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Case Report: Normoglycemic Diabetic Ketoacidosis Post Gastric Botulinum Toxin Injection for Weight Loss

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***Abstract*— True normoglycemic diabetic ketoacidosis (when the blood glucose is below 200 mg/dl) is relatively uncommon and in type 2 diabetes mellitus (T2DM) can be caused by starvation due to various reason, like prolonged fasting, malnutrition, persistent vomiting,post bariatric gastric surgery, chronic alcohol intake, Atkins diet, pregnancy and eating disorder. It is also encountered following the endoscopic procedure using gastric botulinum toxin injection as part of non-surgical bariatric procedure for weight loss in obese people. This procedure can be unsafe in diabetic patients as it is difficult to achieve glycemic control due to unpredicted gastric emptying time and the ability of the individual to have adequate nutrition. We report a case with normoglycemic diabetic ketoacidosis precipitated by starvation post gastric botulinum toxin injection in a patient with T2DM. On presentation patient was acidotic with positive blood ketones and a blood glucose levels of 106 mg/dl, after correction of acidosis the patient was discharged. This case highlights the need to assess the acid-based status even with normal blood glucose levels, especially in those who have received a gastric botulinum toxin injection resulting in poor oral intake.**

***Index Terms*— Botulinum toxin, ketoacidosis, starvation, type 2 diabetes mellitus.**

I. INTRODUCTION

Diabetic ketoacidosis (DKA) was formerly considered a hallmark of type 1 Diabetes Mellitus (T1DM), but it also occurs in individuals who lack immunologic features of T1DM and who can subsequently be treated with oral glucose-lowering agents[1].

DKA is associated with absolute or relative insulin deficiency, volume depletion, and acid-base abnormalities. Nausea and vomiting are often prominent, and their presence in an individual with diabetes warrants laboratory evaluation for DKA[1].

Diagnostic criteria of DKA as approved by American Diabetes Associations are hyperglycaemia (blood glucose of >250mg/dl), Metabolic acidosis (bicarbonate <15 meq/L and arterial PH <7.3), and ketosis (moderate ketonuria or ketonemia)[2]. However some cases of DKA have normal glucose levels, in the study of Munro et al and Jenkins et al, The possible cause for the normal or relatively low glucose was the low calorie intake triggered by starvation and persistent vomitingtogether with continuation of insulin treatment[2-4].

In present days obesity is the major cause of morbidity and there have been many recent advances for weight loss therapies as a cure for morbid obesity both non-surgical and surgical interventions, of which gastric Botox is one of them[5].

Gastric Botox is a new endoscopic procedure that speeds up weight loss by using Botox to temporarily relax the muscles of the stomach (the same botulinum toxin used to smooth facial wrinkles)[5]. Botulinum toxin will cause the muscles to contract less vigorously, making the person feel full more quickly and for longer than usual and greatly reducing the overall amount of food consumption[6]. Although persistent vomiting and inability to eat well can be one of the adverse effect of this procedure, making the diabetic more vulnerable for glycemic excursions[6]. We present here a case of normoglycemic ketoacidosis that highlights the need for assessment of acid-base status in patient with diabetes presenting post gastric botulinum toxin injection with nausea, persistent vomiting and reduced oral intake.

II. CASE HISTORY

A 45 year old female patient diagnosed to have T2DM one year back on oral diabetic medications, presented with history of reduced appetite, generalized weakness, drowsiness, fatigue, nausea, persistent vomiting and abdominal discomfort over the previous two weeks, she lost about 5 kg since procedure. She had undergone a gastric botulinum toxin procedure for weight loss about three weeks back following which she started experiencing the above symptoms.

She was severely dehydrated on the initial examination with normal blood glucose level (106 mg/dl), NA+ 130; k+ 3.4; Cl 102; PH 7.14; Serum HCO3- 7; Beta-Hydroxybutrate 10; Urine ketones 4 and HB A1C 10.2.The laboratory finding was suggestive of metabolic acidosis with high anion gap and her serum was positive for ketone bodies. Her body weight is 80 kg, height 165cm and BMI of 29.

A diagnosis of normoglycemic diabetic ketoacidosis was made with the precipitating factor thought to be the gastric botulinum toxin injection, patient was treated accordingly with intravenous fluid and low dose insulin infusion and she recovered within 24 hours and her glycemic status was within the normal range during the course of her hospital stay.She was discharged after 72 hours after receiving dietary instructions and an advice to avoid dehydration by taking plenty of fluids and liquid diet.

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III. DISCUSSION

DKA results from relative or absolute insulin deficiency combined with counterregulatory hormone excess (glucagon, catecholamines, cortisol, and growth hormone). Both insulin deficiency and glucagon excess, in particular, are necessary for DKA to develop. The decreased ratio of insulin to glucagon promotes gluconeogenesis, glycogenolysis, and ketone body formation in the liver, as well as increase in substrate delivery from fat and muscle (free fatty acids, amino acids) to the liver[1].

DKA is most often seen due to reduction in calorie intake which can be related to vomiting and poor oral intake caused by precipitating factors like infection, stress, non-compliance to medications or sometimes caused by worsening ketoacidosis itself[1].

During the period of low calorie intake, diabetic patients who continue taking enough dose of medication to maintain normoglycemia, but are unable to hold the ketone body formation can present with DKA even with mild hyperglycaemia or sometimes with relative normoglycemia [2],[3],[7]. In a situation of prolonged fasting, the glycogen depletion contributes to the normoglycemia as metabolic acidosis continues to develop [8],[9], lipolysis and the free fatty acid production are accelerated during fasting and insulin is less effective in suppressing the lipolysis and the ketogenesis resulting in more acidosis [10],[11]. Chronic liver disease and Glycogen storage disorder can reduce glycogen stores and can result in normoglycemic ketoacidosis and should be considered as a differential diagnosis [12],[13]. Pregnancy is also considered to be a state of accelerated starvation [14], and with the presence of increased insulin resistance the lipolysis and the ketogenesis will be more during pregnancy [15], so the diabetic patient can easily present with normoglycemic ketoacidosis especially during her early pregnancy as the nausea, vomiting and the decreased oral intake are more exaggerated [16],[17].

There may be a considerable overlap between the normoglycemic DKA and starvation ketoacidosis, as the relative normoglycemia in normoglycemic DKA occurs as a result of prolonged fasting [2-4]. The initial management must be as in any case of ketoacidosis, to correct the fluid and the electrolytes abnormalities and re-establish the carbohydrates metabolism. Higher percentage of dextrose 10-20 % are required to facilitate the concomitant administration of a relatively large amount of insulin that are needed for acidosis correction [2],[7],[17],[18].

Many obese individuals are opting for the endoscopic intervention procedure for weight loss[1],[5].

Botulinum toxin A has been used as a medical therapy for a few decades. In paediatrics it is commonly used to treat spastic disorders associated with cerebral palsy [19]. A novel use for Botulinum toxin A has been for gastrointestinal conditions targeting the lower oesophageal sphincter and more recently the internal anal sphincter, in order to decrease tone and/or increase relaxation[20-22]. It has recently been suggested that the use of intrapyloric botulinum toxin A injections (IPBI) may be a medical alternative to some surgical procedures[20-23]. IPBI effects on the pylorus muscle seem to be mediated by decreasing contractility and acetylcholine release from cholinergic nerves at low doses, and directly affecting the muscle tone at higher doses[21],[23]. The effect of Botulinum toxin A may not be limited just to the pyloric muscle. It has also been reported to be absorbed from stomach and intestine producing peripheral neuromuscular blockade [22],[23].

Recently there has been also use of gastric botulinum toxin for weight loss through endoscopic procedure. It is speeds up weight loss by using botulinum toxin to temporarily relax the muscles of the stomach[5]. Botox will cause the muscles to contract less vigorously, making the person feel full more quickly and for longer than usual -- greatly reducing the overall amount of food consumption. In fact due to gastric botulinum toxin injection there is difficulty in controlling blood glucose in diabetic patient resulting in hyperglycaemic episodes several hours after the meals[6].

IV. CONCLUSION

Diabetic Ketoacidosis following a gastric botulinum toxin injection is a rare and less reported complication, Physician should have a high index of suspicion in diabetics post gastric bypass who present with recurrent episodes of vomiting.

All diabetics who are undergoing botulinum toxin treatment should be counselled beforehand regarding frequent blood glucose monitoring, and the need to have small frequent meals and to maintain adequate hydration after the procedure. Normal blood glucose levels should not deter the physician from embarking on a search for a possibility of normoglycemic keto acidosis.

Management is similar as any case of ketoacidosis, primarily to correct the fluid and the electrolytes abnormalities and re-establish the carbohydrates metabolism. Higher percentage of dextrose 10-20 % is required to facilitate the concomitant administration of insulin that is needed for acidosis correction.

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