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A rare case of familial dysbetalipoproteinemia associated with heterozygous E2/E4 genotype

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Background: Familial dysbetalipoproteinemia is a genetic lipid disorder characterized by both elevated serum cholesterol and triglyceride (TG)due to accumulated remnant lipoproteins by mutation in apolipoprotein(apo)E gene. In humans,three common apoE isoforms have been described,designated E2,E3,and E4. Homozygosity for apoE2 is the commonest genotype. Here we present a case of dysbetalipoproteinemia associated with rare genotype. **Methods:** Serum laboratory measurements including total cholesterol(TC),HDL-C,TG,and LDL-C were analyzed enzymatically after overnight fasting. Serum apolipoproteins were measured by an immunoturbidometric method. Lipoprotein electrophoresis was performed by Hydragel 15 lipoprotein(E) Analyzer. ApoE genotyping was performed by allele-specific polymerase chain reaction method. **Results:** A 37-year-old man was referred to the department of endocrinology to deal with elevated cholesterol levels. He had no family history of dyslipidemia or established cardiovascular disease, while physical examination was unremarkable except cutaneous papules on forearms(Fig 1). Markedly elevated levels of TC(924mg/dL),TG(6246mg/dL),apoE(> 12mg/dL),apoCII(> 10mg/dL), HDL-C(> 130mg/dL) were observed, while LDL-C(46mg/dL), apoA1(44mg/dL) and apoB(71mg/dL) levels were within normal range. Besides, he was simultaneously diagnosed with diabetes by 75g oral glucose tolerance test and 12.4% of HbA1c. Skin biopsy was performed on cutaneous papules and the pathologic diagnosis was consistent with eruptive xanthoma. Lipoprotein electrophoresis depicted 6.8% of alpha lipoprotein, 83.2% of beta/pre-beta lipoproteins, and 10% of chylomicrons,which appear as a broad beta band(Fig.2). Finally, the diagnosis of dysbetalipoproteinemia was verified by apoE2/E4 heterozygosity genotype. The patient received rosuvastatin 10mg and fenofibrate 160mg once a day with multiple insulin injections. After five weeks of treatment, his skin lesions disappeared and serum lipid profiles were normalized. **Conclusion:** We present a rare case of dysbetalipoproteinemia associated with apoE2/E4 genotype. Dysbetalipoproteinemia should be considered in patients who presented extremely high TG level

Figure 1. Eruptive xanthomas on patients' forearm

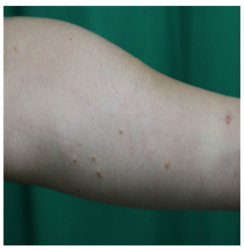
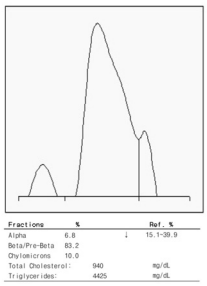


Figure 2. Lipoprotein electrophoresis demonstrating broad β band



Fractions	%		Ref., %
Alpha	6.8	↓	15.1-39.9
Beta/Pre-Beta	83.2		
Chylomicrons	10.0		
Total Cholesterol:	940		mg/dL
Triglycerides:	4425		mg/dL

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Case of euglycemic diabetic ketoacidosis precipitated by a sodium-glucose cotransporter 2 inhibitor

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Introduction: Inhibitors of sodium–glucose cotransporter 2 (SGLT2) decrease plasma glucose by blocking the reabsorption of glucose at the proximal tubule in kidney. However, in May 2015, the Food and Drug Administration (FDA) issued a drug safety communication that SGLT2 inhibitors may lead to diabetic ketoacidosis (DKA). We present the case of euglycemic DKA developed shortly after the treatment of a SGLT2 inhibitor. **Case:** A 36-year-old male presented with general weakness and weight loss during the last 2 weeks. He had no significant medical history. His capillary blood glucose was 417 mg/dl, hemoglobin A1C levels was 11.6% and urine ketones were positive at local clinic. Anion gap or arterial blood gas (ABG) analysis was not checked. He was diagnosed with type 2 diabetes mellitus (T2DM), was started on empagliflozin 5mg, metformin 500mg once a day. After 2 days on empagliflozin, he presented to our outpatient department with visual disturbance, nausea, anorexia and sweating. On physical examination he had stable vital signs with dry mucous membrane, clear breath sounds with no abdominal tenderness. His initial capillary blood glucose level was 178 mg/dL, ABG analysis showed high-anion gap acidosis with a pH of 7.26, and bicarbonate 8.7 mmol/L, an anion gap of 31.3, and lactate of 0.8 mmol/L and ketones were elevated in blood and were positive in urine. He was diagnosed with euglycemic diabetic ketoacidosis, probably due to recent administration of a SGLT2 inhibitor. He was treated with isotonic saline with additional dextrose fluid, and was started on intravenous insulin therapy. After ketoacidosis was improved, insulin drip was discontinued on the second hospital day. He was discharged home on hospital day 8 with metformin, insulin aspart. **Conclusion:** In this case, we learn that DKA can be abruptly developed in T2DM patients treated with SGLT2 inhibitors. Therefore, we should be aware that SGLT2 inhibitors can cause or aggravate DKA. Before prescribing SGLT2 inhibitors, physicians should carefully evaluate whether patients have symptoms and signs suggestive of metabolic acidosis, and perform necessary tests such as urine ketones, anion gap or ABG analysis.

Table 1. Laboratory data at admission

variable	value
Physical examination	
Age (y)	36
Height (cm)	153
Body mass index (kg/m2)	21.7
Arterial blood gas analysis	
pH	7.2
pCO2 (mmHg)	19
pO2 (mmHg)	107
HCO3 (mEq/L)	8.7
Base excess (mEq/L)	-16.1
Routine complete blood cell	
White blood cell(/mm2)	8900
Hemoglobin (g/dL)	17.4
Platelet(/mm2)	241
Blood Chemistry	
Sodium (mEq/L)	134
Potassium (mEq/L)	4.9
Chloride (mEq/L)	94
Blood urea nitrogen (mg/dL)	17.7
Creatinine (mg/dL)	0.85
Glucose (mg/dL)	193
Glycosylated Albumin (%)	40.4
C-peptide (ng/mL)	0.76
GAD II Ab (U/mL)	0.23
Total cholesterol (mg/dL)	182
Triglyceride (mg/dL)	159
High density lipoprotein (mg/dL)	36
Lactic acid (mg/dL)	0.8
Ketone (mmol/L)	3.5
C-reactive protein (mg/dL)	0.09
HbA1c (%)	12.4
Urinalysis	
Specific gravity	1.043
pH	6.0
Glucose	4+
Ketone body	3+