DISTAL RENAL TUBULAR ACIDOSIS A RARELY DIAGNOSED CAUSE OF FAILURE TO THRIVE: A REPORT OF THREE CASES

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SUMMARY

Three cases of distal renal tubular acidosis aged between 6 - 12weeks are described. The presenting features included lethargy, refusal to feed, marked periodic respiration, vomiting and recurrent episode of unexplained metabolic acidosis. A constant feature was failure to thrive despite caloric intake in excess of normal requirements. The diagnosis of distal renal tubular acidosis was based on a urine P^H>5.5 in freshly voided urine despite the presence of metabolic acidosis. All the babies responded promptly to sodium bicarbonate supplement. An increased suspicion of distal tabular acidosis in the evaluation of children in early infancy for failure to thrive is therefore advised.

Keywords: *Renal tubule, Acidosis, Failure to thrive, Bicarbonate*

INTRODUCTION

Children who fail to thrive are a common diagnostic problem in Paediatric practice. Primary or non-organic failure to thrive due to inadequate calorie intake accounts for the majority of the cases seen.[1] However, the cases due to organic (or secondary) failure to thrive constitute a small proportion, encompassing malfunction in any of the organs or systems of the body. Most of these secondary cases have a variety of differential diagnoses, therefore a child with secondary failure to thrive poses as a diagnostic deliemma.[2] In the tropical region such as ours where there is widespread prevalence of chronic or recurrent infections, non-infectious causes or secondary causes of failure to thrive are not often promptly recognized. This report presents three infants seen over one and half years with failure to thrive secondary to distal renal tubular acidosis (DRTA) and is presented to help raise awareness and the index of suspicion of this unusual cause.

CASE REPORTS

Case I

A U was a male infant who presented at age of 6 weeks with two day history of lethargy and refusal to feed. Baby was a product of eight month gestation. Antenatal history was uneventful and delivery took place in a general hospital. Breastfeeding was not exclusive; water was given in the first 24hours of life. The Apgar scores and birth weight were not known. Physical examination revealed a lethargic and cachexic infant. The weight on admission was 1.3Kg, length was 46cm and the initial laboratory findings included PCV of 45 percent, total white cell count of 8,280/mm^3 with 60% neutrophils, 32% lymphocytes and 6% of monocytes. Blood and urine culture yielded no growth. Random blood sugar was normal he was then commenced on naso-gastric tube feeding and treated with antibiotics (Ampiclox and Genticin) for one week. There was no weight gain over twenty-two days despite the caloric intake in excess of normal requirement. Serum chemistry revealed normal Na^+ of 135mmol/L, K^+ 3.0mmol/L, creatinine 20µmol/L. The bicarbonate level was low 15mmol/L and a simultaneous urine specimen P^H8.0. Further treatment was with oral sodium bicarbonate (4mmol/1kg/24hrs) and after about ten days of commencing bicarbonate there was weight gain and the patient was discharged against medical advice.

Case II

A B was a ten week old male infant who presented with diarrhoea of two days duration, with deep and fast breathing on day of admission. Antenatal history was uneventful and delivery was at home by a Nurse. Physical examination revealed a mildly dehydrated and wasted infant weighing 2.5kg. The breathing was acidotic. He was managed with intravenous fluids and bicarbonate. The sepsis work up was positive. Blood culture yielded Staphylococcus aureus and the patient was therefore placed on Ampiclox and genticin for seven days. The diarrhea subsided and the respiratory pattern became normal within 24hours of admission. The weight on admission increased to 2.7kg following rehydration and by the eight day of admission the weight was 2.85kg. The patient was therefore discharged on ninth day of admission with a one-week appointment to be seen in the follow-up clinic.

At presentation at the follow-up clinic, the patient came with history of recurrent diarrhea with 5% weight loss and acidotic breathing. Urinalysis showed P^H of 6.5 and specific gravity of 1001. The creatinine

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was 32µmol/L. Intravenous sodium bicarbonate 4mmol/kg was given and continued with oral bicarbonate supplementation at 8mmol/kg/day. With this treatment there was resolution of acidosis and the weight gain was dramatic.

Case III

AM presented at 3months with failure to thrive. She was a product of term pregnancy with no peri-natal problems, birth weight was not known. Physical examination revealed a small for age infant, weight was 2.5kg less than the fifth percentile. The baby was admitted in order to supervise her feeding. After three weeks, the weight increased to only 2.7kg despite a caloric intake of 120kcal/kg/day and the absence of any obvious systemic illness. The serum urea and electrolytes check showed that $HC0_3$ was 18mmol/L with a urine P^H = 5.8. The other electrolytes were essentially normal. After 48hrs, a review of the electrolytes showed that $HC0_3$ was 16mmol/L and the P^H of urine was 6.8. A diagnosis of distal renal tubular acidosis was made. The patient was commenced on sodium bicarbonate 8mmol/kg/day orally and there was prompt weight gain.

DISCUSSION:

Renal tubular acidosis is characterized by normal anion gap, hyperchloraemic metabolic acidosis and associated failure to thrive secondary to growth failure as well as anorexia.[3] Distal renal tubular acidosis is a primary abnormality of failure to lower P^H in the presence of systemic acidosis because of impaired distal tubular H^+ secretion.[4] Reabsorption of bicarbonate is generally normal but because of the elevated urine P^H, a degree of bicarbonaturia can be present.[4] Further evaluation can be achieved with acid loading, urine to blood Co_2 tension[5] and frusemide challenge test. Recent research has shown that patients with recessive distal renal tubular acidosis have mutations in the genes encoding subunits of the H^+- ATPase in the intercalated cells, this therefore explains the failure of H^+ secretion.[6] There are four distinct types namely; distal or classic or type 1 renal tubular acidosis (RTA), type 3 RTA, is a hybrid of types 1 and 2 and type 4 is accompanied by hyperkalaemia in contrast to others. The urine P^H alone is considered a useful screening test of renal acidification. Infants (older than 14days) who have a higher endogenous acid production generally have a urine P^H less than 6.0.

Therefore, a urine P^H of $\geq$ 5.5 despite acidosis is diagnostic of distal RTA. The constant feature in our three patients was failure to thrive that persisted in spite of caloric intakes of 130 150kcal/kg/day. Two of our patients had urine $P^H \geq 6.5$ despite concomitant acidosis, thus confirming distal renal tubular acidosis (DRTA).

The third patient presented with P^H 5.8, there is the need to confirm diagnosis by ammonium chloride loading test. This particular test could not be done because of lack of reagents for this test at the period.

Under poor socio-economic conditions maternal under-nutrition is associated with a decreased birth weight and often an inadequate breast milk production.[8] The infants of these mothers are at risk for primary failure to thrive. Also, at about 16weeks of age when breast milk production has slowed down, nutritionally adequate weaning diet may not have been introduced due to the Baby Friendly Hospital Initiative (BFHI) programme that encourages exclusive breast feeding. When growth failure starts during the early infancy period, it may be due to a wide range of underlying diseases. However, when there are no clues to specific organ or system involvement, then hypermetabolic states such as anaemia and low grade or cryptic infections like urinary or fungal infections need to be considered. In the absence of these hypermetabolic states, various inborn errors of metabolism are the most likely aetiology. Metabolic acidosis, a common feature of several inborn error of metabolism presenting in the neonatal period is usually severe and progressive and commonly has other findings in addition to failure to thrive and acidosis. With primary renal tubular acidosis, there is no obvious systemic disorder and associated findings are related to the renal tubular dysfunction.[9]

Sepsis evaluation was positive in one of the cases and was placed on antibiotics for seven days without improvement. There were no findings suggestive of inborn error of metabolism. All the patients responded to 8-10mmol/kg/day of bicarbonate therapy; growth velocity increased by 140-170g/week during period of sodium bicarbonate.

Distal renal tubular acidosis if undiagnosed leads to continued growth retardation, rickets, polymigard nephrocalcinosis. Adequate treatment can improve most of the symptoms; the nephrocalcinosis may be irreversible and may lead to chronic renal failure (CRF). Therefore, since distal renal tubular acidosis can be treated cheaply and effectively, early recognition of primary DRTA is of foremost clinical importance. This will be possible with attention to the non-specific symptoms of vomiting, polyuria, dehydration and particularly failure to thrive and a high index of suspicion.

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