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Key Words

Diabetic Ketoacidosis; Diabetic Ketoalkalosis; Metabolic Alkalosis; Chlorthalidone

Case Report

An Unknown Enemy in A Known Frontier

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Abstract

Diabetic Ketoalkalosis (DKAlk), a rare condition characterized by the coexistence of diabetic ketoacidosis and metabolic alkalosis, can obscure the classic presentation of ketoacidosis. We report the case of a 55-year-old male with type 2 diabetes and hypertension who presented with altered mental status, petechial rash, and drowsiness. Laboratory findings revealed severe hyperglycemia (777 mg/dL), elevated serum ketones (acetone 9.6), metabolic alkalosis (high anion gap: 26.8 mmol/L), and hypokalemia. The patient had a history of chlorthalidone use and tested positive for dengue fever. The metabolic alkalosis was attributed to diuretic-induced chloride depletion and activation of the renin-angiotensin-aldosterone system, which masked the underlying ketoacidosis. Treatment included standard diabetic ketoacidosis management with fluid resuscitation, insulin, and electrolyte correction. The patient improved significantly and was discharged on day four with an insulin regimen. This case underscores the importance of thorough acid-base analysis in hyperglycemic patients with atypical blood gas findings, particularly in the context of diuretic use or concurrent illnesses. Early recognition and prompt treatment of DKAlk are essential for favourable outcomes.

Introduction

Diabetes mellitus is one of the Top 10 causes of mortality in the world. The age-standardised disability adjusted life years (DALY) rate for diabetes increased in India by 39·6% (32·1–46·7) from 1990 to 2016, which was the highest increase among major non-communicable diseases [1]. Diabetic ketoacidosis remains one of the most frequently encountered complications of Diabetes that requires admission to intensive care unit. Diabetic ketoacidosis must have all the 3 components of the classic triad of capillary blood glucose > 200 mg/dL(>11mmol/L), venous pH of less than 7.3 and/or bicarbonate < 15 mmol/L, capillary ketone of >3mmol/L or urine ketones of ++ or more [2]. However, it could atypically present as an alkalaemia in patients with intractable vomiting, diuretic use, and hyperaldosteronism [3]. We present a probable first case of Diabetic ketoalkalosis secondary to diuretic use on a background of dengue fever.

Case Report

A 55-year gentleman known hypertensive and type 2 diabetes mellitus presented with altered mental status for last 3 days, generalised petechial rash for last 2 days and worsening drowsiness and slurred speech for 1 day. He had a history of slip and fall 3days back. On arrival to emergency his airway was patent and breathing spontaneously. His admission vitals were pulse rate 106beats/min, blood pressure 140/90mmhg, respiratory rate 19breaths/min and room air saturation of 98%. He was afebrile. On examination he was drowsy but arousable, no pallor, icterus, clubbing, cyanosis, and generalised lymphadenopathy. His presentation GCS was 13/15 (E3V4M6). His pupils were bilateral equal 2mm in size and were reactive to light. His plantar reflexes were flexors and moving all four limbs, sensory and cerebellar examination could not be done in view of his altered mentation. Other systemic examination was within normal limits. His bedside random blood sugar was 485mg/dl. His arterial blood gas revealed metabolic alkalosis with high anion gap lactic acidosis, his anion gap was twenty-four, corrected anion gap {to albumin which was 2.9}-26.8mmol/L.

His lab sugars were 777mg/dl and serum ketones {Acetone} were 9.6 and his HbA1C is 11.4. As a part of evaluation for his metabolic alkalosis we have sent urinary chloride which was 11mmol/L, which was <20 and is suggestive of "chloride responsive metabolic alkalosis". His initial laboratory investigations revealed Hb-14.9g/dl.TLC-7300/mm^3, platelets-1,02,000/mm^3, sodium-128mmol/L, potassium-2.9mmol/L, chloride-68.2mmol/L, magnesium-1.5mg/dl, calcium 8.4mg/dl, phosphorous 0.96, Urine analysis showed glucose 3+ and ketones 2+.

We made a provisional diagnosis of

- Diabetic ketosis with chloride responsive metabolic alkalosis and High anion gap metabolic acidosis, with dyselectrolytemia
- Altered mental status.
- Thrombocytopenia with petechial rash

We treated him as per Diabetic ketoacidosis protocolised fluids, insulin with electrolyte {potassium, phosphorous, magnesium} supplementation. As a part of evaluation for why he had this masked metabolic acidosis, we investigated his drug history and found he was on chlorthalidone for hypertension which explained his metabolic alkalosis with dyselectrolytemia and was stopped. MRI brain was done to evaluate the cause for drowsiness
revealed left occipito-temporal subacute hematoma.

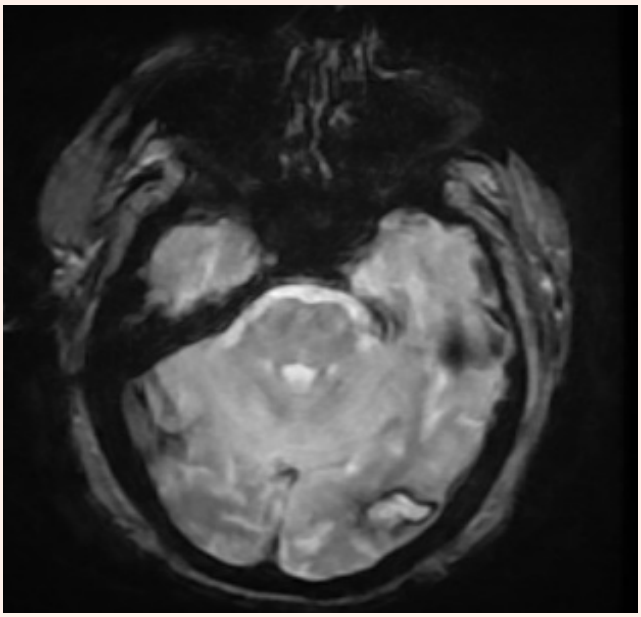
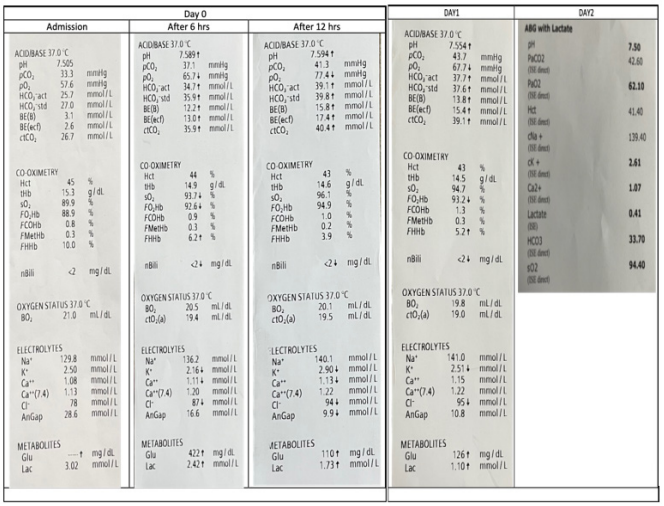


Fig.1: MRI BRAIN – GRE sequence

In view of thrombocytopenia and petechial rash, evaluation for tropical fevers was sent of which Dengue quantitative IgM was reported to be strongly positive 13.6{>11 positive}, which also could have contributed to his metabolic alkalosis (Contraction alkalosis) So, a possible diagnosis of dengue fever with Intracranial hematoma {? Fall related} with Diabetic ketoalkalosis with dyselectrolytemia was made. After aggressive hydration his lactates normalised after 6 hours and was continued with insulin infusion along with electrolyte supplementation. GRBS monitoring done every hour. His serial ABGs showed persistent metabolic alkalosis, due to longer half-life of chlorthalidone (40-60hrs). He was continued on IV fluids and insulin infusion. His urine and serum ketones became negative in next 2 days. He became fully conscious and was started on insulin subcutaneous scale and was shifted out of intensive care unit. On day four patient was discharged with fixed dose insulin s/c scale.

Table 1: Serial ABGs



Day 0			DAY1	DAY2
Admission	After 6 hrs	After 12 hrs		
ACID/BASE 37.0 °C	ACID/BASE 37.0 °C	ACID/BASE 37.0 °C	ACID/BASE 37.0 °C	ABG with Lactate
pH 7.505	pH 7.589↑	pH 7.594↑	pH 7.554↑	pH 7.50
pCO_2 33.3 mmHg	pCO_2 37.1 mmHg	pCO_2 41.3 mmHg	pCO_2 43.7 mmHg	PaCO2 42.60
pO_2 57.6 mmHg	pO_2 65.7↓ mmHg	pO_2 77.4↓ mmHg	pO_2 67.7↓ mmHg	PaO2 62.10
HCO_3^-act 25.7 mmol/L	HCO_3^-act 34.7↑ mmol/L	HCO_3^-act 39.1↑ mmol/L	HCO_3^-act 37.7↑ mmol/L	
HCO_3^-std 27.0 mmol/L	HCO_3^-std 35.9↑ mmol/L	HCO_3^-std 39.8↑ mmol/L	HCO_3^-std 37.6↑ mmol/L	Hct 41.40
BE(B) 3.1 mmol/L	BE(B) 12.2↑ mmol/L	BE(B) 15.8↑ mmol/L	BE(B) 13.8↑ mmol/L	cNa+ 139.40
BE(ecf) 2.6 mmol/L	BE(ecf) 13.0↑ mmol/L	BE(ecf) 17.4↑ mmol/L	BE(ecf) 15.4↑ mmol/L	cK+ 2.61
$ctCO_2$ 26.7 mmol/L	$ctCO_2$ 35.9↑ mmol/L	$ctCO_2$ 40.4↑ mmol/L	$ctCO_2$ 39.1↑ mmol/L	cCa2+ 1.07
CO-OXIMETRY	CO-OXIMETRY	CO-OXIMETRY	CO-OXIMETRY	Lactate 0.41
Hct 45 %	Hct 44 %	Hct 43 %	Hct 43 %	(SID)
tHb 15.3 g/dL	tHb 14.9 g/dL	tHb 14.6 g/dL	tHb 14.5 g/dL	HCO3 33.70
sO_2 89.9 %	sO_2 93.7↑ %	sO_2 96.1 %	sO_2 94.7 %	sO2 94.40
FO_2Hb 88.9 %	FO_2Hb 92.6↑ %	FO_2Hb 94.9 %	FO_2Hb 93.2↓ %	
FCOHb 0.8 %	FCOHb 0.9 %	FCOHb 1.0 %	FCOHb 1.3 %	
FMetHb 0.3 %	FMetHb 0.3 %	FMetHb 0.2 %	FMetHb 0.3 %	
FHHb 10.0 %	FHHb 6.2↑ %	FHHb 3.9 %	FHHb 5.2↑ %	
nBili <2 mg/dL	nBili <2↓ mg/dL	nBili <2↓ mg/dL	nBili <2↓ mg/dL	
OXYGEN STATUS 37.0 °C	OXYGEN STATUS 37.0 °C	OXYGEN STATUS 37.0 °C	OXYGEN STATUS 37.0 °C	
BO_2 21.0 mL/dL	BO_2 20.5 mL/dL	BO_2 20.1 mL/dL	BO_2 19.8 mL/dL	
	$ctO_2(a)$ 19.4 mL/dL	$ctO_2(a)$ 19.5 mL/dL	$ctO_2(a)$ 19.0 mL/dL	
ELECTROLYTES	ELECTROLYTES	ELECTROLYTES	ELECTROLYTES	
Na^+ 129.8 mmol/L	Na^+ 136.2 mmol/L	Na^+ 140.1 mmol/L	Na^+ 141.0 mmol/L	
K^+ 2.50 mmol/L	K^+ 2.16↓ mmol/L	K^+ 2.90↓ mmol/L	K^+ 2.51↓ mmol/L	
Ca^{++} 1.08 mmol/L	Ca^{++} 1.11↓ mmol/L	Ca^{++} 1.13↓ mmol/L	Ca^{++} 1.15 mmol/L	
$Ca^{++}(7.4)$ 1.13 mmol/L	$Ca^{++}(7.4)$ 1.20 mmol/L	$Ca^{++}(7.4)$ 1.22 mmol/L	$Ca^{++}(7.4)$ 1.22 mmol/L	
Cl^- 78 mmol/L	Cl^- 87↓ mmol/L	Cl^- 94↓ mmol/L	Cl^- 95↓ mmol/L	
AnGap 28.6 mmol/L	AnGap 16.6 mmol/L	AnGap 9.9↓ mmol/L	AnGap 10.8 mmol/L	
METABOLITES	METABOLITES	METABOLITES	METABOLITES	
Glu —↑ mg/dL	Glu 422↑ mg/dL	Glu 110↑ mg/dL	Glu 126↑ mg/dL	
Lac 3.02 mmol/L	Lac 2.42↑ mmol/L	Lac 1.73↑ mmol/L	Lac 1.10↑ mmol/L	

Table 2: Serial labs

Discussion

Diabetes mellitus is characterised by hyperglycemia due to lack of insulin or decreased tissue sensitivity to insulin. One of the more severe and commonly feared complications is Diabetic Ketoacidosis (DKA), a hallmark of type 1 diabetes though seen in type 2 diabetes and is the result of uncontrolled production of ketone bodies (3-hydroxybuturate, acetoacetic acid and acetone), leading to metabolic acidosis [4]. Ketoalkalosis (also called "masked DKA" or "alkaline ketoacidosis") refers to cases of ketoacidosis in which the acidosis is overridden by a coexisting alkalosis. Several factors participate in the alkaline masking of the ketoacidosis. Common features are vomiting and activation of the renin-angiotensin-aldosterone system because of hypovolemia leading to loss of hydrogen and chloride ions. Diabetic Keto-Alkalosis (DKAlk) was first described by Bleicher in 1967 [5]. Since then, there have been >30 cases of diabetic ketoalkalosis reported and continues to be a rare pathology for the clinicians to recognise [6].

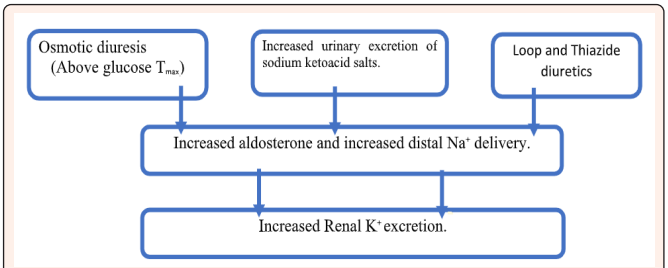


Fig 2: Coupling effect of Na^+ and aldosterone in uncontrolled diabetes.

Both volume depletion and diuretic use as seen in our case act by a common mechanism of activating the renin–angiotensin–aldosterone system which stimulates renal tubules for sodium reabsorption, bicarbonate reabsorption and new bicarbonate generation, the latter two effects are accomplished by the secretion of hydrogen ions into the tubular lumen [7]. Hyperaldosteronism will, in turn, induce hypokalaemia which contributes to the generation of metabolic alkalosis by shifting hydrogen ions

from the extracellular fluid to the intracellular fluid in exchange for potassium and by increasing renal bicarbonate reabsorption [7,8]. When we look at varied arterial blood gas presentation of Dengue fever around 7.36% patients had metabolic alkalosis [9], which also could have contributed to our patient's metabolic alkalosis in addition to diuretics. Chlortalidone is slowly absorbed from the gastrointestinal tract after oral ingestion. It has a long half-life (40-60hours) and therefore a prolonged diuretic action [10]. Second, chlorthalidone being present in the blood for a longer period might permit more drug exposure in tissue compartments where the drug has its effects [11]. This complex interplay presents as metabolic alkalosis despite having a high anion gap metabolic acidosis and ketosis. In most of the cases that were previously published, diabetic ketoacidosis was masked by an alkalotic picture with vomiting being the primary clinical presentation. Whereas in our case chronic use of diuretic and Dengue fever was thought to be the reasons behind this unusual presentation. Treatment of diabetic ketoalkalosis doesn't differ from the treatment of DKA and intravenous fluid administration remains as the mainstay of treatment along with insulin infusion, electrolyte correction and hourly GRBS monitoring. Since diabetic ketoalkalosis is a less known entity with limited availability of literature, it is common to underdiagnose a patient who presents with such a clinical presentation and may lead to delayed treatment. By presenting this case we hope that it will contribute to a better understanding of atypical acid base interaction that might occur in the background setting of diuretic use or vomiting or hyperaldosteronism. To conclude, an initial presentation with alkalosis in blood gas of a hyperglycemic patient should prompt the physician to evaluate for masked diabetic ketoacidosis, which is a life-threatening condition if not identified and treated early.

Conclusion

By presenting this case we hope that it will contribute to a better understanding of atypical acid base interaction that might occur in the background setting of diuretic use or vomiting or hyperaldosteronism. An initial presentation with alkalosis in blood gas of a hyperglycemic patient should prompt the physician to evaluate for masked diabetic ketoacidosis, which is a life-threatening condition if not identified and treated early.

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