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A Rare Presentation of Type 1 Diabetes; "Children with Severe Hyperlipidemia" and Management of Hyperlipidemia: Case Report

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Diabetic ketoacidosis is the most common, life-threatening, acute complication of diabetes mellitus. Severe hyperlipidemia, causing lipemic serum, is rarely seen in case of diabetic ketoacidosis. Here, we will discuss a 10-years old girl who presented with ketoacidosis and had milky plasma appearance and severe hyperlipidemia. There was a milky appearance in blood sample drawn for biochemistry studies. In laboratory, blood sample could not be evaluated due to excessively lipemic sample; thus, repeated measurement was performed. In the second measurement, glucose, triglyceride, total cholesterol, LDL-cholesterol and HDL-cholesterol levels were found to be elevated. Diabetic ketoacidosis was considered as initial clinical diagnosis in our unconscious patient with acidotic respiration and acetone odor. With this case presentation we emphasized that serum lipid levels should be measured in diabetic ketoacidosis and diabetic children with poor glucose control. Additionally, we wanted to share management of hyperlipidemia in this case. It also should be kept in mind that blood measurements can be inaccurate in hyperlipidemic conditions; thus, stimulating the laboratory in the presence of hyperlipidemia may require a second measurement.

***Key Words**: Diabetic ketoacidosis, hyperlipidemia, children*

Nadir Bir Tip 1 Diyabet Sunumu; Şiddetli Hiperlipidemi Çocuklar ve Hiperlipideminin Yönetimi: Olgu Sunumu

Diyabetik ketoasidoz, diyabetin en sık, yaşamı tehdit eden, akut bir komplikasyonudur. Lipemik seruma yol açan şiddetli hiperlipidemi, nadiren diyabetik ketoasidoz vakalarında görülür. Burada, ketoasidoz ile başvuran ve sütlü plazma görünümü ve şiddetli hiperlipidemisi olan 10 yaşında bir kız sunulmuştur. Biyokimya çalışmaları için alınmış kan örneğinde süt görünümü vardı. Laboratuvarda, aşırı lipemik numune nedeniyle kan örneği değerlendirilemedi; bu nedenle, yenilenmiş ölçüm yapıldı. İkinci ölçümde, glukoz, trigliserid, toplam kolesterol, düşük yoğunluklu lipoprotein (LDL-kolesterol) ve yüksek yoğunluklu lipoprotein (HDL kolesterol) seviyelerinin yükselmiş olduğu tespit edildi. Diyabetik ketoasidoz, asidotik solunum ve aseton kokusu olan bilinçsiz hastamızda ilk klinik tanı olarak kabul edildi. Bu olgu sunumu ile serum lipit düzeylerinin diyabetik ketoasidozda ve düşük glikoz kontrollü diyabetik çocuklarda ölçülmesi gerektiğini vurguladık. Ayrıca, bu vakada hiperlipidemi yönetimini paylaşmak istedik. Aynı zamanda, kan ölçümlerinin hiperlipidemi koşullarında hatalı olabileceği akılda tutulmalıdır; böylece, hiperlipidemi varlığında laboratuvarı stimüle etmek ikinci bir ölçüm gerektirebilir.

***Anahtar Kelimeler:** Diyabetik ketoasidoz, hiperlipidemi, çocuklar*

Introduction

Type 1 diabetes mellitus is the most commonly seen endocrine-metabolism disease of childhood which is characterized by impaired energy homeostasis due to insulin deficiency and diabetic ketoacidosis which is the most commonly seen, life-threatening, acute complication of diabetes mellitus. Over 30% of the patients with newly diagnosed diabetes mellitus manifests by diabetic ketoacidosis. Mild hyperlipidemia in association with diabetic ketoacidosis is a common condition. However, severe hyperlipidemia and milky appearance of plasma is extremely rare (1). Particularly in children, there is limited number of cases with an association of severe hyperlipidemia and diabetic ketoacidosis. We presented a case which was diagnosed as type 1 diabetes mellitus and exhibited an association of ketoacidosis and severe hyperlipidemia by laboratory and clinical findings.

Case Presentation

A 10-years old girl was presented to pediatric emergency department with complaints of vomiting, headache and loss of conscious. She had no fever or diarrhea. Her parents reported that she had polydipsia and polyuria during last 2 days. There was no known risk factor for diabetes mellitus and hyperlipidemia in her personal and family history. In the initial examination loss of conscious, superficial and rapid respiration (kussmaul respiration), severe dehydration and acetone odor were detected; therefore, the patient was admitted to intensive care unit. In the physical

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Table 1. Shows the laboratory values of patient on admission and follow up period

	Reference Range	On admission		On follow-up	
		Day 1	Day 6	1 months after	1 years after
Triglyceride	0-200 mg/dL	8000	843	120	52.1
Total cholesterol	0-200 mg/dL	>1000	731	130	131
LDL-cholesterol	50-159 mg/dL	>800	53	60	65
HDL-cholesterol	35-65 mg/dL	>190	28.2	30	56
Creatinine	0.1-1.5 mg/dL	5	0.39	0.3	0.52
Sodium	135-146 mEq/dL	148	134	138	138
Potassium	3.5-5.1 mEq/dL	0.49	4.6	4	4.42
Chloride	98-108 mEq/dL	132	97.9	102	102
Calcium	8.2-10.5 mg/dL	0.95	10	9	9.82
AST	0-37 U/L	258	4	25	14
ALT	0-41 U/L	185	3.9	35	23

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, HDL: High density lipoprotein, LDL: low density lipoprotein

examination, following findings were recorded: heart rate, 140 beats/minute; blood pressure 110/70 mmHg; respiration rate 52/minute; body temperature 37°C. Mucosa was dry and capillary filling time was longer than 3 seconds. In auscultation, breath sounds were bilaterally equal, without any abnormal sounds. In abdominal palpation, abdomen was found to be free and no organomegaly was detected. Height was 130 cm (10^{th} percentile) and weight was 24 kg (3-10^{th} percentile). There was no pathological finding in the rest of physical examination. There was a milky appearance in blood sample taken for biochemistry studies. In laboratory, glucose 456 mg/dL, triglyceride (8000 mg/dL; reference range: 0-200 mg/dL), total cholesterol (>1000 mg/dL; reference range: 0-200 mg/dL), low-density lipoprotein (LDL) cholesterol (>800 mg/dL; reference range: 50-159 mg/dL), high-density lipoprotein (HDL) cholesterol (>190 mg/dL; reference range: 35-65 mg/dL), chloride (132 mEq/L; reference range: 98-108 mEq/L), calcium (0,95 mg/dL; reference range: 8.2-10.5 mg/dL), aspartat aminotransferase (AST) (258 U/L reference range: 0-37 U/L), alanine aminotransferase (ALT) (185 U/L; reference range: 0-41 U/) levels were found to be elevated. Complete blood count, coagulation tests and thyroid function tests were normal. BUN, creatinine, total protein, albumin and uric acid levels were also normal. In the urinalysis, the following findings were recorded: color, yellow; density, 1020; glucose, 3+; protein, 2+; hemoglobin, 3+; ketone, 3+. In the blood gas analysis, pH and HCO_3 were found as 6.99 and 5 mmol/L, respectively. She had acidemia, ketonuria and clinical findings consistent to diabetic ketoacidosis. In accordance with the management protocol of diabetic ketoacidosis, intravenous fluid and insulin treatment was initiated. Intravenous insulin treatment was replaced by subcutaneous insulin treatment and oral nutrition was permitted on the 24 hour after initiation of intravenous fluid and insulin treatment, when patient became conscious and Ph; >7.30, HCO_3; >15 mmol/L, ketone; negative. At the two week of follow-up, triglyceride, total cholesterol and LDL-cholesterol levels gradually returned to normal levels. No treatment was given for hyperlipidemia during this period. Table 1 presents baseline values at admission and final values.

Discussion

As diabetic patients with a known diabetes mellitus presents with diabetic ketoacidosis, patients with new onset diabetes mellitus may also manifest with diabetic ketoacidosis. Insulin is involved in protein and lipid metabolism, as well as glucose metabolism. Impaired lipid metabolism in diabetes mellitus has been known for several years (2, 3). Insulin decreases the use of free fat acids in cytogenesis in liver by inhibiting lipolysis. Also, it enhances degradation of chylomicrons by stimulating lipoprotein lipase. Lipoprotein lipase is an extracellular enzyme which is primarily located at fat tissue and capillary wall of heart and skeletal muscles. Lipoprotein lipase hydrolyzes triglyceride to monoglyceride, fat acid and glycerol. Fat acids are taken by fat tissue and muscles, where they are either used or stored. Chylomicron residues are taken by liver, where they are converted to apolipoprotein, cholesterol esters, cholesterol, fat acids and amino acids. Very low density lipoproteins (VLDLs) synthesized from triglycerides are transported to peripheral tissues and degraded by lipoprotein lipase. Insulin facilitates storage of triglycerides as fat tissue by acting on peripheral lipoprotein lipase (4). In case of insulin insufficiency such as uncontrolled diabetes mellitus, mobilization of fat acids is markedly increased, while usage is decreased. This results in increased fat acid load in liver. In patients with insulin insufficiency, enhanced lipolysis and decreased fat acid use and clearance result in hyperlipidemia. As in our case, insulin deficiency causes severe hyperlipidemia in patients with newly onset type 1 diabetes mellitus presented with diabetic ketoacidosis.

Severe hyperlipidemia has a higher morbidity and mortality when it is complicated by pancreatitis and leads diabetic ketoacidosis (5-8). Garnier et al. (9) reported that plasma lipid levels were decreased to normal values by insulin therapy in an adult patient with type V hyperlipidemia who presented with diabetic ketoacidosis

and pancreatitis. Cole et al. (10) reported that hypertriglyceridemia was successfully treated by using low dose unfractionated heparin in an adult patient presented with diabetic ketoacidosis and severe hypertriglyceridemia. Blackett et al. (11) reported that they treated a child with diabetic ketoacidosis and hyperlipidemia via insulin treatment alone. In our case, we think the primary illness was diabetes mellitus not primary hyperlipidemia. Therefore we treated the patient with only fluid and insulin treatment. With this treatment the hyperlipidemic and hyperglycemic state were getting to normal gradually. We also did not think pancreatitis due to normal amylase levels.

Severe lipemia impedes accurate measurements in laboratory test by 3 mechanism: 1) dispersion of light due to turbidity; 2) decrease in sample viscosity and; 3) division between polar and non-polar phases (12). Some biochemical parameters are found as high, while some others as low in hyperlipidemia. This is termed as biochemical interference. In a case report by Waseem et al. (13), it was found that serum sodium, potassium, chloride and bicarbonate values were low, whereas serum creatinine, triglyceride, total cholesterol were high. In that report, the authors managed their patient by insulin infusion and intravenous fluid therapy according to standard diabetic ketoacidosis protocol. After resolution of diabetic ketoacidosis, hyperlipidemia resolved and serum electrolyte levels returned to normal. In our center, blood glucose measurements are performed by enzymatic hexokinase method. When technical methods were investigated, no information was found about interaction between hyperlipidemia and blood glucose measurements or electrolyte levels. There is information suggesting that lipid levels above 250 mg/dL may lead false-elevation in AST, ALT and creatinine values.

Abnormally higher triglyceride levels suggest lipoprotein lipase or apolipoprotein C II deficiency. In severe hyperlipidemia caused by insulin deficiency as in diabetes mellitus, a decrease in lipid levels is anticipated when control of diabetes mellitus is achieved or diabetic ketoacidosis is treated. If severe hyperlipidemia persists despite treatment of insulin deficiency, further evaluations are needed for differential diagnosis. In our case, lipid levels returned to normal with insulin therapy and at follow-up hyperlipidemia did not recur in.

In children, association of severe hyperlipidemia and diabetic ketoacidosis manifested as lipemic serum has been rarely reported. Diabetic ketoacidosis is a condition which is related to high mortality and morbidity. Serum lipid levels must be measured in children with diabetic ketoacidosis or in those with poorly controlled diabetes mellitus. We observed that hyperlipidemia due to diabetes can be controlled successfully with insulin treatment**.**

Declaration of Interest

There is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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