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CASE REPORT

Reduced retinal blood flow-velocity in severe hyperlipidemia measured by the retinal function imager

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Introduction

Severe hyperlipidemia is associated with rare ocular manifestations, including iris and retinal xanthomas, lipid keratopathy, and lipemia retinalis. The later condition of lipemic discolorization of the retinal vessels and fundus has rarely been described in cases of severe hypertriglyceridemia [1]. We report here a case of a patient with lipemia retinalis where retinal blood flow velocity was measured in the acute phase and after a reduction in triglyceride level was achieved.

Materials and method

A 43-year-old Caucasian male was admitted to the hospital due to new-onset diabetes mellitus, with blood glucose levels of 507 mg/dl. The patient's father died from chronic heart failure at the age of 81 years, and both his mother and sister suffer from dyslipidemia of unknown nature with no evidence of thrombo-embolic complications. Past history included hypertension and obstructive sleep apnea syndrome. Blood pressure was 135/81 mmHg and mean arterial pressure [MAP = diastolic + 1/3 (systolic–diastolic)] was 99 mmHg; heart rate (HR) was 96 bpm. The patient was referred to the ophthalmology clinic for retinal evaluation to rule out diabetic retinopathy. The patient had no visual complaints. Visual acuity was 6/7.5 in the right eye and 6/6 in the left eye. Anterior segments were normal, the lens was clear, and intraocular pressure was 21 mmHg in both eyes. Retinal examination of both eyes revealed a salmon-colored fundus with milky-colored retinal arteries and veins. No color difference was apparent between the arteries and veins. RPE changes of the macula were consistent with lipemia retinalis (Fig. 1a). No signs of diabetic retinopathy were observed. Eruptive xanthomatous lesions were found on his skin. Laboratory testing revealed a serum triglyceride level of 22,680 mg/dl. Due to the extreme high content of triglycerides in the early phase, measurement of cholesterol level was not possible technically.

The patient was treated with a low-fat and carbohydrates diet. Lipids control was obtained by bezafibrate and glycemic control by insulin, metformin and repaglinide.

Four weeks after treatment initiation, serum triglycerides level decreased to 717 mg/dl. Retinal vessel color returned to normal, and yellow deposits appeared in both foveas (Fig. 1b). Blood pressure was 130/80 mmHg (MAP = 96.7 mmHg), HR was 73 bpm and intraocular pressure was 18 mmHg in both eyes. Cholesterol levels were mildly elevated: total cholesterol — 209 mg/dl; LDL — 181 mg/dl; HDL — 46 mg/dl.

Retinal blood flow velocity measurements in the early phase and 4 weeks after were performed with the Retinal Function Imager (RFI, Optical Imaging, Ltd). This instrument measures retinal blood flow velocity non-invasively by tracing the movement of red blood cells [2]. The velocity (mm/sec) in secondary and tertiary branches of arteries and veins in the macula was measured. A comparison of the velocity in common segments at both time points was performed, after confirming normal distribution of the data, using paired Student's *t*-test analysis. Regional velocity differences in the macula were

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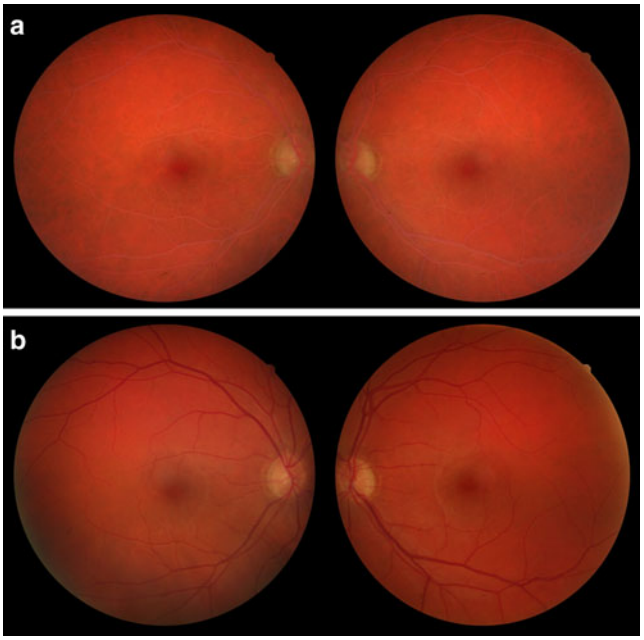

Fig. 1 **a** A color fundus image of the retina on day of presentation, note the milky appearance of retinal vessels and salmon-colored background. **b** Follow-up fundus image 4 weeks later, showing normal-appearing retina

studied using Mann–Whitney U test. The heart rate (HR) measurements were recorded directly from the RFI instrument. Significance was set to $p<0.05$.

Results

The velocity in 29 vascular segments was measured at both time points (11 arterial, 18 venous segments). The average velocity (± standard deviation) in the arterial segments on admission was 3.28±0.71 mm/sec and 1.85±0.40 mm/sec in the venous segments (Fig. 2a). This was slower than the average values that were published for the healthy population in both arteries (4.19±0.99 mm/sec) and veins (3.03±0.59) [2]. After 4 weeks, when lipids levels decreased, the velocity increased to 3.68±0.94 mm/sec ($p=0.02$) in the arterial segments and 2.29±0.44 mm/sec ($p=0.0006$, Fig. 2b) in the venous segments. There were no differences in the velocity in the superior and inferior hemi-macula at both time points. However, the arterial velocity in the nasal hemi-macula was higher than in the temporal region in the post-treatment measurement ($p=0.02$).

Discussion

Lipemia retinalis is a rare ocular manifestation of severely increased serum triglycerides. As found in most cases [1], our patient did not have any symptoms, and visual acuity was preserved, although in some cases a reversible deficit of electroretinogram response has been described [3]. Severe hypertriglyceridemia can develop due to familial disorder or secondary to other metabolic disorders, or due to drugs and other causes. Based on patient's lipid profile and family history, one cannot rule out the existence of a genetic disorder in the lipids metabolism until a genetic evaluation is performed. However, the fact that such high triglycerides levels did not induce clinical thrombo-embolic complications until the age of 43 years suggests a secondary cause. The most plausible cause is poorly controlled diabetes mellitus.

The arterial and venous retinal blood flow velocity was attenuated in the state of lipemia retinalis, which resolved to normal values after the reduction in the triglycerides concentration. Arterial and venous retinal blood flow velocity has been reported to be positively correlated to HR, and arterial retinal blood flow velocity has been reported to be positively correlated also to MAP [2]. Since HR and MAP were lower at the follow-up visit, retinal velocity is expected to be lower based on HR and MAP changes alone. The arterial regional differences in velocity in the follow-up visit could be a result of difference in anatomical location in respect to arterial origin, where nasal segments are more proximal than the temporal segments, and therefore the velocity is faster as has been described in healthy subjects [4]. We did not find any previous report on retinal blood flow velocity in lipemia retinalis. Endothelial dysfunction was induced by acute hypertriglyceridemia in subjects with mild baseline hypertriglyceridemia and not in normotriglyceridemic subjects [5]. Induced acute hypertriglyceridemia in healthy subjects resulted in a short-term increase in retinal blood flow due to local vasodilatation [6], although free fatty acid level has a larger effect than triglycerides level [7]. In these reports, the triglyceride levels were acutely increased up to 700 mg/Dl. In the case presented here, changes in triglyceride levels were not acute, and the magnitude was 100-fold larger. Therefore, it is not surprising that the change observed in retinal blood flow velocity has an opposite direction. Triglycerides are mobilized in the blood by chylomicrons, which are the largest lipoprotein (size range from 0.1 to 1.2microns). It has been shown that high levels of triglycerides increases plasma viscosity [8]. It has also been shown that dyslipidemia (mainly high levels of LDL cholesterol) alter erythrocyte flexibility and permeability, and cause decrease in flow velocity [9] In another study, atherogenic diets rich in saturated fat and cholesterol influenced the blood viscosity and erythrocyte aggregability. Plasma triglyceride levels correlated significantly with erythrocyte rouleaux formation rate, which increased blood viscosity [10]. As the RFI traces erythrocyte movement, the high viscosity of plasma and changes in the physical properties of erythrocytes reduce red blood cell mobility.

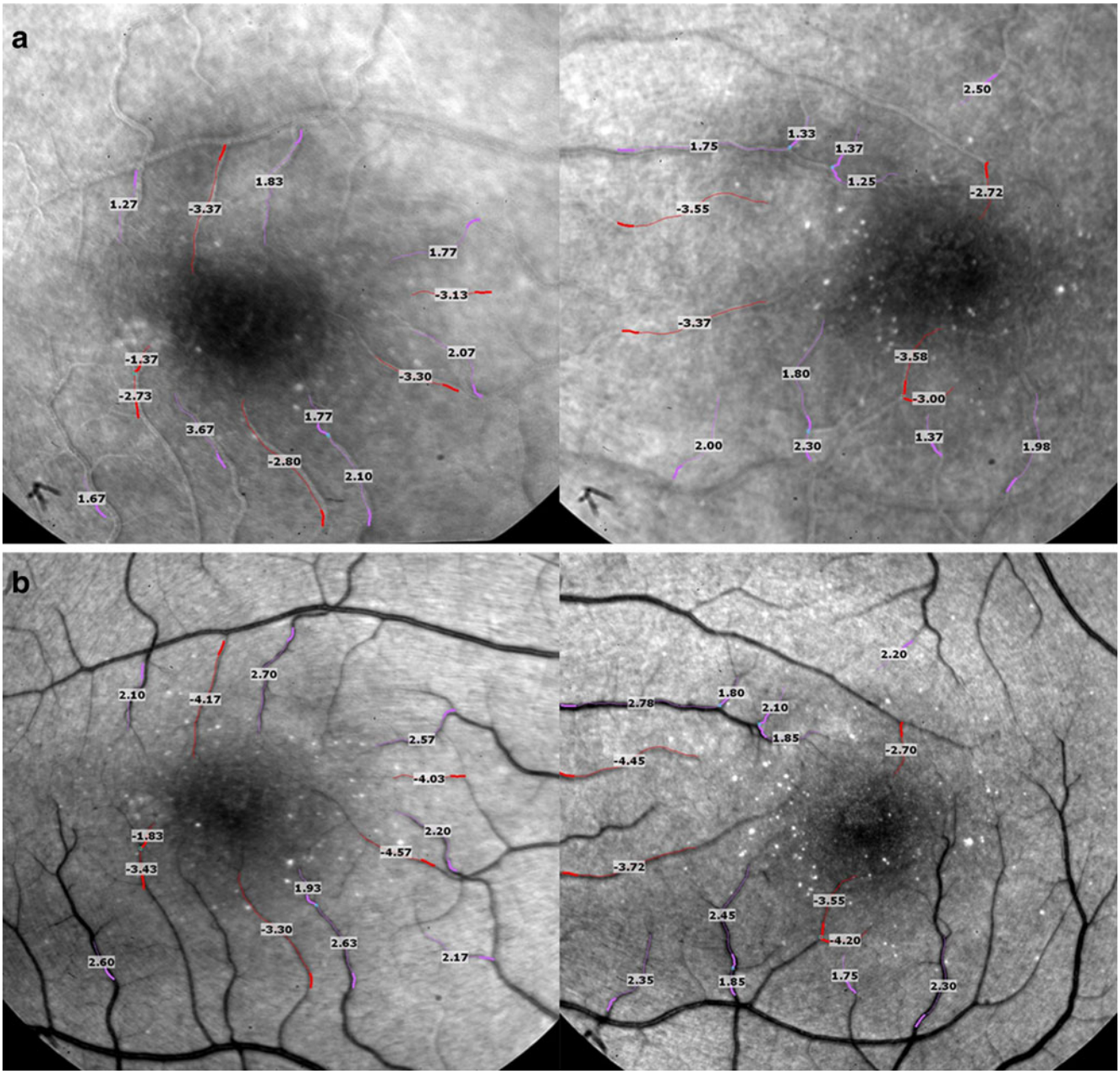

Fig. 2 **a** An RFI image with retinal blood flow velocity measurements on the day of presentation. Arterial segments are marked in *red* and venous segments are marked in *purple*. Blood flow velocity values are measured in mm/sec. **b** Follow-up RFI image 4 weeks later, showing a significant increase in blood flow velocity values in the same segments of arteries and veins

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