea.

patients complain of visual symptoms [14]. On the contrary, for early-onset FSHD patients, the expert panel recommended yearly ophthalmologic examinations until the patient can report potential visual alterations.

Accordingly, applying these recommendations, an adult FSHD patient with no visual symptoms and a first negative ocular screening should not seek further ophthalmological attention if asymptomatic. Nonetheless, as we have presented in this case report, vascular abnormalities, particularly peripheral ischemic areas, can manifest at any moment during a patient's lifetime and can lead to sight-threatening complications, such as retinal neovascularization or neovascular glaucoma.

We believe instructing FSHD patients to seek medical attention only if they report visual symptoms is insufficient. Peripheral ischemic retinal areas do not necessarily manifest as symptomatic in terms of decreased visual acuity, and thus patients may report ocular symptoms when the retinal disease is already at an advanced stage.

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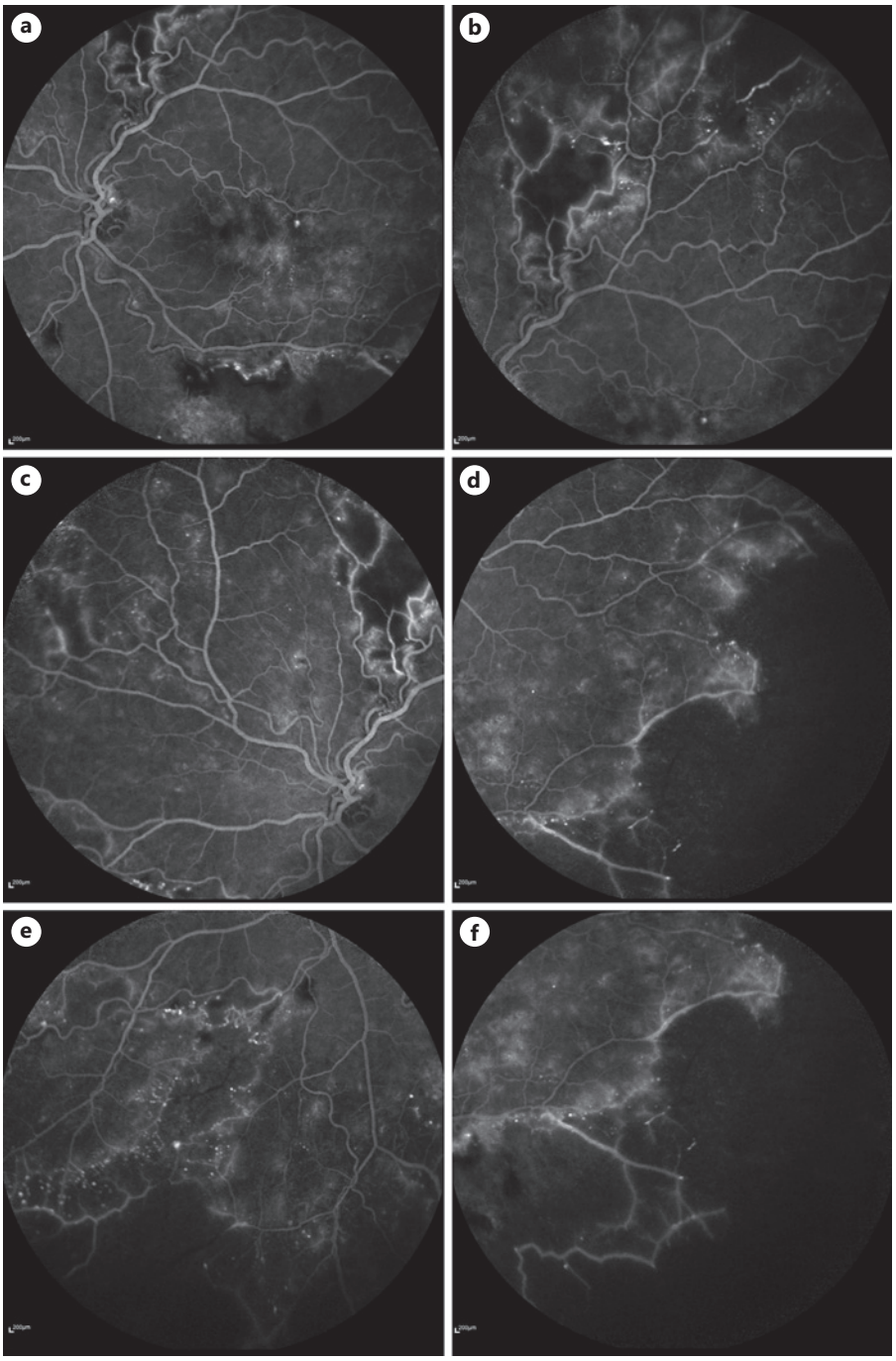

Fig. 2. Fluorescein angiography of the left eye showing posterior pole (**a**), superior (**b**), nasal (**c**), temporal (**d**), inferior (**e**), and inferotemporal (**f**) retinal quadrants. All images were taken between 70 and 120" post dye injection with the 55° lens using the Heidelberg Spectralis® device. **a** Presence of a hyperfluorescent microaneurysm along with diffuse dye leakage within the area of macular edema. Perivascular leakage, microaneurysms, and extensive non perfused retinal areas can be appreciated in all quadrants (**b**–**f**).

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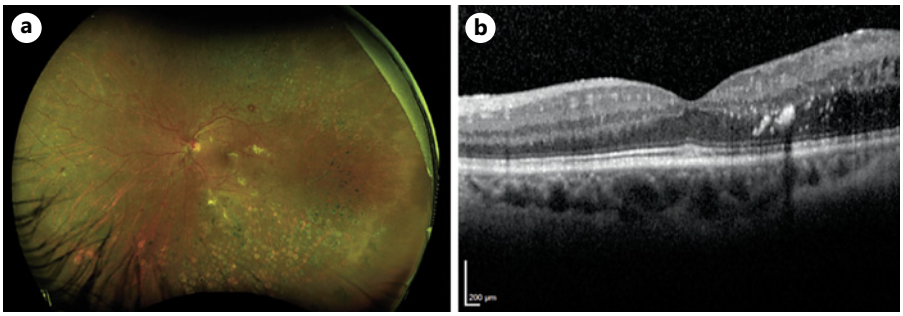

Fig. 3. a Optos® wide field fundus image of the left eye after panretinal photocoagulation. **b** Heidelberg Spectralis® OCT image of the left eye after panretinal photocoagulation.

Our patient's previous ocular history had been unremarkable, and she did not experience any visual impairment for 44 years. Nevertheless, a visit to our ophthalmology department for subjective decreased visual acuity in the left eye led to the diagnosis of Coats-like disease with extensive peripheral retinal ischemia.

Conclusion

FSHD patients usually undergo regular and meticulous medical follow-ups by internal medicine or rheumatology specialists. Based on current international guidelines, ophthalmologists should perform an initial evaluation, and if the patient is asymptomatic, no further ocular screening is recommended in adulthood. We believe that this management is insufficient, and based on our experience, we recommend performing regular yearly clinical ophthalmological visits for adult FSHD patients. Although rare, ocular manifestations of FSHD can lead to potential sight-threatening complications if not detected early. Timely diagnosis and, if needed, prompt ocular therapeutic interventions are warranted for any case of Coats-like disease in FSHD.

Summary Statement

FSHD type 1 patients can develop Coats-like retinal disease without experiencing early ocular warning symptoms. There are no established guidelines for ophthalmological check-ups for such patients, who are at risk of developing retinal complications throughout their life. We suggest annual dilated fundoscopy to allow early detection of retinal ischemic complications that warrant laser photocoagulation to prevent long-term ocular neovascular complications.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. This study protocol was reviewed and the need for approval was waived by the Ethics Committee of Canton Ticino, Switzerland.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Francesca Bruzzone and Tim Beltraminelli conceived and wrote the manuscript with inputs from Alex Casanova and Moreno Menghini; Francesca Bruzzone, Tim Beltraminelli, Alex Casanova, and Moreno Menghini performed patient clinical evaluation, provided intellectual input, and reviewed the data.

Data Availability Statement

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

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