Falsely Normal Anion Gap in Severe Salicylate Poisoning Caused by Laboratory Interference

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Severe salicylate poisoning is classically associated with an anion gap metabolic acidosis. However, high serum salicylate levels can cause false increase of laboratory chloride results on some analyzers. We present 2 cases of life-threatening salicylate poisoning with an apparently normal anion gap caused by an important laboratory interference. These cases highlight that the diagnosis of severe salicylism must be considered in all patients presenting with metabolic acidosis, even in the absence of an increased anion gap. [Ann Emerg Med. 2011;58:280-281.]

INTRODUCTION

Salicylates are present in many prescription and over-the-counter medications and are used commonly for their anti-inflammatory and analgesic properties. More than 20,000 salicylate exposures were reported to US poison centers in 2009.1 Salicylate toxicity is classically associated with an anion gap metabolic acidosis. We describe 2 cases of life-threatening acute aspirin overdose in patients with a normal anion gap.

CASE REPORT

Case 1

A 33-year-old woman presented after a reported ingestion of a bottle of aspirin and alcohol approximately 2 hours before arrival. She presented tachypneic (respiratory rate=29 breaths/min), with normal mental status. Ten minutes after arrival in the emergency department (ED), the patient experienced a 15-second generalized tonic-clonic seizure. This was followed 10 minutes later by a reported episode of pulseless wide-complex tachycardia, which resolved after administration of 150 mEq of intravenous sodium bicarbonate. A sodium bicarbonate infusion was initiated. Her laboratory values returned shortly, with levels of sodium 139 mmol/L, chloride 123 mmol/L, serum bicarbonate 13 mmol/L, and serum glucose 102 mg/dL. Her serum salicylate level was 110 mg/dL. An arterial blood gas result showed a significant metabolic acidosis and respiratory alkalosis (pH 7.21, pCO2 32 mm Hg, pO2 152 mm Hg, calculated serum bicarbonate 12 mmol/L). She received hemodialysis, during which her apparent hyperchloremia resolved, resulting in an increase in her calculated anion gap (Figure 1). The patient recovered fully.

Case 2

A 52-year-old man was brought in by ambulance to the ED after his supervisor called the police when he did not arrive at work in the morning. EMS found the patient at home drowsy but still alert and oriented to person, place, and time. On ED arrival, he was tachypneic (respiratory rate=20 breaths/min) and diaphoretic. He denied ingestions other than alcohol use 12 hours before with his usual dose of diazepam. Shortly thereafter, his initial laboratory values returned, with levels of sodium 142 mmol/L, chloride 111 mmol/L, serum bicarbonate 22 mmol/L (calculated anion gap 9 mmol/L), and serum glucose 115 mg/dL. His serum salicylate level was 54.6 mg/dL. At that point, the patient admitted to ingesting 150 tablets of 325 mg of aspirin 14 hours before. His arterial blood gas showed both metabolic acidosis and a primary respiratory alkalosis (pH 7.41, pCO2 25 mm Hg, pO2 93 mm Hg, calculated serum bicarbonate 16 mmol/L). He continued to absorb salicylate during the next 11 hours achieving a highest recorded concentration of 95.3 mg/dL. Increasing salicylate levels were accompanied by a paradoxic decrease in the calculated anion...
gap. The patient underwent hemodialysis and recovered fully. Analysis of data from both cases showed an apparent linear relationship between serum salicylate concentrations and measured serum chloride levels (Figure 2).

DISCUSSION

We present 2 cases of moderate to severe salicylate poisoning in which patients had a normal anion gap and apparent hyperchloremia. Other causes of hyperchloremia, including renal, oncologic, and endocrine disorders, were ruled out through history, physical, and laboratory evaluation, suggesting that increased serum salicylate was the cause of the apparent hyperchloremia. Rare previous reports in the nephrology and clinical chemistry literature have described a false increase in serum chloride measurements that occurs in the presence of high concentrations of salicylate.2-5 This interference appears to occur with some ion-selective electrodes but not others and may be due to loss of selectivity over the operational life of the chloride electrode, as well as competition between salicylate and chloride ions to bind to albumin.4 Our laboratory uses a widely used Siemens Dimension Vista analyzer (Neward, DE), which uses a proprietary ion-sensitive chloride electrode. With this analyzer, salicylate levels of 20 mg/dL are known to produce a 4% increase in reported chloride levels, and salicylate levels of 60 mg/dL are known to produce a 15% false increase in serum chloride.6 The data from our patients produce a linear relationship between salicylate concentrations and chloride values similar to that reported in other articles (Figure 2).4,5 Review of maintenance records showed that the electrode on our hospital’s analyzer had been recently changed, in accordance with user manual instructions.

Metabolic acidosis caused by an accumulation of salicylic acid, lactic acid, and ketone bodies is a hallmark feature of severe salicylate poisoning. Salicylate poisoning classically results in an increased anion gap.7 One retrospective study suggested that screening for salicylism is not needed because significant cases would be detected by an increased anion gap.8 However, our cases clearly show that an increased anion gap cannot be relied on as an indicator of salicylate intoxication in all cases. Physicians caring for patients with severe salicylate poisoning should be aware that the anion gap may be falsely normal in this population because of pseudohyperchloremia. In cases of poisoning with incomplete history, the diagnosis of severe salicylism should be considered in the setting of metabolic acidosis, even if the anion gap is normal.

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