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Insulin Therapy for Acute Pancreatitis in a Patient with Lipase Maturation Factor 1 Mutation: A Case Report

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CASE REPORT

Insulin Therapy for Acute Pancreatitis in a Patient With Lipase Maturation Factor 1 Mutation: A Case Report☆

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Abstract

Acute pancreatitis is a frequent cause of hospital admission, managed with intravenous (IV) fluids, analgesia, and oral feeding when tolerated. In patients with hypertriglyceridemia-induced pancreatitis, insulin and other therapies may be necessary for disease resolution. We present a case of a patient with severe acute pancreatitis and euglycemic diabetic ketoacidosis (DKA) with known lipase maturation factor 1 (LMF1) gene mutations, which can impact insulin efficacy on triglyceride metabolism through altered lipoprotein lipase activity, successfully treated with intravenous insulin. This case highlights the effectiveness of insulin therapy even in those with LMF1 gene mutations.

Keywords: Pancreatitis, Hypertriglyceridemia, LMF1 gene, Lipoprotein lipase, Insulin

1. Introduction

Prior research into the implications of lipase maturation factor 1 (LMF1) mutations comes from animal studies. However, we need studies clarifying the clinical manifestations associated with this mutation in hospitalized patients. Manifestations of LMF1 gene mutations include hypertriglyceridemia, pancreatitis, and atherosclerotic heart disease.[1] Presently, there is insufficient data regarding the prevalence of the LMF1 gene mutation in the general population. Therefore, it cannot be determined how commonly patients with hypertriglyceridemia have an underlying LMF1 mutation. Here, we aim to describe the clinical course and treatment of a patient with an LMF1 mutation who presented with acute pancreatitis and euglycemic diabetic ketoacidosis (DKA).

Our patient had a mutation in the LMF1 gene, which codes for a transmembrane protein in the endoplasmic reticulum that is involved with the production of lipoprotein lipase, hepatic lipase, and endothelial lipase.[2] Unsurprisingly, the deficiency in lipase in patients with a deleterious mutation in LMF1 leads to severe hypertriglyceridemia.[3]

At triglyceride levels above 1000 mg/dL, patients begin to develop chylomicronemia syndrome. Among the features of chylomicronemia syndrome are recurrent pancreatitis, abdominal pain, nausea, and vomiting independent of pancreatitis, lipemia retinalis, and hepatosplenomegaly.[4]

It has been well-established that insulin use can significantly lower triglyceride levels in the general patient population,[5] and a growing body of evidence supports the use of insulin drips as a mainstay of treatment in adult patients presenting with hypertriglyceridemia-induced pancreatitis.[6] Presently, the American College of Gastroenterology (ACG) does not specifically include insulin therapy formally for the management guidelines for hypertriglyceridemia-induced pancreatitis, although review articles have supported the efficacy of intravenous insulin in its management.[7,8] We highlight a unique case of hypertriglyceridemia-induced pancreatitis

☆ This case report has not been previously presented at any professional meetings.

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effectively managed with insulin in the setting of LMF1 gene mutation (in which intravenous insulin may not be expected to work).

2. Case report

Our patient is a 38-year-old male with a past medical history of pancreatitis secondary to hypertriglyceridemia complicated by necrotizing pancreatitis and pseudocyst, insulin-dependent type II diabetes diagnosed by Endocrinology at age 30, complicated by retinopathy, hypertriglyceridemia with LMF1 gene mutation, and obesity, who presented to the Emergency Department (ED) with a one-day history of sharp epigastric pain radiating to the back, nausea, vomiting, and subjective fevers and chills. Upon arrival, he was afebrile, had a blood pressure of 153/95 mmHg, a heart rate of 127 beats per minute, and had a normal oxygen saturation on room air, body mass index (BMI) 37.5. On physical exam, he was in no acute distress and had a soft, non-distended abdomen, with epigastric and right upper quadrant tenderness to palpation. Labs showed lipase 1134 units/L, LDL 66 mg/dL, HDL 10 mg/dL, triglycerides 2773 mg/dL, A1c 6.8%, anion gap 19 mEq/L, glucose 155 mg/dL, AST >4202 U/L, ALT >3899 U/L, total bilirubin 1.7 mg/dL, bicarbonate 14 mmol/L, HIV and HCV negative, acetaminophen level negative, urine drug screen positive for opiates after having received them in the ED. Urinalysis demonstrated 3+ ketones. CT abdomen findings were consistent with acute pancreatitis with peripancreatic fluid collection. RUQ US demonstrated no cholelithiasis, acute cholecystitis, or ductal dilation. The patient was compliant with all his outpatient medications including his basal and prandial insulin regimen, fenofibrate, metformin, empagliflozin, rosuvastatin, omega-3 fatty acid, lisinopril, and ergocalciferol.

The patient was admitted to the medical ICU for hypertriglyceridemia-induced acute pancreatitis in the setting of euglycemic DKA with a blood glucose of 155 mg/dL, bicarbonate 14 mmol/L, 3+ ketonuria, and arterial pH 7.3 with concurrent use of an SGLT2 inhibitor, empagliflozin. The patient received an insulin drip and IV fluids for management. The patient had three prior hospital stays, about 12 months apart from each other, the most recent being 12 months prior, for hypertriglyceridemia-induced pancreatitis which were managed similarly with insulin drip in the ICU that led to resolution of symptoms. His anion gap closed within 24 h of therapy initiation this admission, and his triglycerides improved to 464 mg/dL within four days of treatment. His liver enzymes normalized on repeat lab draws 4 h after admission, to AST 15 U/L, ALT 21 U/L and remained normal during his hospital stay. Given the rapid normalization of labs, history, physical exam, and negative workup for other etiologies of liver injury, the initial liver enzyme elevation was suspected to be a lab error. His symptom improvement correlated with these findings. His treatment transitioned to subcutaneous insulin once triglycerides dropped below 500 mg/dL. His home fenofibrate and omega 3 acid ethyl esters were continued at his home doses during his hospital stay and at discharge. The medicine team optimized his statin therapy to atorvastatin 80 mg daily. Atorvastatin was started in the hospital and continued upon discharge once his liver enzymes normalized. He was eventually discharged home with the resolution of pain and resumption of oral intake.

3. Discussion

The management of this patient centered on insulin to treat his hypertriglyceridemia and euglycemic DKA. Insulin lowers triglyceride levels by increasing the activity of lipoprotein lipase (which breaks down chylomicrons and very low-density lipoprotein in the blood) and by inhibiting the activity of hormone-sensitive lipase (which releases free fatty acids from adipose cells into the bloodstream).[9] However, lipoprotein lipase levels are found to be severely reduced in patients with mutations in the LMF1 gene, such as this patient.[10] No strong evidence has yet been published regarding efficacy of insulin use in patients with LMF1 mutations, and thus clinicians may falsely presume such patients would have less therapeutic success with insulin therapy. Despite having a mutation in the LMF1 gene and having experienced hypertriglyceridemia-induced pancreatitis several times, our patient did experience significant improvement in both glycemic control and hypertriglyceridemia with insulin therapy. This finding suggests insulin effectively reduces triglyceride levels, even in patients with LMF1 mutations. This case report is the first documented example of insulin therapy successfully lowering triglyceride levels and subsequently treating acute hypertriglyceridemia-induced pancreatitis in a human subject with LMF1 mutation.

In conclusion, this case supports the use of insulin to treat hypertriglyceridemia-induced pancreatitis in patients with LMF1 mutations (who will be subsequently deficient in lipoprotein lipase, a central component of the mechanism through which insulin

lowers blood triglyceride levels). Further investigation may be needed to understand how insulin is effective in patients with LMF1 mutations presenting with hypertriglyceridemia-induced pancreatitis.

Ethics information

All ethical practices were strictly followed by the authors.

Support

The authors have no sources of support to disclose.

Informed consent

Informed consent was obtained from the patient for publication of case details.

Conflict of interest

The authors have no conflict of interest to disclose.

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