Wide anion gap metabolic acidosis caused by food protein allergy in infants: A 2-case report

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ABSTRACT

Two infants (aged 12 and 16 months) presented with failure to thrive was reported in this study. Clinically, both infants looked normal and neither had respiratory dyspnea. However, wide anion gap metabolic acidosis was observed in the sera of both children, and both had acidic urinary pH. Specific IgE to cow’s milk protein, egg white, and egg yolk was negative in the first infant, while in the second infant specific IgE to cow’s milk protein was positive. The patch test for cow’s milk protein and egg yolk were also positive in the second infant. Metabolic acidosis was markedly improved in both children after discontinuation of cow’s milk and egg. There was recurrence of metabolic acidosis in the first infant after he was reintroduced to cow’s milk. Both children thrived and had no metabolic acidosis after dairy product and egg restriction and could tolerate cow’s milk and egg after one year of food restriction.

Key words: Food protein allergy, infant, loss of appetite, metabolic acidosis, wide anion gap.

INTRODUCTION

Metabolic acidosis is a clinical disturbance that is characterized by an increase in plasma acidity. Although severe episodes can be life-threatening, metabolic acidosis is sometimes a mild condition that can only be detected by blood sampling. Metabolic acidosis can be the caused by different conditions including ketoacidosis, lactic acidosis, renal tubular acidosis and hyperchloremic acidosis. The serum anion gap has been used to identify errors in the measurement of electrolytes, to detect paraproteins and to evaluate patients with suspected acid-base disorders (Kraut and Nagami, 2013). Here, we report two infant-aged children presented with failure to thrive, and both had blood investigation that revealed wide anion gap metabolic acidosis.

CASE REPORT

Case 1

A 12-month-old female infant was referred to the hospital due to a failure to gain weight for 3 months. He was diagnosed with transient renal tubular acidosis at six months of age, and took Shohi’s solution since the diagnosis. Her parents subsequently observed a marked decrease in his appetite during the 3-months period prior to his visit to the hospital. His past history was unremarkable. On physical examination, his weight and length were 9,000 g and 73 cm, respectively. Vital signs were temperature 36.5°C, respiratory rate 28/min, blood pressure 100/70 mmHg and heart rate 92/min. He was active, fully conscious, not distressed, and had no pallor or jaundice. Other examinations and complete blood count were unremarkable. Urinalysis revealed a pH of 5, with all of the other values being normal. His first serum electrolyte investigation showed 136 mmol/L sodium, 4.2 mmol/L potassium, 102 mmol/L chloride and 15 mmol/L bicarbonate. The anion gap was 19. Blood test for specific IgE to cow’s milk, soy protein, egg white, egg yolk, and wheat were all negative. Dairy products and egg were subsequently eliminated from his diet. Four weeks later, his appetite returned to normal, and his serum electrolytes were 139 mmol/L sodium, 4.5 mmol/L potassium, 103 mmol/L chloride, and 25 mmol/L.
bicarbonate, while the anion gap was 11. The Shohl’s solution was then discontinued and his subsequent serum electrolyte levels remained normal. Three months later, he was challenged with cow’s milk and his serum bicarbonate dropped to 15 mmol/L.

Acidosis was improved by dietary restriction of dairy products and after 5 months of dietary restriction, his parents reintroduced whole egg into his diet, which led to generalized urticaria. After 1 year of food restriction, he could tolerate dairy products and egg without metabolic acidosis.

Case 2

A 16-months-old, male infant was referred to the hospital due to failure to gain weight for 4 months. He had otherwise been thriving well since birth. Since weaning, he has been regularly consuming regular baby foods and whole cow’s milk daily. On physical examination, his weight and length were 10 kg and 79 cm, respectively. His vital signs were temperature 36.8°C; respiratory rate 30/min, blood pressure 90/60 mmHg, and heart rate 90/min. He was active, alert and had no pallor or jaundice. His first complete blood count showed eosinophil count of 1,200/mm³. Urinary analysis showed a pH of 5, with normal results for all other values.

Serum electrolytes were 140 mmol/L sodium, 4.6 mmol/L potassium, 104 mmol/L chloride and 17 mmol/L bicarbonate. The anion gap was 19. Specific IgE was positive to cow’s milk but negative to egg. Patch tests for cow’s milk and egg yolk were positive and after elimination of dairy products and egg from his diet for 1 month, his serum electrolytes were 140 mmol/L sodium, 4.6 mmol/L potassium, 104 mmol/L chloride, and 22 mmol/L bicarbonate. The anion gap was 14. His appetite returned to normal and he increased body weight to 11 kg within 6 months. After one year of food restriction, dairy products and egg were reintroduced into his diet after which there was no recurrence of metabolic acidosis.

DISCUSSION

The two cases described in the report were almost identical. Both children were thriving until more solid foods were gradually introduced into their diets. Except for loss of appetite, no other clinical findings of metabolic acidosis were observed in either patient. According to our review of the literature, only two other infants have been reported with metabolic acidosis caused by food protein allergy (Masson and Cecile, 1996; Rizk et al., 1999). These patients were often misdiagnosed of renal tubular acidosis, and Shohl’s solution was prescribed to treat acidosis. Although Shohl’s solution could increase the serum bicarbonate in our patients, those levels were still below normal. The poor appetite observed in our patients did not improve until after the correct diagnosis was made, diet restrictions were imposed, and their metabolic acidosis subsided.

Since their urine pH levels were within acidic range, we were of the view that acidosis was caused by loss of bicarbonate in the urine. Moreover, loss of bicarbonate through the gastrointestinal tract was not considered since neither of the patients had diarrhea. Both of the immediately aforementioned conditions are almost always associated with normal anion gaps, which was not the case in our patients. The wide anion gap metabolic acidosis in our patients suggests the presence of organic acids in the blood circulatory system.

Masson and Cecile (1996) and Rizk et al. (1999) reported lactic acidosis in infants with cow’s milk protein intolerance. The plausible explanation for this condition is allergic reactions to foods in the small bowel, which causes malabsorption of dietary carbohydrates. The residual carbohydrate was then fermented by the bacteria in the large bowel, which results in the formation of lactic acid in the stool (Davidovics et al., 2017; Puwanant et al., 2005). The lactic acid was thereafter absorbed into the circulation thereby causing wide anion gap metabolic acidosis. The most reliable method for diagnosing food protein intolerance is the withdrawal of suspected foods, with subsequent observation for improvement in symptoms. Both of our patients showed marked improvement in metabolic acidosis within 2 weeks after withdrawal of dairy products and egg, which were both high-suspicion foods. In addition to normalization of their serum bicarbonate levels, their appetites also returned to normal. Both children began to gain weight after restriction of the suspected foods. After 1 year of avoidance of dairy products and egg, both foods were successfully reintroduced into the diets of both children with no observed reemergence of metabolic acidosis.

Clinical manifestations including failure to thrive and loss of appetite increased suspicion for the presence of wide anion gap metabolic acidosis caused by food protein allergy. Both children in this report returned to normal after diagnosis and restriction of suspected allergenic foods. After 1 year, both children were able to tolerate all restricted and non-restricted foods without recurrence of metabolic acidosis. Until now, there is no available report on the mechanism of the ‘wide anion gap’ metabolic acidosis in food allergy. There were reports of severe lactic acidosis in cow’s milk protein intolerance. The ‘wide anion gap metabolic acidosis’ is an unique manifestation of this disease which has not been reported before.

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REFERENCES


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