Euglycemic DKA in MODY Patient: Empagliflozin to Blame.

Angela Magdaleno
Lehigh Valley Health Network, angela.magdaleno@lvhn.org

Sandhya Venkataraman DO
Lehigh Valley Health Network, Sandhya.Venkataraman@lvhn.org

Gretchen Perilli MD
Lehigh Valley Health Network, gretchen_a.perilli@lvhn.org

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Euglycemic DKA in MODY Patient: Empagliflozin to Blame

Angela Magdaleno, DO, Sandhya Venkataraman, DO and Gretchen Perilli, MD

Lehigh Valley Health Network, Allentown, Pennsylvania

BACKGROUND

- Diabetic ketoacidosis (DKA) occurs when the body's requirements for insulin are higher than the insulin available for use, resulting in lipolysis, ketogenesis, and ketoacidosis
- DKA is classically associated with Type 1 diabetes mellitus (DM), but can occur in any patient with diabetes
- Euglycemic DKA is defined by ketosis, metabolic acidosis, and a blood glucose level less than 200 mg/dL
- Euglycemic DKA is concerning as it can be easily misdiagnosed and mistreated
- Few cases have demonstrated a possible relationship between empagliflozin and euglycemic DKA
- Empagliflozin is a sodium glucose co-transporter (SLGT-2) inhibitor in the proximal convoluted tubule of the kidney to reduce reabsorbed filtered glucose, resulting in decreased serum glucose levels.

CASE PRESENTATION

42 year old female with mature onset diabetes of the young (MODY) type 2 presented to the emergency room with complaints of nausea, vomiting and epigastric abdominal pain worsening over four days. She was diagnosed with gestational DM at age 34 and post-partum was unsuccessfully treated with a variety of oral medications. She underwent testing which revealed a glucokinase mutation consistent with MODY type 2. Recently, she was started on empagliflozin-linagliptin in addition to a diet of less than 60 grams of carbohydrates per day. On admission, imaging was unrevealing, and she was diagnosed with gastroenteritis. Her serum glucose was 106 mg/dL, potassium was 4.6 mmol/L, bicarbonate was 21 mmol/L, anion gap was 14, and lipase was normal. Urinalysis revealed glucose of 500 mg/dL, ketones > 160 mg/dL, and specific gravity >1.030. Venous blood gas revealed metabolic acidosis. Beta hydroxybutyrate was 2.71 mmol/L. The patient was diagnosed with euglycemic DKA. Endocrinology discontinued empagliflozin, emphasizing that the only treatment required for MODY type 2 is diet restriction. Her symptoms improved, labs normalized, and she was discharged.

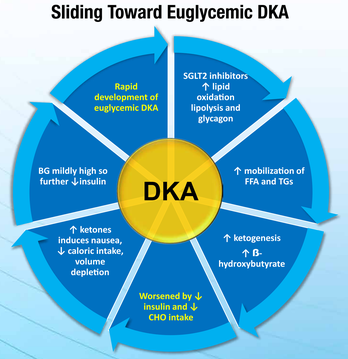

Figure: Demonstration of the cascade of clinical events and metabolic changes that contribute sequentially to progressive clinical deterioration and develoment of full-blown episodes of euDKA. BG, blood glucose; CHO, carbohydrate; TGs, triglycerides.

Table 1 - Genetic and Clinical Characteristics of MODY Subgroups

	MODY 1	MODY 2	MODY 3	MODY 4	MODY 5
Genetics	HNF-4α (20q13)	Glucokinase (7p15)	HNF-1α (12q24)	IPF-1 (13q12)	HNF-1ß (17cen-q21)
Prevalence	5%	15%	70%	< 1%	2%
Severity	Progressive IGT	Mild,stable hyperglycemia	Progressive IGT	Progressive IGT	Progressive IGT
Onset	12-35 years	Birth	12-28 years	14-40 years	12-28 years
Microvascular Complications	+	Rare	+	+	+renal
Treatment	Progressive need	Pregnancy	Progressive need	Progressive need	Progressive need

DISCUSSION

- This case demonstrates a deadly combination of inappropriate SGLT-2 inhibitor use causing decreased serum glucose levels in a MODY type 2 patient resulting in euglycemic DKA
- MODY Type 2 results from a defective glucokinase enzyme, therefore increased serum glucose levels are required to trigger insulin secretion
- Patients with MODY Type 2 often present with mild fasting hyperglycemia, which is required to stimulate insulin secretion
- In this case, empagliflozin resulted in decreased serum glucose and increased glucosuria. As a result, the body's demands for insulin were higher than the amount of insulin being secreted due to defective glucokinase enzyme, inducing DKA.

Image References:

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