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ORIGINAL RESEARCH

Cerebrovascular Accident Complicating Diabetic Ketoacidosis in a Nigerian Adolescent: A Case Report and Review of the Literature

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Summary

Cerebrovascular accident (CVA) is a rare neurological complication of diabetic ketoacidosis (DKA) in the paediatric population. The risk of developing CVA in DKA patients is often increased due to abnormalities in coagulation factors, platelet activation, blood volume and flow, and vascular reactivity. Cerebral oedema, the most common neurological complication of DKA, may also predispose to CVA. We report the case of a -12-year-old adolescent with DKA complicated by CVA. She developed features of right hemispheric CVA while on admission and had radiological confirmation of an ischaemic CVA. This report highlights that cerebrovascular accidents in DKA can easily be missed or confused with cerebral oedema.

Keywords: Cerebral Oedema, Cerebrovascular disease, Hemiplegia, Hyperglycaemia, Stroke, Type 1 Diabetes mellitus.

Introduction

Diabetic ketoacidosis (DKA) is a well-reported complication of diabetes mellitus in resource-poor and advanced countries. [1 - 3] It is a medical emergency that combines the primary underlying mechanism of insulin deficiency with hyperglycaemia, metabolic acidosis, accumulated ketones in the blood or urine and increased anion gap. [4] In a study carried out by Ahuja *et al*., infections and non-compliance with insulin therapy were the most common risk factors for DKA in children.[5] Other risk factors associated with DKA include socioeconomic disadvantage, female gender, adolescence, high glycosylated haemoglobin (HbA1c), eating disorders and depression. [6] Cerebrovascular accident (CVA) is a rare complication of paediatric DKA. It accounts for about one-tenth of intra-cerebral complications in DKA. [7]

The systemic inflammation in DKA causes vascular endothelial damage, coagulopathy and elevation of inflammatory markers such as C-Reactive Protein, cytokines (IL6, IL1β, TNFa), and complement activation. [4, 8, 9] Furthermore, the oxidative stress induced by hyperglycaemia and ketosis may lead to tissue ischaemia. [9] Therefore, patients with DKA are predisposed to a higher risk of developing blood hyperviscosity and vascular injury, potential causes of ischaemic

CVA and haemorrhagic CVA, respectively. Diabetic ketoacidosis complicated by CVA is not necessarily accompanied by cerebral oedema [9], although it may mimic it on presentation as both conditions have overlapping clinical features. Therefore, it is crucial to distinguish CVA in DKA from cerebral oedema as the approach to management differs.

We report the case of a -12-year- old female adolescent with DKA complicated by CVA.

Case Description

AP, a known patient with Type 1 Diabetes mellitus (T1DM), diagnosed a year prior, presented at the Children Emergency Unit of the Lagos State University Teaching Hospital (LASUTH) in March 2019 with complaints of fever and vomiting of two days duration, generalized body weakness of a day duration, an episode of convulsion and unresponsiveness about 5 hours before presentation. Before referral, she had received an unknown quantity of intravenous fluids in a private hospital.

At presentation, she was unconscious with a Glasgow Coma Score (GCS) of 3/15, and her pupils were sluggishly reactive to light. Lateralizing signs were not observed at presentation. Based on CDC growth charts, the body length and weight were 151cm (47^{th} percentile, SD -0.07) and 49kg (76^{th} percentile. S.D.0.73), respectively. [10] She was febrile (38.3^{O} C), had deep breathing with tachypnoea (respiratory rate of 60 cycles per minute), tachycardia (heart rate of 160 beats per minute but a normal blood pressure of 110/70mmHg. The random blood glucose at admission was 338mg/dl. The full blood count showed neutrophilia (Table I). A diagnosis of DKA with cerebral oedema secondary to sepsis in a known patient with T1DM was made.

Table I: Summary of the results of laboratory investigations at the point of admission

Parameters	*Result*	*Comment*	*Reference*
Na	140mmol/l	Normal	133.0-150.0mmol/l
K	4.2mmol/l	Normal	3.5-5.0mmol/l
Cl	106mmol/l	Normal	96.0-110.0mmol/l
Hco3	5mmol/l	Low	18.0-32.0mmol/l
Urea	27mg/dl	Normal	10.0-50.0mg/dl
Creatinine	1.34mg/dl	High	0.5-1.10mg/dl
PCV	38%	Normal	37-47%
TWBC	27,900cells/mm^3	High	4000-11000cells/mm^3
Neutrophils	82.7%	High	40-75%
Lymphocytes	7.3%	Low	20-45%
Others	10%	High	0-7%
Platelets	231,000/mm^3	Normal	150,000-450000/mm^3
Urine Ketone	3+	High	Negative

Na – Sodium, K - Potassium, Cl - Chloride, HCO_3 -Bicarbonate, PCV - Packed Cell Volume, TWBC - Total White Blood Cells.

AP was commenced on intravenous Normal Saline at 10ml/kg in the first hour, with deficit and maintenance fluid given over the next 48 hours. She also received three doses of intravenous mannitol (0.5mg/kg) over 24 hours, along with furosemide to treat early-onset cerebral oedema. Hyperglycaemia was corrected as per the unit protocol with subcutaneous soluble insulin. She was placed on broad-

spectrum antibiotics (Intravenous Ceftriaxone 1g twice daily).

Subsequently, the random blood glucose range over the next three days was between 169mg/dl and 394mg/dl and fever had subsided by the third day of admission. Consciousness level gradually improved and was recorded as GCS of 10/15 on the third day of admission, at which time paresis of the left side of the body was noted. She regained full consciousness on the fifth day of admission with the persistence of the weakness of the left side of the body. A diagnosis of a right hemispheric ischaemic stroke was made and was confirmed by neuroimaging, which showed the presence of multiple lacunar infarcts in both cerebral hemispheres. (Figure 1) She regained full muscle activity by the tenth day of admission and was later discharged on subcutaneous basal-bolus insulin. No neurological sequela was noticed two years later.

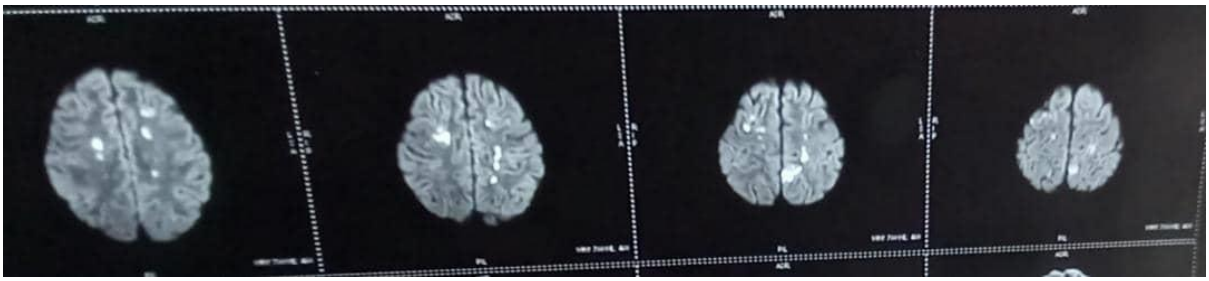

Figure 1: Coronal view of Brain MRI showing multiple small foci of restricted diffusion in both cerebral hemispheres

Discussion

Cerebral oedema is the most reported of the rare complications of DKA in children. [11] Perhaps CVA, another rare complication of DKA, has received less attention in the literature because it may have been frequently missed. Both complications share clinical features of generalized body weakness, headache, confusion, altered sensorium and increased respiratory rate. [8] These notable common features make diagnosis and distinction between the two conditions challenging, particularly when the patient cannot communicate. The diagnosis of DKA-related cerebral oedema in the index patient was based on the history of copious intravenous fluid infusion, unconsciousness, tachypnoea and sluggish pupillary reflex in a known patient with T1DM. These have earlier been described as early signs of DKA-related cerebral oedema. [12] Some reports also indicate that children who have had higher fluid volume and rapid correction of hyperglycaemia are more prone to develop overt cerebral oedema. [13] All researchers may not share this view as other reports indicate that cerebral oedema may occur from early ischaemic brain damage followed by reperfusion injury during treatment. [11, 14]

It is difficult to determine the onset of CVA in the index patient as she presented in an unconscious state. The focal sign of paresis, which led to the diagnosis, was only discovered as she regained consciousness and moved her limbs actively. This feature occurs in the minority of patients as less than 30% of patients with DKA-associated CVA have characteristic focal neurologic deficits. [9] Even though the mechanism of ischaemic CVA in children is not yet fully understood, DKA has been associated with tissue ischaemia. [8] Risk factors for CVA include metabolic abnormalities,

sickle cell anaemia, congenital heart disease, coagulopathies and infections.[4] The index patient had two risk factors: metabolic acidosis and leucocytosis.

An early brain MRI is highly recommended to confirm the diagnosis of CVA and ascertain the outset of CVA and other neurological impairment in patients with DKA. [11] In addition, CVA should be suspected in patients with DKA who do not respond to conventional treatment. The index patient had brain imaging studies that confirmed the diagnosis of CVA. Unfortunately, this may not be possible in resource-poor settings. Therefore all clinicians should have a high index of suspicion for CVA when managing children with DKA.

The clinical presentation of the index patient is similar to the report of Oludare *et al*. [15] in Southwestern Nigeria. The cases were referred for higher-level management, but they developed focal neurological deficits, which alerted the clinicians to brain imaging. Both patients, however, made a full recovery before discharge. Without a doubt, many of such cases may have been missed. It is also possible that some CVA mortality may have been erroneously attributed to DKA- associated cerebral oedema. [16]

It is essential to maintain hydration in all patients with DKA as hyperglycaemia and dehydration are potentially prothrombotic states and are associated with increased risk of intravascular thromboembolism. [8] Generally, the use of thrombolytic agents, adequate hydration, diet restrictions, infection control, physiotherapy, temperature and glycaemic control are important measures in managing children with DKA and CVA. [8] The use of thrombolytic agents for the treatment of paediatric CVA remains controversial, as few studies have documented its use. [11, 17] The index patient had careful attention paid to all the afore-mentioned measures but did not receive any thrombolytic agent.

Conclusion

A cerebrovascular accident, a rare complication of DKA, can occur as a complication of cerebral oedema or as an isolated case without cerebral oedema. Clinicians managing children with DKA should be aware of this complication as it can negatively affect the outcome and prolong hospital stay.

Declaration: Parental consent was obtained to publish the report.

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