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Severe Alkalemia (pH 7.85): Compatible with Life? A Triple Acid-Base Conundrum

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ABSTRACT

Acid- Base disorders are a common occurrence seen in emergency medicine. An infrequent occurrence is one with a triple acid base disorder in which one of the derangement predominates to generate an alkalemia with a pH of > 7.60. Severe alkalemia with a pH > 7.65 is associated with a high mortality rate. Early recognition and aggressive management of the underlying acid base disorders is imperative for survival. Here we describe a case in which a patient presented with a gapped metabolic acidosis, presumed secondary to diabetic ketoacidosis, as well as a concurrent severe metabolic alkalosis with a pH of 7.85 and a respiratory alkalosis, which was secondary to a paradoxical unexpected respiratory response.

INTRODUCTION

Mixed acid-base disturbances commonly result from failure of compensatory mechanisms, too little or too much compensation Metabolic alkalosis is seen frequently with excessive vomiting, milk-alkali syndrome, nasogastric suctioning, diuresis, post-hypercapnia states, severe hypokalemia, contraction alkalosis, chlorouretics, laxative abuse, villous adenoma, cystic fibrosis etc [1, 2]. Extreme alkalemia with arterial pH> 7.55 is associated with a mortality rate of > 45% and an arterial pH> 7.65 is associated with mortality rates in excess of 80% [3]. Metabolic alkalosis can be divided into “chloride responsive” versus “ chloride resistant” based on the urine chloride. Chloride responsive alkalosis is often due to intravascular volume loss or contraction alkalosis [4]. Acute compensation for metabolic alkalosis includes the respiratory system [1]. Untreated metabolic alkalemia is life threatening and can lead to seizures and even death.

CASE PRESENTATION

A 55 year old female with past medical history of IDDM, gastroparesis, and chronic pancreatitis presented with one day history of abdominal pain in the right lower quadrant and around the colostomy site. The patient had associated dry heaving, significantly reduced oral intake secondary to dry heaving and shortness of breath. The patient noted that she has needed to empty her ileostomy bag more frequently over the past week. Patient stated she was compliant with taking her insulin, but had not taken it that day. Review of systems was negative except as above.

The patient’s past medical history was significant for diastolic heart failure, insulin dependent diabetes mellitus, gastroparesis, chronic pancreatitis, and breast cancer. Her surgical history consisted of having a lumpectomy (2005), appendectomy (2007), cholecystectomy (2008), a Whipple procedure, J-tube

placement, and a diverting colostomy (2012). Patient lives with her husband and denied any smoking, alcohol, or illicit drug use.

On physical examination, patient was normotensive with a heart rate of 87 with tachypnea with normal pulse ox and normothermia, was ill appearing and cacechtic. Patient was uncomfortable due to pain. Patient had dry mucus membranes and had pain over abdomen diffusely without rebound or guarding. Patient did have reduced bowel sounds. Patient's ostomy site was unremarkable.

A central line was placed due to difficult access. While the central line was being placed, the patient began showing signs of confusion. The first arterial blood gas returned the following values: pH > 7.85, pCO_2 < 19mmHg, pO_2 113 mmHg, bicarbonate 31mmol. A second arterial blood gas was ordered, which showed a pH > 7.85, pCO_2 21mmHg, pO_2 99mmHg, bicarbonate of 31 mmol. The basic metabolic profile returned the following values: glucose 594 mg/dL, sodium 124mmol/L, potassium 5.1 mmol/L, chloride 68 mmol/L, bicarbonate 33 mmol/L, blood urea nitrogen 44mg/dL, creatinine 3.90mg/dL, calcium 6.8 mg/dL, phosphorus 6.4 mg/dL, magnesium 0.9 mg/dL, lactate of 4.3, and moderate amount of acetone in blood. Liver function test, lipase, urinalysis, coagulation profile were unremarkable.

ER COURSE

Based on the laboratory results a diagnosis of a triple acid base disorder was made. She was found to have a severe primary metabolic alkalosis with a secondary respiratory alkalosis and a tertiary gapped metabolic acidosis. Despite being alkalotic, the patient had an anion gap of 23, with expected bicarbonate from this disorder of 14, if she had a simple gapped acidosis. Yet her actual bicarbonate level was 31, therefore indicating a severe primary metabolic alkalosis, as well as a respiratory alkalosis from her presumed diabetic ketoacidosis. At this time the patient received four liters bolus of normal saline along with being started on an insulin drip. The patient was electively intubated and sedated to precisely control her minute ventilation with the intent of increasing her PCO_2 and thereby decrease her pH quickly. While preparing for intubation, the patient had an acute onset of generalized seizure activity for which patient received lorazepam two milligrams intravenously for four doses total, which controlled the seizures. The patient was successfully intubated. The pulmonary critical care team as well as the nephrology team were contacted for vent assistance as well as metabolic derangements. Patient respiratory rate was set to 6 to help retain carbon dioxide.

Several hours after fluid administration and initiation of mechanical ventilation, patient's blood gas had normalized with a pH of 7.47 and bicarbonate had decreased to 27. Her ICU stay consisted of aggressive volume resuscitation with normal saline, to increase her intravascular volume and replete her large chloride deficit. She remained sedated through the night, in order to prevent her from "over-breathing" the ventilator and increasing her minute ventilation. She received multiple liters of normal saline intravenously and in the morning she was weaned off propofol and successfully extubated.

DISCUSSION

Triple acid-base disorders are not an uncommon phenomenon in patients who delay seeking medical care with conditions that have a predisposition for metabolic derangements. The patient that presented to our emergency room had alkalemia severe enough to mask the gapped metabolic acidosis. However, the clinician must always remember to calculate the anion gap for each patient regardless of the initial serum bicarbonate. Metabolic alkalosis is produced by a gain in bicarbonate or loss in hydrogen ion. Etiologies of metabolic alkalosis are traditionally divided into two categories based upon its relationship with urine chloride concentrations. Chloride responsive metabolic alkalosis is typically caused by loss of GI hydrogen ions secondary to vomiting or excessive nasogastric suctioning, congenital chloride diarrhea, volume contraction, diuretic use, and post hypercapnia. Chloride resistant metabolic alkalosis is typically caused by bicarbonate retention, severe hypokalemia, hyperaldosteronism, Barter and Gittleman syndromes, and milk-alkali syndrome. A review of literature revealed that acidbase disorders are a common phenomenon, but severe metabolic alkalemia is less common. With a pH of 7.55 mortality rate is 40% and with a pH of 7.65 mortality rate is in excess of 80% [1, 3].

Chloride responsive metabolic alkalosis can be defined as a metabolic alkalosis with a concomitant urine chloride concentration of less than 15 mEq/L. Chloride responsive metabolic alkalosis tends to create a more clinically relevant alkalosis [3]. The underlying etiology of the loss of hydrogen ion comes from the kidneys or gastrointestinal tract, vomiting or excessive nasogastric suctioning results in a direct loss of hydrochloric acid. Severe vomiting typically produces hypokalemia and hyponatremia in addition to the loss of hydrogen and chloride ions. The compensatory mechanism of the kidneys results in increased sodium resorption at the expense of increased hydrogen ion losses. Potassium depletion independently augments bicarbonate resorption at the proximal convoluted tubule with a resultant increase in ammonia production fur-

ther enhancing hydrogen ion excretion [5]. It is this urinary hydrogen loss which creates the paradoxical aciduria that is frequently encountered in severe metabolic alkalosis.

Although diarrhea and lower gastrointestinal losses typically produce a loss of bicarbonate ions thus producing a metabolic acidosis, it must be noted that in certain disease states, severe diarrhea can elicit a chloride responsive metabolic acidosis. This is best understood in patients with villous adenoma. Villous adenomas of the colon usually produce a hyperchloremic metabolic acidosis because of the loss of large volumes of colonic fluid rich in potassium and bicarbonate. However, 10 to 20% of these tumors will secrete chloride rather than bicarbonate with potassium, and thus result in metabolic alkalosis. These patients possess a down regulated adenoma gene. The adenoma gene directs synthesis of an intestinal anion transporter or a regulator of such a transporter. The exact mechanism is unclear. A similar phenomenon is seen in other patients with a described congenital chloride wasting diarrhea. Compounding this chloride loss, severe diarrhea often produces a clinically significant hypokalemia. Severe hypokalemia produces an intracellular acidosis, and bicarbonate ions are shifted intracellularly thus worsening the alkalosis.

It must be noted that metabolic alkalosis from both upper and lower gastrointestinal losses is quite frequently compounded by concomitant volume contraction. Volume contraction is a potent mechanism for metabolic alkalosis especially when the etiology has a component of hydrogen ion loss as seen in persistent intractable vomiting. The mechanism of volume contraction producing a metabolic alkalosis is typically explained by two separate mechanisms. The first mechanism is based upon knowledge of the extracellular fluid compartment being relatively bicarbonate poor. Depletion of extracellular volume will produce an increased loss of water in relationship to bicarbonate thus producing a net alkalosis. Secondly it must be noted that renal compensation for volume loss also likely plays a role in the resultant alkalosis. Hypovolemia produces a decrease in renal blood flow and stimulates the renin angiotensin aldosterone axis. Renin secretion is increased and stimulates an increase in the sodium hydrogen exchange as well as an increase in bicarbonate reabsorption in the proximal tubule. Aldosterone secretion is also increased and stimulates the hydrogen-ATPase within the intercalated cells of the collecting duct. This produces an increase in hydrogen secretion in the distal tubule as well as an increased catabolism of bicarbonate which is immediately resorbed.

Although our patient suffered from severe lower gastrointestinal losses via her ileostomy, it is unlikely that her alkalosis was secondary to a congenital chloride wasting diarrhea or a villous adenoma. Severe volume contraction combined with upper gastrointestinal hydrogen ion losses secondary to vomiting is the most likely explanation of her severe alkalemia.

Severe alkalemia with a pH > 7.6 can result in compromise of cerebral and myocardial perfusion. This occurs due to arteriolar vasoconstriction. Neurologic manifestations that occur include headache, tetany, altered sensorium, seizures, lethargy, and delirium. Some of these manifestations are due to decreased ionized calcium. Immediate recognition and treatment is necessary to prevent further damage to these organs. If respiratory response is appropriate and bicarbonate levels are greater than 45 mmol/L, with a pH > 7.55, the goal is to decrease bicarbonate levels below 40 mmol/L as well as stopping the ongoing process leading to the metabolic alkalosis such as treating emesis with an anti-emetic or an H2 blocker or proton pump inhibitor if there is active gastric drainage. Simultaneously fluids should be given in the form of NaCl or KCl if needed, to help with azotemia and to induce bicarbonaturia [6]. Schwartz et al looked at the pathogenesis produced by chloride depletion alkalosis and noted that chloride repletion with NaCl or KCl fully corrected chloride depletion alkalosis in maintenance phase. Volume expansion was studied in rats where they had chloride depletion alkalosis and were given 5% dextrose with 6% albumin or isotonic chloride solution. The rats that had the former infusate, had persistent chloride depletion alkalosis despite an increase in extra-cellular fluid, whereas the latter infusate corrected the alkalosis [4].

A unique aspect to this case is the presence of a respiratory alkalosis concomitant to the underlying primary metabolic alkalosis. This is physiologically paradoxical to the overall clinical picture. Alkalemia triggers a decrease in minute ventilation to allow for respiratory compensation by retention of carbon dioxide. Upon presentation the patient was documented to be profoundly tachypenic with a respiratory rate in the 40's. Under normal physiologic circumstances this degree of alkalemia would be expected to produce a very low respiratory rate. This phenomenon is the compensatory central respiratory suppression precipitating a feeling of breathlessness or air hunger, and therefore producing the tachypnea responsible for her respiratory alkalosis [7, 8]. Upon initiation of mechanical ventilation with adequate sedation utilizing propofol, the patient was found to be essentially apneic on the ventilator. The change in respiratory rate was likely due to adequate sedation removing the anxiety and breathlessness associated with such a severe alkalosis. This was unlikely due to direct propofol induced respiratory suppression. Respiratory suppression due to propofol administration is dose dependent and typically not seen at the dosages administered for inten-

sive care unit sedation [9, 10]. It has been previously noted that compensatory hypoventilation is inconsistent and controversial in the setting of severe metabolic alkalosis [11]. Upon further evaluation one may assert that the anxiety associated with air hunger and resultant respiratory alkalosis supersedes the compensatory hypoventilatory mechanism driven by severe alkalemia.

Acid base management needs to be approached in the same, step-wise algorithm with each patient presenting to the emergency room. First, the clinician must determine if the two sets of data (arterial blood gas and serum basic metabolic profile) were drawn concomitantly, in order to ensure accuracy of the data. The bicarbonate on the ABG and serum should be within 2 mEq/L of each other. Then, the change in plasma sodium and chloride from normal values needs to be determined. If sodium changes alone, then it is a primary "hydration" problem. If the chloride change is not reflected by a similar change in sodium, then an acid-base disorder is present. Next, the anion gap should be calculated. In a simple gapped acidosis, the increase in anion gap should be approximately equal to the decrease in the bicarbonate. Our patient's expected bicarbonate was 14, yet the actual was 31, indicating a concurrent severe metabolic alkalosis. Next, the decrease in chloride in a metabolic alkalosis should be approximately equal to the increase in bicarbonate. Lastly, the degree of compensation can be determined based on which is the most severe and primary disorder. In our patient, this was chloride responsive metabolic alkalosis. Therefore the formula to determine compensation is pCO_2 = 0.9 x (HCO3-) + 9 +/- 2. Our patient's expected $paCO_2$ was 36, however was actually 21, indicating a third respiratory alkalosis disorder [12-14]. This patient that presented to the emergency room, in the acute setting had gapped metabolic acidosis due to diabetic ketoacidosis, respiratory alkalosis and a severe primary metabolic alkalosis, which was mainly due to two etiologies. Both resulted in a chloride depleted state. The chloride depletion likely was secondary to excessive emesis of one week duration with associated increase in ileostomy drainage, which led to severe volume contraction precipitating chloride loss. Most life-threatening metabolic alkalosis are chloride responsive. The patient in the emergency department needed two things, intravascular volume replacement and chloride repletion, which was provided in the form of four liters of normal saline infused simultaneously wide open. The patient was also electively intubated to control her minute ventilation. Given the isotonic saline replacement, and permissive hypercapnia through mechanical ventilation, patient's metabolic/respiratory derangements dramatically improved over the course of the day. Patient was admitted in the intensive care unit and later extubated the next day and a couple of weeks later discharged.

CONCLUSION

Life-threatening alkalemia is uncommon in the emergency department setting, however early recognition and treatment is imperative for patient survival. Quickly, based on a physical examination and the urine chloride, all metabolic alkalosis can be divided into chloride responsive and chloride resistant [15-17]. Typically severe life threatening causes are chloride responsive. Thus, with the exception of patients presenting with gross volume overload on physical exam, early and adequate fluid resuscitation with isotonic saline is a critical first step in therapy. Normal saline administration should not be delayed awaiting urinary chloride concentrations despite the potential for altering the true concentration prior to fluid resuscitation. Elective intubation of the patient allowing for ventilatory control and resulting permissive hypercapnia further assists in normalizing serum pH while simultaneously repleting serum chloride as was the case in the case presented. Triple acid base disturbances represent an interesting part of acid base management. The clinician must always remember to calculate the anion gap before any other calculations are completed, regardless of the serum pH or bicarbonate concentrations. Then the primary disorder can be deduced and compensation calculations after that. By following the same, simple acid base algorithm with each and every patient, complex acid-base disorder will more likely be identified.

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