

Moderate Hypertriglyceridemia Revealed by Acute Chest Syndrome, a Milky Appearance Serum and Prior History of Recurrent Acute Pancreatitis in a Type 2 Diabetes Black Patient: A Case Report

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Abstract

Although the “triglyceride paradox” states that hypertriglyceridemia is less frequent in Blacks and the risk of pancreatitis increases with severe hypertriglyceridemia, we herein report on a case of moderate hypertriglyceridemia revealed by an acute chest syndrome and a milky appearance serum in a 47-year-old type 2 diabetes black patient with prior history of recurrent acute pancreatitis. In addition to insulin therapy and coronary angioplasty, the combination of a statin and a fibrate resulted two months later in a substantial improvement in triglyceride levels and a normal serum appearance.

Keywords

Moderate Hypertriglyceridemia, Acute Chest Syndrome, Pancreatitis, Fibrates, Black African

1. Introduction

Dyslipidemia in T2DM is characterized by an atherogenic profile with elevated low-density lipoprotein-cholesterol (LDL-c), elevated triglycerides (TG) and decreased high-density lipoprotein-cholesterol (HDL-c) and increases the risk of both coronary artery disease (CAD) [1] and pancreatitis [2]. Indeed, modest increase in TG levels has been reported to be associated with CVD risk whereas severe hypertriglyceridemia (TG > 11.3 mmol/l) increases the risk of pancreatitis [1] [3]. If the role of HTG in promoting

pancreatitis is well accepted, controversy still remains about CVD [3]. However, the clustering of HTG with other components of the metabolic syndrome such as elevated small dense LDL-c particles and low HDL-c could explain the increased CVD risk conferred by HTG [4]. Although the so-called “triglyceride paradox” states that hypertriglyceridemia (HTG) is less frequent in blacks [5] [6], we herein report on a case of moderate HTG revealed by an acute chest syndrome and a milky appearance serum in a 47 years old poorly controlled T2DM black patient with prior history of recurrent acute pancreatitis referred to the outpatient clinic of the Division of Cardiology of the University of Kinshasa Hospital.

2. Case Report

IB is a 47 years old black patient with type 2 diabetes under mixed insulin since 1994. In August 2014, due to an acute chest pain on walking that usually relieves 3 to 4 minutes after stopping walking, his general practitioner from Brazzaville, Republic of Congo referred him to the outpatient clinic of the Division of Cardiology/University of Kinshasa Hospital for, Republic of Congo. His past medical history is characterized by a history of recurrent acute pancreatitis (2002 and 2003) and hypertension (2009) successfully controlled with a combination of angiotensin converting enzyme inhibitor (Ramipril 10 mg) and thiazide diuretic (Hydrochlorothiazide 12.5 mg). He was not smoking or consuming alcohol and has no physical activity in leisure time. Physical examination revealed a body mass index (BMI), waist circumference (WC), seated blood pressure (BP), pulse rate of 29 Kg/m², 98 cm, 142/89 mm Hg and 98 bpm, respectively (**Table 1**). Cardiac and pulmonary sounds were normal; there was no abdominal tenderness, hepatomegaly nor splenomegaly; pedal and posterior arterial pulses were normally perceived and symmetric. Cardiac ultrasound was normal and electrocardiogram findings of negative T waves at leads D1, aVL, V1, V4, V5 and V6 were suggestive of inferior and lateral ischemia. The diagnosis of acute chest syndrome complicating a metabolic syndrome (MetS) was retained and patient was prescribed, in addition to current anti-hypertensive treatment, an oral cardio-selective beta-blocker (Atenolol 10 mg), nitrate compound (Isosorbide dinitrate 10 mg), statin (Simvastatin 10 mg) and antiplatelet (Clodopigrel 75 mg) with progressive relieve of chest pain. A venipuncture that draw a milky appearance blood sample (**Figure 1(a)**) was performed and blood chemistry showed fasting plasma glucose (FPG) 21 mmol/l, serum creatinine 159 μ mol with estimated glomerular filtration rate (eGFR) by abbreviated modification of diet in renal disease equation (MDRD) 52 ml/min/1.73 m², tri-iodothyroxine (T3) 0.95 ng/ml, tetra-iodothyroxine (T4) 103 nmol/l and thyroid stimulating hormone (TSH) 0.8 IU/ml. Lipid and lipoprotein profile was as follows: total cholesterol (TC) 9.87 mmol/l, LDL-c 5.14 mmol/l, HDL-c 1.0 mmol/l, non-HDL-c 8.86 mmol/l, TG 8.09 mmol/l (**Table 2**). The analysis of these laboratory tests revealed a mixed dyslipidemia (elevated TG and LDL-c) with low HDL-c and a reduced kidney function. Abdominal ultrasound showed pancreatic micro-calcifications suggestive of asymptomatic chronic pancreatitis. Finally, the diagnosis of acute coronary syndrome (ACS) complicating a T2DM-associated

Table 1. Sociodemographic and clinical characteristics of the patient at the first visit.

Variable	
Age, years	47
Past medical history:	
-Diabetes (1994)	
-Acute pancreatitis (2002, 2009)	
-Hypertension (2009)	
BMI, Kg/m ²	29
Waist circumference, cm	98
SBP, mm Hg	149
DBP, mm Hg	89
Pulse rate, bpm	98
FPG, mmol/l	21
Serum creatinine, μ mol/l	159
GFR-MDRD, ml/min/1.73 m ²	52
Triiodothyroxin (T3), ng/ml	0.95
Tetraiodothyroxin (T4), nmol/l	106
FSH, IU/l	0.80

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; GFR, glomerular filtration rate; MDRD, modification of diet in renal disease; Follicle stimulating hormone; IU, international unit.



Figure 1. Serum appearance before (a) and after (b) two months treatment with the combination of statin and fibrate (Fenofibrate).

Table 2. Lipid and lipoprotein profile before and two months after the addition of a fibrate to the statin.

Variable	Before fibrate	After fibrate
Total cholesterol mmol/l	9.87	6.80
LDL-c, mmol/l	5.14	3.37
HDL-c, mmol/l	1.00	1.26
Non HDL-c, mmol/l	8.86	5.29
TG, mmol/l	8.09	4.86

Abbreviations: LDL-c, low-density lipoprotein-cholesterol; HDL-c, high-density lipoprotein-cholesterol; TG, triglycerides.

mixed dyslipidemia with mainly HTG as a component of MetS was retained. Thiazide diuretic and beta-blocker, drugs known to alter glucose and lipid metabolism, were stopped and replaced by oral low release indapamide (2.5 mg) and an angiotensin converting enzyme inhibitor Ramipril (10 mg), respectively. Since statins do not effectively lower TG levels, a fibrate (Oral Fenofibrate 160 mg once daily) was added to statin. Two months later (November 2014), the patient was feeling better and has no complaints. Venipuncture drawn a red blood sample (**Figure 1(b)**) and laboratory parameters were as follows: FPG 8 mg/dl, blood urea nitrogen (BUN) 6.8 mmol/l, creatinine 124 μ mol/l, eGFR-MDRD 69.8 ml/min/1.73 m², TC 6.56 mmol/l, LDL-c 3.97 mmol/l, HDL-c 1.26 mmol/l, non-HDL-c 5.29 mmol/l, TG 4.8.6 mmol/l (**Table 2**). As coronary angiography was not available in Kinshasa, the patient travelled abroad to Lazio in Italy where coronary angiography evidenced an occlusion of descendant anterior coronary artery and a stenosis of circumflex artery. Coronary angioplasty with stent was performed on January 10, 2015 and patient was prescribed oral cardioaspirin 100 mg, Lopressor 100 mg, Ramipril 10 mg, Eskim 1000 mg, Atorvastatin 40 mg, Pantoprazole 40 mg and subcutaneous Novorapid 18 IU thrice daily and Levemir 18 IU once daily. At discharge, the patient was feeling better and went back to Brazzaville under the surveillance of his general practitioner.

3. Discussion

We reported on a 47-year-old patient with type 2 diabetes with prior history of acute pancreatitis presenting with an acute chest pain and very important hypertriglyceridemia with a milky appearance serum.

3.1. Clinical Findings

Lipid profile made of increased levels of both cholesterol and TG observed in the present T2DM diabetes case is a well-known feature of mixed dyslipidemia and does translate underlying insulin resistance state [1]. Indeed, insulin resistance has been reported to be associated with an increase in serum TG through several mechanisms including reduced insulin-dependent inhibition of lipolysis in adipocytes, increased TG

and very-low lipoprotein density cholesterol (VLDL-c) production by the liver, and impaired insulin-dependent activation of lipoprotein lipase and hydrolysis of TG-rich lipoprotein particles with subsequent fasting and postprandial HTG [7]. In the absence of genetic testing, contributing factors to HTG in the present case could be physical inactivity, central obesity, uncontrolled hypertension and diabetes, reduced kidney function, and the use of drugs known to alter lipid metabolism such as thiazide diuretic and beta blocker; diet could be another factor but it was not formally evaluated in the present case [7].

A milky appearance of serum in the present case does suggest high levels of chylomicrons as observed in type V hyperlipoproteinemia [8]. Chylomicronemia syndrome defined as TG levels above 11.3 mmol/l plus one of either eruptive xanthoma, lipemia retinalis or abdominal pain/pancreatitis is a complication of HTG usually considered as rare [8]. However, a serum milky in color can be seen with TG levels between \sim 11.3 mmol/l since chylomicrons are formed at TG levels $>$ 5.65 mmol/l [9]. In this regard, Zhang *et al.* [9] in a retrospective clinical study of 224 patients with hypertriglyceridemia pancreatitis that TG \geq 5.65 mmol/l should raise a high degree of suspicion of HTG, especially if no other etiology of acute pancreatitis is apparent.

Patient's past-medical history was characterized by two episodes of acute pancreatitis. Hypertriglyceridemia is a well-established cause of acute pancreatitis, accounting for 1% - 4% to 9% of patients who present with acute pancreatitis [10] [11] [12] [13]. Although the exact pathway by which HTG causes acute pancreatitis remains poorly understood, two potential mechanisms have been suggested [9] [14]. The first one relies on the hydrolysis of excess TG by pancreatic lipase causing accumulation of free fatty acids in the pancreas; the latter in turn cause acinar cell and pancreatic capillary injury. The resultant ischemia creates an acidic environment, which further enhance free fatty acid toxicity. The second one is that increased chylomicron-induced hyperviscosity in the pancreatic capillaries leads to ischemia [9] [14].

Acute retrosternal chest pain experienced by the patient could be related to the coexistence of multiple CVD risk factors clustering in metabolic syndrome. However, HTG could be one of the most important factors in the development and progression of the dynamic process of atherosclerosis [1]. The Prospective Cardiovascular Munster (PROCAM) study [15] found increases in risk as TG levels rose from 2.3 mmol/l to 9.0 mmol/l after adjustment for other risk factors for cardiovascular disease. A strong independent relation between plasma TG levels and likelihood of cardiovascular disease has been reported in other studies [15]. Meta-analyses of thousands of patients followed up for more than 10 years showed that a TG elevation of 1 mmol/l increased the risk of cardiovascular disease by 32% in men and 76% in women, independent of HDL-c levels [15]. Although the role of HTG in promoting CVD remains still a matter of controversy, recent studies reported a consistent strong positive relationship between TG levels (especially non fasting TG) and CVD [16]. Indeed, HTG has been reported to be associated with low HDL-c and increased levels of the more atherogenic small dense LDL-c particles with subsequent oxidative stress, inflammation and prothrombotic state, all well-known characteristic features of the atherosclerosis process [1] [17].

3.2. Therapeutic Aspects

3.2.1. Insulin Therapy

Despite the presence of metabolic syndrome suggestive of underlying insulin resistance, the present case was paradoxically receiving insulin to control his T2DM. In case of severe T2DM-associated HTG and poorly controlled diabetes as in the present, continuous intravenous insulin infusion has been reported to be beneficial in reducing plasma glucose and serum TG [11]. A recent study, a group of 15 patients with a median TG of 26.23 mmol/l has their TG levels corrected to a median of 5.75 mmol/l at discharge with an average 48h of continuous insulin infusion [18]. Since TG levels in the present patient were below those reported in aforementioned study, subcutaneous insulin was preferred to continuous intravenous insulin.

3.2.2. Lipid Lowering Therapy and Hypertriglyceridemia

Improvement in serum appearance and lipid profile was observed in the present case two months after the initiation of lipid lowering therapy with a statin and a fibrate. Although statins have some TG lowering effects at higher doses, ranging from 20% to 28%, they are not effective enough to remove the risk of pancreatitis in patients with severe HTG and should not be used in their own as first line agents [2]. In these patients, fibrates are the most efficacious first line pharmacotherapy for HTG, and typically lower TG levels rapidly and effectively [2]. Meta-analyses as well as the ACCORD study suggest that fibrates are useful for the treatment of HTG in diabetic patients [7] [19] [20]. Fenofibrate consistently decreased TG levels to a significantly greater extent than placebo; significantly greater increases in HDL-c levels and significantly greater reductions in LDL-c and total cholesterol levels were also seen in some trials [20]. The beneficial effects of fenofibrate on lipid profile are mediated by mainly the activation of peroxisome proliferator-activated receptor-alpha [21]. Fibrates are generally well tolerated and rarely cause myopathy or hepatic toxicity as showed by safety data from the FIELD study as well the ACCORD lipid trial [14] [21].

3.2.3. Antihypertensive Therapy

Beta blocker and thiazide diuretic, drugs known to alter glucose and lipid metabolism, were replaced by an angiotensin converting enzyme inhibitor Ramipril and another diuretic indapamide known to have beneficial or neutral effects on glucose and lipid metabolism. Angiotensin 2 alters insulin secretion and sensitivity through the production of pro-inflammatory cytokines and reactive oxygen species with subsequent oxidative [22]. Thus, the inhibition of renin angiotensin system can improve alterations in glucose and lipid metabolism in diabetes [22].

4. Conclusion

A milky serum appearance in the context of acute abdominal pain should guide the doctor to a diagnosis of acute pancreatitis, and to propose the triglyceride assay. We have shown here that the complications of hypertriglyceridemia can be seen in black patients, even at relatively moderate rates of triglycerides.

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Authors' Contribution

LFB wrote the manuscript, KEV collected data and revised the manuscript, MJR revised the manuscript, KFM revised the manuscript.

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