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LIPEMIA RETINALIS DURING CHEMOTHERAPY WITH ADJUNCTIVE GLUCOCORTICOID TREATMENT IN A PATIENT WITH COLON CARCINOMA

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Purpose: The purpose of this report is to describe a case of lipemia retinalis due to decompensating hyperlipidemia that occurred during chemotherapy in a patient with metastatic colon carcinoma.

Methods: Retrospective case report.

Results: A 55-year-old non–insulin-dependent diabetic man with well-controlled hyperlipidemia presented himself with temporarily blurred vision in both eyes occurring during chemotherapy. He was found to have lipemia retinalis in his both eyes. Blood tests revealed elevated cholesterol and triglyceride levels exceeding 8,200 mg/dL. He received six cycles of FOLFIRI/bevacizumab and accompanying dexamethasone because of colon cancer with pulmonary metastases. Lipemia retinalis had resolved after a 6-week follow-up when chemotherapy was finished, and the patients' triglyceride and glucose levels decreased to normal values.

Conclusion: Lipemia retinalis associated with visual impairment may occur during chemotherapy under accompanying treatment with dexamethasone. Even if patients with hyperlipidemia are metabolically well-controlled with oral medication, treatment with dexamethasone can potentially lead to decompensation of hyperlipidemia causing secondary lipemia retinalis.

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Hyperlipidemia is characterized by increased levels of serum concentrations of cholesterol or triglycerides and known as a major factor of premature vessel atherosclerosis. Lipemia retinalis is a rare retinal manifestation of hypertriglyceridemia. Retinal vessels appear creamy whitish colored due to the effect of light scattering by triglyceride-laden chylomicrons.[1] In clinical practice, lipemia retinalis caused by chylomicronemia in hyperlipidemia is often observed in patients with metabolic syndrome. However, associations with primary hyperlipidemia or secondary factors causing high levels of triglycerides are also well-documented.[2,3]

Case Report

A 55-year-old white man presented to our department with temporarily blurred vision in both eyes. Ocular history of the patient was unremarkable, and his best-corrected visual acuity was 100/100 in both eyes. Slit-lamp examination demonstrated normal anterior segments, and intraocular pressures were measured at 16 mmHg in both eyes. His medical history included metastatic colon cancer treated with surgery and chemotherapy, diabetes mellitus, and hyperlipidemia well-controlled with statins (atorvastatin 40 mg once per day).

Dilated funduscopic examination revealed normal optic discs, white creamy retinal vessels, and arterial narrowing with arteriovenous crossing abnormalities but no signs of diabetic retinopathy. Furthermore, optical coherence tomography was unremarkable, and there was no evidence for diabetic macular edema. The clinical picture was consistent with lipemia retinalis (Figure 1, A and B).

Before our ophthalmologic examination, the patient was treated with six cycles of chemotherapy with FOLFIRI/bevacizumab

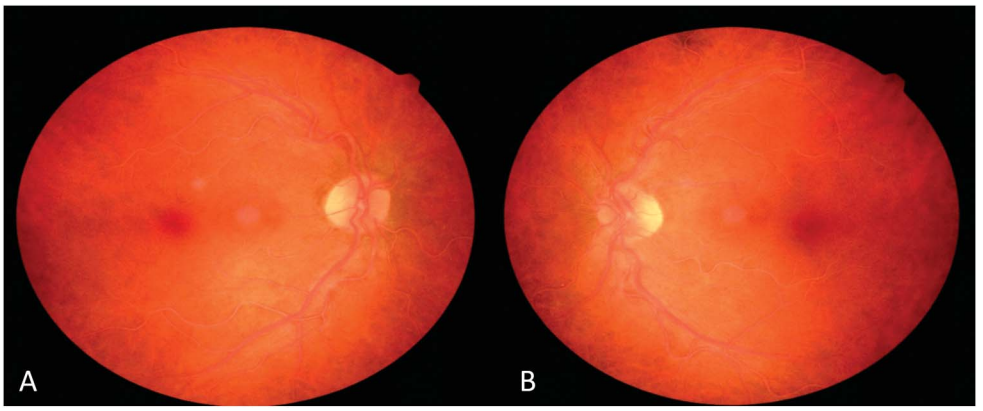

Fig. 1. Fundus photograph of right (**A**) and left (**B**) eye with signs of lipemia retinalis. Characteristic white creamy vessels are visible, making it difficult to distinguish the arteries from the veins.

because of newly occurring pulmonary metastases. The chemotherapy consisted of bevacizumab, irinotecan, and 5-fluorouracil. In addition, he received intravenous therapy with dexamethasone (8 mg every 2 weeks) for treatment of the side effects of the chemotherapy. The patient was referred to the Department of Internal Medicine to perform further diagnosis and treatment; were laboratory evaluation revealed highly increased levels of cholesterol (681 mg/dL) and triglycerides (8,258 mg/dL). It seems the chemotherapy with concomitant treatment with dexamethasone led to metabolic decompensation in hyperlipidemia.

The patient presented himself again to our department 6 weeks later, reporting that his visual problems had vanished. Fundus examination revealed reversion of the alterations of the retinal vessels due to lipemia (Figure 2, A and B). Metabolic control of the triglycerides was achieved (triglycerides were 605 mg/dL and cholesterol was 167 mg/dL on the day of examination) since he quitted chemotherapy and intravenous dexamethasone. In addition, his lipid-lowering therapy had been re-evaluated and changed to cholib 145/40 mg tablets once per day (combination of simvastatin and fenofibrate).

Discussion

Lipemia retinalis is a rare ocular finding characterized by creamy white colored retinal blood vessels, which was first described in 1880 by Heyl.[4] It is associated with elevated levels of plasma triglycerides and occurs in certain types of both primary and secondary hyperlipidemia. In early stages of lipemia retinalis (triglyceride levels of 2,500–3,499 mg/dL), only the peripheral retinal vessels appear creamy and thin. As triglyceride levels increase (3,500–5,000 mg/dL), lipemia spreads out to the posterior pole and the creamy color of the vessels extends toward the optic disc. With triglyceride levels exceeding 5,000 mg/dL, the retina becomes salmon-colored with creamy whitish arteries and veins distinguishable only by size.[1,2]

Although the exact correlation of the incidence of lipemia retinalis and the level of plasma triglycerides is not completely understood, the retinal changes are known as a direct consequence of the elevated levels of circulating chylomicrons in the retinal vessels. Chylomicrons are large lipoproteins, which serve to transport triglycerides in the circulatory system after intestinal absorption. The slightly smaller macromolecules very low-density lipoproteins also play an important role. These lipoproteins are involved in the process of transportation of fat in the metabolism but do not seem to contribute to the fundal appearance.[5]

However, it has been observed that not all patients with even highly elevated levels of chylomicrons and triglycerides present lipemia retinalis, suggesting that other factors, such as changes in hematocrit and difference in translucency of the retinal and choroidal vessels, have to be considered.[5] Rayner et al[1] assumed the light-scattering effect of chylomicrons is responsible for the clinical picture of lipemia retinalis in the fundi.

Most lipemia retinalis cases are asymptomatic, but in fact, also patients with initially deteriorated visual acuity were reported.[6] In general, only advanced and persistent lipemia is known to cause decrease in visual acuity or might even lead to complete loss of vision after massive irreversible lipid exsudation.[1]

Regarding current literature, several cases of lipemia retinalis caused by chylomicronemia in hyperlipidemia due to uncontrolled diabetes mellitus or due to primary hyperlipidemia or even caused by impairment of lipid metabolism during a viral illness were described.[1,3]

This is the first report to our knowledge of an association between symptomatic lipemia retinalis and

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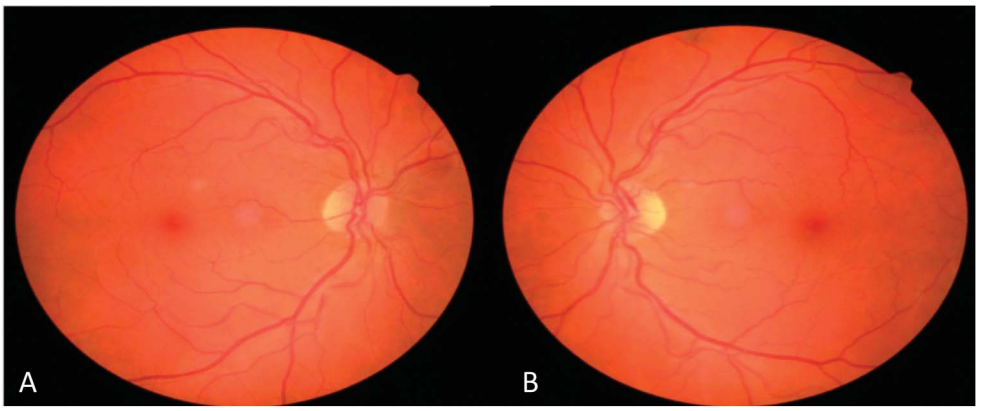

Fig. 2. Fundus photograph of right (**A**) and left (**B**) eye, 6 weeks after initial presentation and under appropriate lipid-lowering medication. The lipemia retinalis had resolved, and the retinal vessels abnormalities returned to normal appearance.

decompensated hyperlipidemia related to treatment with chemotherapy and accompanying treatment with dexamethasone in a patient with metastatic colon cancer. The present data do not reveal any causal linkage between chemotherapy with FOLFOX/bevacizumab and secondary hyperlipidemia, so lipemia retinalis in our patient is believed to be a consequence of decompensated hyperlipidemia after chronic therapy with dexamethasone over a period of 5 months.

Previously, Chahande et al described a case of a 14-year-old diabetic boy developing lipemia retinalis because of intravenous treatment with prednisolone (1 mg/kg for 5 days) for multiple intracranial neurocysticerci with perilesional edema. The authors also assume the lipemia in this case was caused by administration of steroids.[7]

Secondary hypertriglyceridemia is known as a result of the supply of glucocorticoids. Glucocorticoid substitution is associated with hypertriglyceridemia, elevated glucose, and higher non–high-density lipoprotein cholesterol levels and can lead to metabolic syndrome, which was proved in a study with GH- and glucocorticoid-replaced hypopituitary patients.[8]

Suggesting underlying mechanisms, studies reported that pharmacological doses of glucocorticoids lead to an increased endogenous glucose production in healthy people by stimulating hepatic gluconeogenic enzymes and augmenting supply of substrates to the liver for gluconeogenesis by peripheral lipolysis and proteolysis.[9,10]

Usually no treatment is required for lipemia retinalis. Once triglyceride levels return to normal, the retinal appearance of lipemia retinalis should quickly resolve without causing decrease in visual acuity or permanent retinal disease.[11] However, lipemia retinalis is a very important sign of a potential life-threatening systemic metabolic disorder, and it is essential to recognize it as a sign of a profound lipid abnormality.

We present the first documentation of lipemia retinalis associated with visual symptoms because of decompensating hyperlipidemia in a patient undergoing chemotherapy with concomitant treatment with dexamethasone, and we want to raise awareness of this probably often underdiagnosed retinal condition. Lipid-lowering therapy is believed to normalize fundal appearance and leads to restoration of visual acuity. It is important to adapt the lipid-lowering medication to obtain appropriate management of the lipid metabolism in patients receiving dexamethasone therapy.

Key words: chemotherapy, colon carcinoma, cortisone, hyperlipidemia, lipemia retinalis.

References

1. Rayner S, Lee N, Leslie D, et al. Lipaemia retinalis: a question of chylomicrons? Eye 1996;10:603–608.
2. Park YH, Lee YC. Lipemia retinalis associated with secondary hyperlipidemia. New Engl J Med 2007;357:10.
3. Gayathri K, Ramalingam PK, Santhakumar R, et al. Lipemia retinalis due to secondary hyperlipidemia in type 1 diabetes mellitus. J Assoc Physicians India 2016;64:83–84.
4. Heyl AG. Intraocular lipaemia. Trans Am Ophthalmol Soc 1880;3:55.
5. Vinger PF, Sachs BA. Ocular manifestations of hyperlipoproteinaemia. Am J Ophthalmol 1970;70:563–572.
6. Rymarz E, Matysik-Woyniak A, Baltaziak L, et al. Lipemia retinalis—an unusual cause of visual acuity deterioration. Med Sci Monit 2012;18:CS72–CS75.
7. Chahande S, Murthy R. Lipemia retinalis following systemic steroids for neurocysticercosis in a juvenile diabetic. Indian J Pediatr 2015;82:298–299.
8. Dullaart RPF, Schols JL, Van Der Steege G, et al. Glucocorticoid replacement is associated with hypertriglycerdiaemia, elevated glucose and higher non-HDL cholesterol and may diminish the association of HDL cholesterol with the -629C>A CETP promoter polymorphism in GH-receiving hypopituitary patients. Clin Endocrinol 2008;69:359–366.
9. Kraus-Friedmann N. Hormonal regulation of hepatic gluconeogenesis. Physiol Rev 1984;64:170–259.
10. Vander Kooi BT, Onuma H, Oeser JK, et al. The glucose-6-phosphatase catalytic subunit gene promoter contains both positive and negative glucocorticoid response elements. Mol Endocrinol 2005;19:3001–3022.
11. Horton M, Thompson K. Lipemia retinalis preceding acute pancreatitis. Optometry 2011;82:475–480.