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CASE REPORT

The Practice of Emergency Medicine

Euglycemic diabetic ketoacidosis in a pregnant woman

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Abstract

Background: Euglycemic diabetic ketoacidosis (EDKA) carries serious risks for mortality and morbidity for both the mother and the baby, and it is essential to recognize it early and start immediate treatment.

Case Presentation: We present a case of EDKA in a 28-week pregnant woman known to have type 1 diabetes. She was found to have severe acidosis with a blood sugar level of 10.6 mmol/L (190.8 mg/dL) and normal anion gap. She was found to have EDKA, which was confirmed later with a depressed venous pH and bicarbonate level and an increased serum ketone level. The patient's acidosis was not improving significantly with 0.05 units/kg/h of insulin infusion, so a full dose of 0.1 unit/kg/h of insulin infusion was started following a full diabetic ketoacidosis (DKA) protocol regardless of her blood sugar level. The patient showed gradual improvement and was discharged home after 4 days, with follow-up with endocrinology and obstetrics.

Conclusion: In conclusion, EDKA is a critical complication of diabetes, especially in pregnant women. Therefore, it is crucial to treat it early and potentially consider following a full DKA protocol using 0.1 unit/kg/h insulin infusion instead of 0.05 unit/kg/h.

KEYWORDS
EDKA, insulin, pregnancy

1 | CASE PRESENTATION

A 26-year-old woman, 28 weeks pregnant, previously diagnosed with type 1 diabetes 5 years ago and currently receiving insulin injections and metformin, came into the emergency department (ED) with complaints of lower abdominal pain persisting for 1 day, accompanied by nausea and multiple episodes of vomiting. Initially, a registered nurse triaged the patient to the minor area because of full beds in the urgent area. The primary concern was to rule out preterm labor. However, the patient denied vaginal bleeding or amniotic fluid leakage, which was later confirmed on examination.

The initial vital signs were as follows: temperature, 97°F; heart rate, 105; respiratory rate, 20; blood pressure, 125/78. On examination, the patient appeared dehydrated, with a soft and non-tender abdomen. Chest examination revealed normal findings, no discharge on vaginal examination, and the cervix was closed.

The initial management focused on rehydration through the administration of 3L of Ringer lactate (RL) boluses given approximately 30 min apart. Considering the patient's severe dehydration and frequent vomiting episodes, a venous blood gas (VBG) and urine dipstick were performed in the minor area to assess for electrolyte disturbances and ketonemia, as part of the nausea and vomiting workup in pregnancy. Additionally, a complete blood count and metabolic panel were completed to investigate for further possible infectious causes, which were later reported to be within normal limits. The VBG results are presented in Table 1.

Furthermore, the urine dipstick revealed +4 ketones. Due to the critical value of metabolic acidosis, the patient was transferred to the

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TABLE 1 The patient's venous blood gas panel.

Parameter	Value
PH	7.17
CO_2	20 mm Hg
O_2	31 mm Hg
Potassium	4.4 mmol/L
Sodium	135 mmol/L
Glucose	10.6 mmol/L (190.8 mg/dL)
Bicarbonate	7.4 mmol/L
Lactate	1.7 mmol/L
Chloride	112 mmol/L

resuscitation bay. The time taken from triaging of the patient and initial treatment and assessment by the first physician in the minor area and shifting to resuscitation bay was 1 h and 20 min. In the resuscitation bay, the patient underwent reassessment, and although vital signs were stable, she exhibited slight tachypnea with a respiratory rate of 26. A bedside ultrasound revealed collapsibility of the inferior vena cava of >50% as the sole significant finding.

Given the patient's dehydration, additional RL boluses were administered, resulting in a total of 6L. Further history-taking revealed that the patient had not taken her insulin injections for 2 days, which she had been non-compliant with since her diagnosis, as reported by her family. She denied fasting or reducing her usual eating habits as well as alcohol consumption. Considering her medical background and the failure of acidosis to improve with adequate hydration, a presumptive diagnosis of euglycemic diabetic ketoacidosis (EDKA) was made. A blood sample was sent for serum ketones, which returned positive with a value of 4 mmol/L (23.24 mg/dL).

Because there are no specific guidelines or clear recommendations available for the management of EDKA, we followed our evidence-based clinical approach (EBCA) for the management of diabetic ketoacidosis (DKA) in adults in the ED. Our EBCA suggested decreasing the insulin infusion to half dose which is 0.05 units/kg/h instead of 0.1 unit/kg/h when the glucose level is below 11 mmol/L (198 mg/dL) and changing the fluid to 5% dextrose. Unfortunately, using this value of insulin, the correction of acidosis progressed slowly.

Consequently, the case was discussed with the medical intensive care unit, and they recommended administering a full dose of 0.1 units/kg/h for rapid correction of acidosis. Following their advice, the patient received a full dose of insulin infusion along with 5% dextrose fluids and potassium supplementation. The patient's general condition improved significantly, with resolution of tachypnea, nausea, vomiting, and abdominal pain. No infectious causes were identified, and the final diagnosis was determined as EDKA resulting from discontinuation of insulin.

Reaching the diagnosis and initiating appropriate management for this patient posed challenges. Vomiting in pregnancy is a common presentation and had the urinary ketones, serum bicarbonate and VBG not been considered in the minor area, the diagnosis could have been delayed, leading to the development of serious complications. Therefore, we strongly recommend expanding the differential diagnosis and taking appropriate measures to address the most likely conditions.

Another challenge was the management itself. Cases of EDKA in the emergency setting are rare, and their management is not a straightforward task. Seeking expert opinions in such cases is crucial for providing optimal patient care.

After consultation with obstetric specialists, fetal monitoring with cardiotocography and obstetric ultrasound were performed with reassuring results. After spending 7 h in the ED, the patient was admitted to the internal medicine ward. Following a 4-day hospital stay, she was discharged home safely. At 37 weeks of gestation, the patient was admitted for labor induction because of her uncontrolled blood sugar readings. While in the obstetric hospital, the patient underwent an emergency caesarian section for a non-reassuring fetal cardiotocography in the first stage of labor; there were no complications post-delivery for both the mother and the baby.

2 | BACKGROUND

DKA continues to be a commonly prevalent case in the ED requiring prompt diagnosis, hospitalization, and management, with the overall hospitalization rate steadily increasing from 2009 to 2014 at an average annual rate of 6.3% as per the Diabetes Surveillance System of the Centers for Disease Control and Prevention.[1]

It is worth mentioning that other conditions can present with metabolic acidosis, which can be divided into high anion gap metabolic acidosis conditions and normal anion gap metabolic acidosis conditions. Normal anion gab conditions including DKA, methanol ingestion, ethanol ingestion, uremia, lactic acidosis, starvation, and aspirin toxicity commonly present with high anion gap metabolic acidosis on the VBG test. Three of these conditions are known to cause high levels of ketone bodies (ketonemia\ketonuria), which are DKA, alcohol intoxication, and starvation.[2]

EDKA is a high anion gap metabolic acidosis condition that poses significant risks during pregnancy, affecting maternal and fetal well-being.[3]

3 | DISCUSSION

Many physiological factors contribute to the development of EDKA. First, pregnancy-induced respiratory alkalosis is compensated by a decline in bicarbonate levels, which induces metabolic acidosis and increases the risk of DKA. Second, pregnancy is considered a diabetogenic and ketogenic state due to insulin resistance, lipolysis higher free fatty acid levels and possibly ketogenesis,[4] together with hormones generated by the placenta and fetus, which can all block the effects of insulin. Third, the demand for insulin production rises as fetal and placental needs increase.[5]

There are two distinct mechanisms regarding potential causes of normal blood glucose levels in pregnant women with euglycemic DKA. The mother's and the fetus's nutritional demands are among the first causes. Increased intake of glucose by the fetus and placenta

can cause the mother's blood glucose level to drop as a result of a reduction in both glycogenolysis and hepatic glucose production.[6] In addition, the starvation state that occurs during pregnancy is more pronounced in the third trimester when the mother's metabolic rate increases by up to 300 kcal per day and can increase the likelihood of ketosis developing.[7]

The second mechanism is related to physiologic changes in body fluids during pregnancy. The hemodilution state that develops during pregnancy due to increased plasma volume might cause a fall in glucose concentration. Plasma volume increases by 40% in the pregnancy period.[8] An increased glomerular filtration rate, which may lead to significant glucose excretion in the urine, is another physiological factor that might contribute to the low glucose level in euglycemic DKA; all these causes combined can lead to the development of EDKA in pregnant women.[7]

Despite not being a common occurrence during pregnancy, DKA represents approximately 1% of diabetes complications in pregnant women[9] and 30% of these cases are euglycemic. Delaying diagnosis will exacerbate the potential of associated complications in both mother and fetus.[10] The exact pathogenesis of these complications is yet to be completely understood, and the literature on them remains minimal. However, severe fetal outcomes have been reported in the short and long term. Short-term ones include fetal hypoxia, cardiac arrhythmias, acidosis, and fetal demise, which have shown to reach up to 35%.[11] Studies of long-term complications have shown a link to lower IQ levels, with one study showing an inverse correlation between the ketone levels in the mother and the IQ score of the infant.[12] Furthermore, long-term complications included intellectual disabilities, including but not limited to autism and neurological problems such as seizure disorders.[10,13,14]

As for the maternal burdens of EDKA, they can be comparable to that of DKA in general. For example, cardiac complications described in the literature include electrolyte imbalance-induced arrhythmias, cardiogenic shock, and myocardial infarction. Other complications can be associated with the emergency cesarean sections that often accompany the diagnosis. Finally, a far less frequently discussed complication of DKA in pregnancy is its psychosocial and emotional impact on the mother and the family. This includes the distress that can come with possible intubation or the risk of losing the infant if the mother herself survives such a critical and life-threatening event.[15,16] Should the infant survive, there is psychological apprehension of possible future medical problems the child might have.

When it comes to the management of EDKA, there are no specifics guidelines or recommendations made by endocrinology societies.[17] This has urged us to look at the literature and see how similar cases have been treated. The most crucial step in the management is the early diagnosis and recognition of the disease itself to prevent severe complications for both the baby and the mother,[18] initial resuscitation with fluid boluses preferably using RL, to reduce the risk of developing hyperchloremic metabolic acidosis when using normal saline for resuscitation. Early use of dextrose 5% and even 10% dextrose is needed if the patient started to develop hypoglycemia with the insulin infusion,[19] our patient needed a total of 6 L RL all given as boluses, initially insulin infusion started at a rate of 0.05 unit/kg/h with 5% dextrose and potassium supplement. This was based on our ED EBCA for the management of adult with DKA according to the recommendation of Modi et al. Later on, the patient was started on 0.1 unit/kg/h of insulin infusion by the medical intensive care unit (MICU) team following a full regular DKA protocol regardless of the serum glucose levels; it is recommended to increase the dose of the insulin infusion if the patient's acidosis is not improving, especially in a patient with type 1 diabetes. Starting insulin infusion at a lower rate might not help improve the acidosis quickly, which was exactly the case in our patient.[19,20]

We have summarized the literature review in the Table S1, looking precisely at the used insulin doses. The articles we reviewed do not clearly show whether a full DKA protocol was used to treat EDKA. Some did not mention the insulin dosages, and some cases had unfavorable outcomes.

4 | CONCLUSION

We presented a case report of a pregnant young woman seeking medical attention at the ED due to nonspecific abdominal pain and vomiting. Subsequent investigation revealed the condition to be EDKA. We comprehensively examined the various approaches to managing EDKA and the associated challenges and reviewed the current literature on the management of EDKA.

Treating EDKA by following the regular DKA protocol will help rapidly correct acidosis. However, further trials should be done to come up with solid recommendations and guidelines on how much insulin should be used for treating EDKA, so the patients will be managed appropriately and have a better prognosis.

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