LIPEMIA RETINALIS IN METABOLIC SYNDROME

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Abstract

A 19-year-old female with a history of pure gonadal dysgenesis and metabolic syndrome was undergoing regular diabetic eye screening. Recent clinical examination revealed bilateral creamy-white retinal vessels, in keeping with the features of lipemia retinalis (LR). Optical coherence tomography (OCT) images also show hyperreflective deposits accumulated in the dilated retinal vessels with a shadowing effect. Further investigations showed a total serum cholesterol level of 24.2 mmol/L and an unreadable triglyceride level due to a lipemic blood sample. Her medications were increased to T. atorvastatin 40 mg at night and T. ezetimibe 10 mg once daily by her physician. Unfortunately, she developed acute pancreatitis secondary to diabetic ketoacidosis with hypertriglyceridemia three months after the diagnosis of LR. LR is a clinical indication of a very high triglyceride level when laboratory testing is not possible. The high comorbidities associated with hypertriglyceridemia and diabetes may warrant close monitoring for cardiovascular disease and life-threatening pancreatitis.

Keywords: Lipemia Retinalis, Hypertriglyceridemia, Metabolic Syndrome, Acute Pancreatitis

Introduction

Lipemia retinalis is a rare presentation of hypertriglyceridemia described as a white and creamy appearance of the retinal arteries and veins, and sometimes the whole fundus (1). Although secondary and genetic factors can elevate triglyceride (TG) levels, metabolic syndrome remains the most common cause of hypertriglyceridemia. Hyperlipidaemia might affect multiple organs, including the cardiovascular system, liver, pancreas, skin, and retina (2, 3). Nevertheless, severe hypertriglyceridemia (> 500 mg/dL) will also increase the risk of acute pancreatitis, which can cause high morbidity and mortality.

In this case report, we describe a patient with metabolic syndrome who presented with asymptomatic lipemia retinalis, fatty liver disease, and eruptive xanthoma and eventually developed acute pancreatitis.

Case report

A 19-year-old girl with underlying pure gonadal dysgenesis and metabolic syndrome (type 1 diabetes mellitus and hypertriglyceridemia—high TG and low high-density lipoprotein (HDL)) was undergoing annual diabetic eye screening. Both conditions were diagnosed two years ago and managed by the gynaecology and endocrinology teams. She was started on oestradiol gel, subcutaneous insulin, oral atorvastatin (20 mg daily), and fenofibrate (145 mg daily). Her chromosomal study showed 46XX with no gross numerical or structural abnormality detected, which ruled out Turner syndrome, one of the common causes of primary amenorrhea with diabetes mellitus. There was no family history of lipid abnormalities. Her eye assessment was normal one year prior (i.e., August 2020) (Figures 1A and 1B), when her total cholesterol (TC) was 5.8 mmol/L (224.3 mg/dL), TG was 9.21 mmol/L (815.8 mg/dL), and HbA1c was 10.3%. Unfortunately, she has not been compliant with her medications.

She was reviewed a year later (i.e., in August 2021). Her best-corrected visual acuity was 20/30 in both eyes with a normal anterior segment. However, bilateral creamy-white retinal vessels were seen during the dilated fundus examination (Figures 2A and 2B), when her TG level was unreadable. Optical coherence tomography (OCT) revealed hyperreflective materials accumulated in the

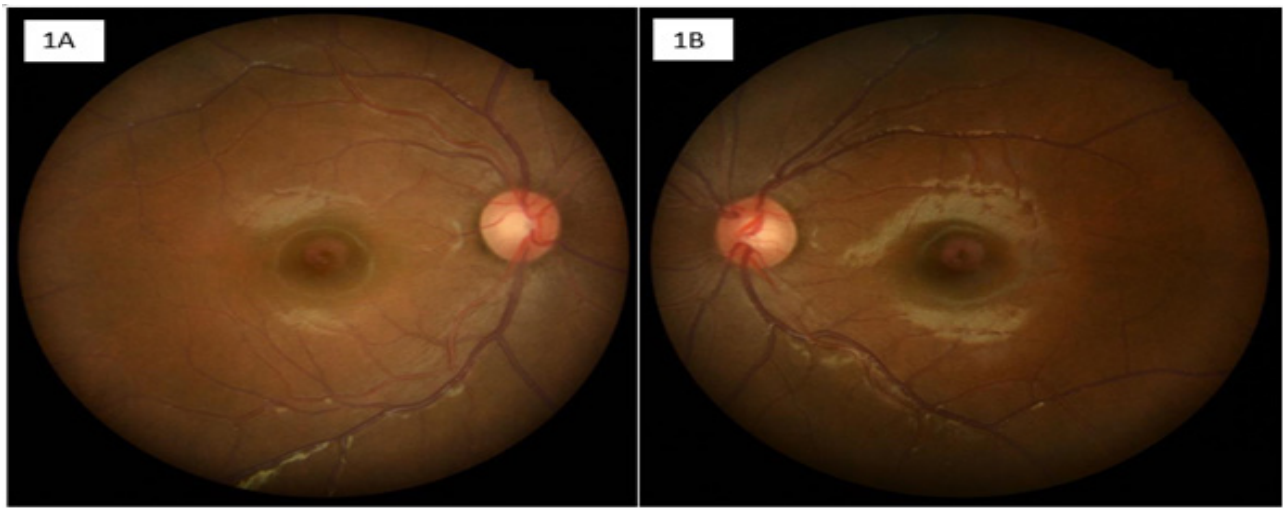

Figure 1A and 1B: Normal fundus photo taken August 2020

dilated superficial retinal capillaries, forming a shadow over the underlying structures (Figures 3A and 3B). Her body mass index was 22. Systemic examinations showed eruptive xanthomas over both forearms (Figure 4). Her cardiovascular system was unremarkable and she had no hepatosplenomegaly. There was a creamy layer of supernatant in the syringe from venepuncture (Figure 5).

Laboratory studies reported a TC of 24.2 mmol/L (935.8 mg/dL) and an HbA1c of 13%. Her lipemic blood sample was unable to provide a TG or LDL level. Her medications were escalated to T. atorvastatin 40 mg ON and T. ezetimibe 10 mg OD by her physician.

Unfortunately, she was diagnosed with acute pancreatitis and left pyelonephritis, together with diabetic ketoacidosis secondary to sepsis, three months after being diagnosed with lipemia retinalis. She presented with left lumbar pain, nausea, and abdominal distension. Her blood sugar was 22 mmol/L, with a blood ketone of 2.1 mmol/L, a high C-reactive protein level of 195 mg/L, and a serum amylase of 162 IU/L. Contrast-enhanced computed tomography of the thorax, abdomen, and pelvis (CECT-TAP) is suggestive of acute pancreatitis with peripancreatic collection, cystitis, and bilaterally enlarged adrenal glands with mild splenomegaly. She was discharged well after completing one week of intravenous Augmentin (1.2 g tds). She was also being referred to a hepatobiliary surgeon for further management.

Otherwise, her fundus examination four months after the treatment showed a normal fundus (same as Figure 1). Her

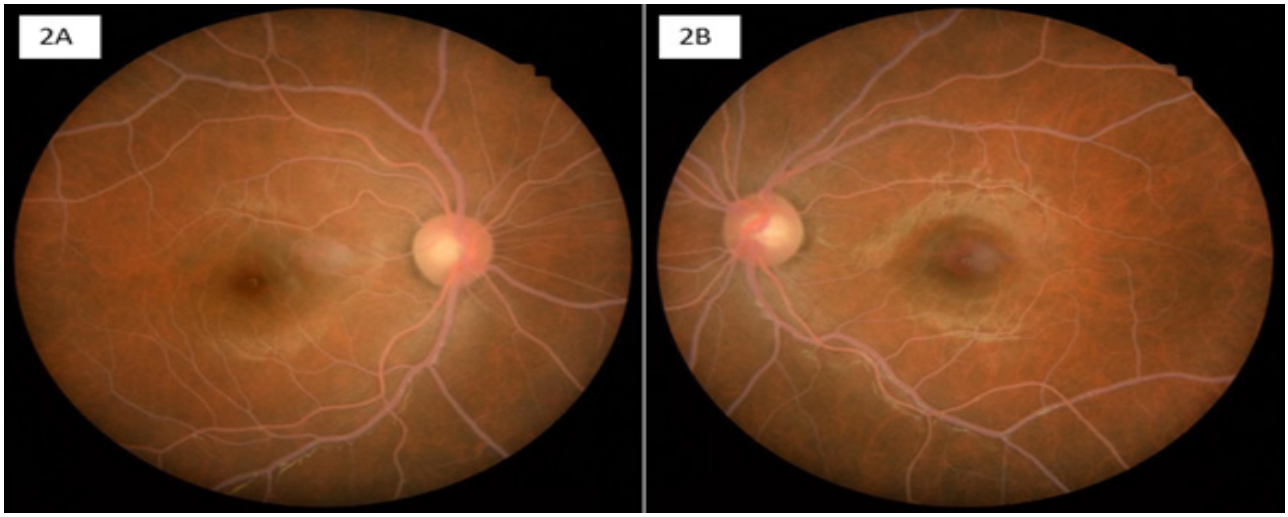

Figure 2A and 2B: Fundus photo taken August 2021 showed bilateral creamy-white retinal vessels

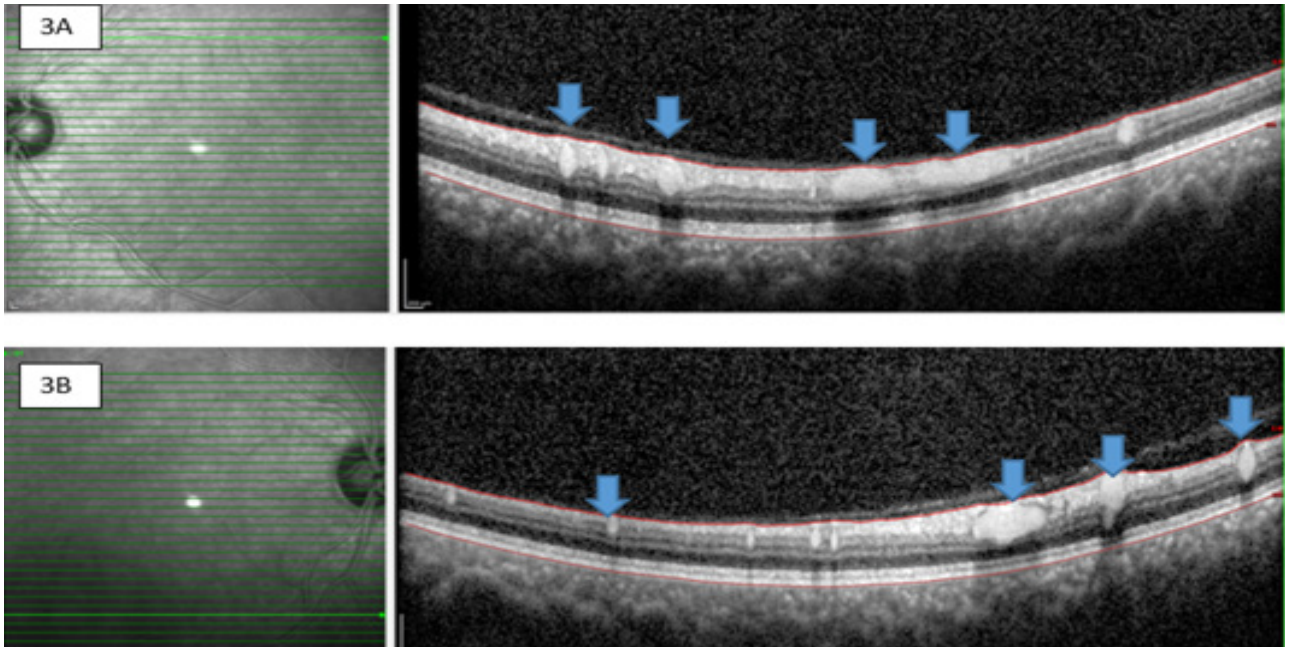

Figure 3A & 3B: Both eyes OCT images showing hyperreflective deposits accumulated in the dilated retinal vessels with shadowing effect (Blue arrow mark)

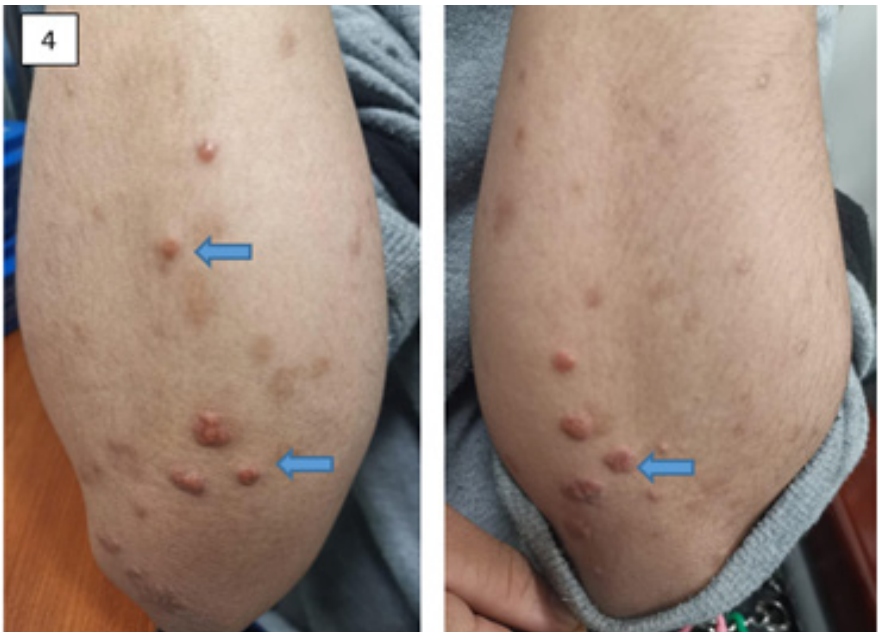

Figure 4: Cluster of eruptive xanthomas over right and left forearms respectively (Blue arrow mark)

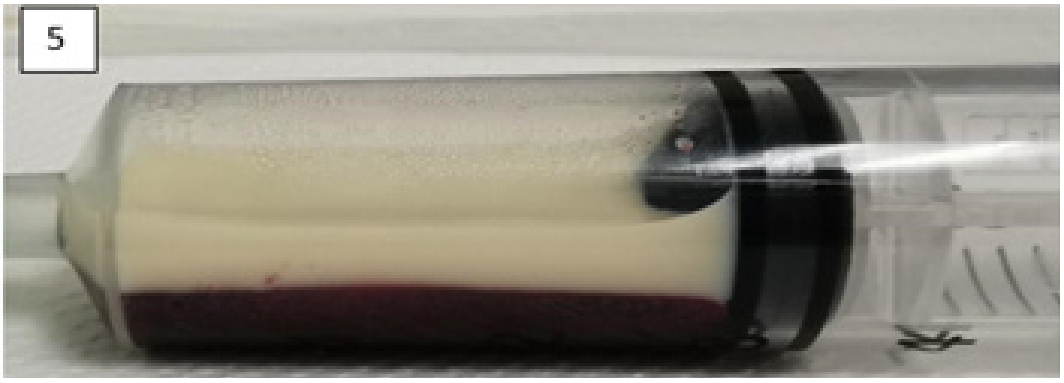

Figure 5: Creamy layer of supernatant in the syringe

TC had decreased to 8.8 mmol/L (340.3 mg/dL), and her TG had reduced to 7.84 mmol/L (694.4 mg/dL). On OCT, the hyperreflective materials in the retinal vessels improved after the treatment (Figure 6).

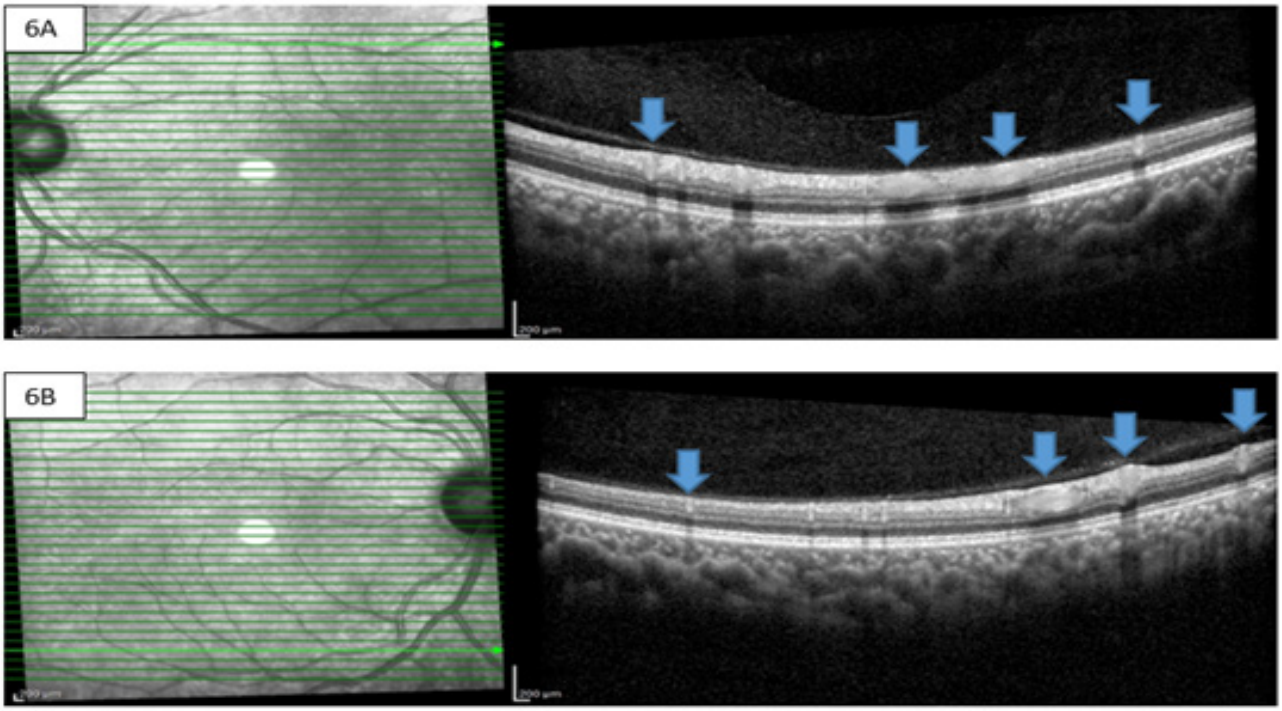

Figure 6A & 6B: Both eyes OCT images showing improving hyperreflective deposits in the retinal vessels with shadowing effect (Blue arrow mark)

Discussion

Dyslipidaemia is a major risk factor for cardiovascular disease (CVD). According to the Malaysia National Health & Morbidity Survey (NHMS) 2019 report, one in five individuals in the 18–19-year age group, or 38.1% of adult Malaysians over the age of 18, had hypercholesterolemia (TC > 5.2 mmol/L) (3). The National Cholesterol Education Programme (ATP III) final report by the American Heart Association classified a triglyceride (TG) level of 150 mg/dL as normal, 150–199 mg/dL as borderline high, 200–499 mg/dL as high, and > 500 mg/dL as very high (1 mmol = 88.5736 mg/dL) (4). Dyslipidaemias may occur primarily or secondary to diseases such as nephrotic syndrome, obstructive liver disease, hypothyroidism, Cushing's syndrome, drugs (oestrogens, oral retinoids), alcoholism, and insulin resistance states (including diabetes mellitus and metabolic syndrome). As seen in our patient, her hypertriglyceridemia was thought to be due to an underlying uncontrolled diabetes mellitus with insulin resistance. Controlling the ideal sugar level with insulin will rapidly reduce the TG level. This pattern of lipid derangement followed by a rapid return to normal TG and cholesterol levels can be attributed to insulin, which is believed to have a significant impact on lipoprotein synthesis and secretion (5). Dyslipidaemia affects multiple organs, including the cardiovascular system, liver, pancreas, skin, and retina (2, 3). This was reflected in our patient as we observed the various complications of dyslipidaemia, including fatty liver disease, acute pancreatitis, eruptive xanthoma, and lipemia retinalis.

Lipemia retinalis was first reported by Heyl in 1880 and was associated with metabolic syndrome and genetic disorders (6). Lipemia retinalis is usually seen when serum TG levels are higher than 2,000 mg/dL (1). The early signs of lipemia retinalis take place in the peripheral retina and extend to the posterior pole as TG levels increase. At TG levels of 2,500–3,499 mg/dL, the peripheral vessels will appear creamy and thin; at levels of 3,500–5,000 mg/dL, the vessels in the posterior pole will assume a creamy colour; and at levels exceeding 5,000 mg/dL, the fundus becomes salmon-coloured, with creamy arteries and veins that may be distinguished by calibre alone. The ocular findings are due to the light scattering from the triglyceride-laden chylomicrons in the plasma. Lipemia retinalis is estimated to be present in 23% of patients with severe hypertriglyceridemia, as a consequence of the accumulation of circulating chylomicrons caused by lipoprotein lipase deficiency (1).

Lipemia retinalis usually does not cause visual impairment, and the discoloration of retinal vessels will be reversed once the serum lipid levels are lowered (7, 8). However, the literature has reported cases associated with retinal vein occlusion, which is likely due to increased viscosity

and sludging of blood in the microvasculature caused by marked chylomicronaemia (7, 9). Lipid-lowering therapy is important in the reversal of the fundus appearance. This is seen in our case report, as our patient had normal visual function despite the fundus changes and the normalisation of fundus appearance following four months of lipid-lowering treatment.

OCT is a helpful ocular imaging tool that could demonstrate hyperreflective materials in the retinal vessel lumen. This was previously postulated to be due to the extravasation of lipid from retinal vessels related to its location and origin: leakage from the retinal capillary network causes accumulation in the inner retinal layers, and leakage from choroidal circulation causes hyperreflective dots to be present in the deeper retinal layers (10). However, as seen in our patient, OCT findings of hyperreflective dots were mainly observed within the retinal vessel lumen in the inner retinal layers (Figure 3), with no leakage noted. This OCT finding usually disappears later than the fundus changes after normalisation of the serum TG level (10). OCT is therefore helpful in exhibiting and indirectly monitoring the presence of chylomicrons in the retinal vessels.

Eruptive xanthomas are painless, yellowish papules surrounded by an erythematous border that present as grouped lesions on the torso, elbows, chest, and buttock regions (11). They are formed by clusters of foamy cells caused by phagocytosis of macrophages as a consequence of increased accumulations of intracellular lipids. This is generally not observed until TG levels are extremely elevated (e.g., > 2,500 mg/dL) (12) and typically resolves within several weeks after TG levels are reduced.

Hypertriglyceridemia is the third most common cause of acute pancreatitis, following gallstones and alcohol use. Acute pancreatitis usually occurs when TG levels are > 1,000 mg/dL (4). The mortality rate of acute pancreatitis can go up to 20% in patients with pancreatic necrosis. The serum TG level is found to be proportionate to the risk and severity of acute pancreatitis. Horton and Thompson also reported a case of lipemia retinalis preceding acute pancreatitis, which is similar to our patient (13). Additionally, it was also reported that hypertriglyceridemia with uncontrolled diabetes appears to be the commonest cause of pancreatitis (14). Thus, control of hyperglycaemia is an important factor in minimising the risk of this potentially life-threatening pancreatitis.

Incidental findings of lipemia retinalis in our patient allowed for timely and prompt intervention, which could possibly have reduced the morbidity rate. Our patient was co-managed aggressively with other disciplines to bring about dietary changes, lifestyle changes, as well as medications to optimize her hypercholesterolemia and diabetes mellitus.

Conclusion

Lipemia retinalis is an important clinical feature that may signify a potentially devastating underlying disorder. Proper management allowed for reversible changes and the reduction of possible complications. It is therefore pertinent to approach and manage the patient holistically.

Acknowledgement

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Competing interests

The authors declare that they have no competing interests.

Ethical Clearance

We obtained approval from the Medical Research and Ethics Committee (MREC) and the Ministry of Health Malaysia (MOH), registered under NMRR ID-21-02392-SVL.

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