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Distal Renal Tubular Acidosis, an Uncommonly diagnosed Cause of Failure to Thrive: Report of Five Cases

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Summary

Ajayi OA, Mokuolu OA. Distal Renal Tubular Acidosis, an Uncommonly diagnosed Cause of Failure to Thrive: Report of Five Cases. *Nigerian Journal of Paediatrics* **2001; 28:21.** Five cases of distal renal tubular acidosis aged between 2½ weeks and 2½ months are described. The presenting features included lethargy, refusal to feed, marked periodic respiration, vomiting and recurrent episodes of unexplained metabolic acidosis. A constant feature was failure to thrive despite caloric intakes in excess of normal requirements. The diagnosis of distal renal tubular acidosis (DRTA) was based on a urine pH>5.5 in a freshly voided urine despite concurrent or induced metabolic acidosis. All the babies responded dramatically to sodium bicarbonate supplement, as baking soda or bicarbonate of soda. The need for increased index of suspicion of DRTA in the evaluation of children in early infancy for failure to thrive and the simplicity of treatment using baking soda is discussed.

Introduction

THE infant or child who is failing to thrive is a common diagnostic problem in paediatric practice. Primary or non-organic failure to thrive (FTT), due to inadequate caloric intake accounts for majority of the cases.[1] Cases of secondary or organic FTT, though constituting a small proportion, encompass malfunction in any of the organs/systems of the body resulting in a long list of differential causes.[2] Most of these aetiological causes are encountered rarely, hence, an infant or child with secondary FTT poses a 'needle in a haystack' diagnostic problem. Furthermore, because of the widespread prevalence of chronic or recurrent infections in the tropics, non-infectious causes of secondary FTT are not usually promptly recognized. This paper presents 5 infants, seen over two years, with early growth failure secondary to distal real tubular acidosis (DRTA), an uncommonly recognized but readily treatable cause of FTT.

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Case Reports

Case One

SR was a male infant who presented at the age of 14 days with a two-day history of lethargy and refusal to feed. The child was said to be a product of a "seven months" gestation. Antenatal history was otherwise uneventful and delivery took place in a private hospital. Breast-feeding had been exclusive. Apgar scores and birth weight were unknown. Physical examination revealed a wasted and lethargic infant with marked periodic breathing. The weight was 1.2kg, length 42cm and occipitofrontal circumference 29cm. Initial laboratory findings included PCV of 42 percent, total white cell count of 9,600/mm^3 with 62 percent neutrophils, 32 percent lymphocytes and 6 percent monocytes. Blood and urine were sterile and the cerebrospinal fluid was normal. Dextrostix was normal. He was commenced on naso-gastric tube feeding and treated with antibiotics consisting of ampicillin, cloxacillin and gentamycin for seven days. Although there was slight improvement in the breathing, the child remained lethargic. There was no weight gain for over two weeks despite caloric intake in excess of normal requirement. Serum chemistry revealed

normal Na^+ of 136mmol/L, K^+ 3.0mmol/L, BUN 1.5mmol/L and creatinine 20umol/L. The HCO_3 level was low, 15mmol/L and a simultaneous urine specimen gave a pH of 8.0. With this finding, treatment, in the form of oral sodium bicarbonate, baking soda (4mmol/kg/day), for DRTA was initiated. There was marked improvement in activity level, and a dramatic weight gain. Withdrawal of sodium bicarbonate led to a significant decline in growth velocity.

Case Two

This was a six-week old infant who presented with diarrhoea of two days duration and deep and fast breathing on the day of admission. Physical examination revealed a mildly dehydrated and wasted infant, weighing 2.3kg. The breathing was acidotic. He was managed initially with intravenous fluids, including sodium bicarbonate. Although sepsis work up was negative, the patient had antibiotics for 7 days. The diarrhoea subsided and the respiratory pattern became normal within 24 hours of admission. The weight on admission increased to 2.45kg (6.5 percent increase) following rehydration. At discharge eight days later, weight was 2.55kg. He was readmitted two days after discharge with a day history of recurrent diarrhoea, 4 percent weight loss and clinical acidosis out of proportion with the degree of dehydration. Urinalysis done on second admission showed a pH of 6.5 and specific gravity of 1001. The BUN was 1.5mmol/L while creatinine was 22umol/L. Intravenous sodium bicarbonate, 4mmol/kg was instituted. Oral bicarbonate supplementation was continued at 8mmol/kg/day. With this regimen there was prompt resolution of the acidosis and dramatic weight gain.

Case Three

The subject is the first of a set of dizygotic twins delivered at 32 weeks gestation, following 5 days history of premature rupture of membrane. Apgar scores were 2 and 3 at 1 and 5 minutes, respectively. She had initial respiratory distress that resolved within 4 hours of birth. Sepsis work-up was negative. Anthropometric measurements at birth were weight 1.45kg, length 42cm and occipitofrontal circumference of 27cm. The patient had a weight loss of 17 percent over two weeks, then a growth velocity of 40g/week during the next 4 weeks, remaining at 7 percent below the birth weight at 4 weeks of age. This was in contrast to the second twin who had an initial weight loss of 8 percent over the first two weeks, then a growth velocity of 90g/week and a subsequent growth velocity of 170g/week. The failure of the patient to thrive in the absence of a primary or obvious secondary cause prompted the screening for DRTA. Freshly voided urine collected gave a pH of 8.0 despite a serum HCO_3 of 15mmol/L. She was commenced on sodium bicarbonate supplement, 8mmol/kg/day,orally. The growth velocity increased to 200g/week.

Case Four

A nine-day old male infant presented with apnoea following a 2-hour history of difficulty in breathing. Gestational age was 34 weeks by maternal dates. Birth weight and details of perinatal history were unknown. He had been on exclusive breastfeeding with no demonstrable faulty breastfeeding technique. The main feature on admission was the tissue wasting and a weight of 1.3kg. He was resuscitated using bag and mask ventilation. Bolus sodium bicarbonate and dextrose were also given to correct possible acidosis and hypoglycaemia, respectively. Subsequent sepsis work-up was negative but he was treated with sultamicillin and gentamycin. The patient's weight increased to 1.45kg by 48 hours of admission. Thereafter, he gained only 50gms during the next 10 days, despite caloric intake of 130-150 kcal/kg/day. Spot urine gave a pH of 6.4, suggesting a diagnosis of DRTA. Oral sodium bicarbonate supplement, at 10mmol/kg/day, was commenced on day 11, and the patient's weight increased to 1.8kg over the following 10 days.

Case Five

SW presented at 2½ months with failure to thrive. He was a product of a term pregnancy with no perinatal problems, birth weight was not known. Physical examination revealed a small for age infant who was otherwise well. Weight was 2.4kg, less than the fifth percentile. The baby was admitted for supervised feeding. After four weeks, the weight had only increased to 2.7kg (growth velocity of 75gm/week) despite caloric intake of 120 kcal/kg/day, and absence of any obvious systemic illness. The patient was consequently investigated for DRTA. The serum HCO_3 was 18mmol/L with a simultaneous urine pH of 5.8. An acidification or ammonium chloride acid loading test was carried out. Ammonium chloride at a dose of 75mmol/m^2 was administered via a nasogastric tube over 30minutes and urine pH was checked hourly for 4 hours. To ensure complete emptying of the bladder, a urinary catheter was passed and aspirated at every hour. The urine pH was static at 5.8 for 4 hours, confirming the diagnosis of DRTA. Oral

Table

Features in 5 Cases of Distal Renal Tubular Acidosis

Feature	*Case* 1	2	3	4	5
Age at presentation (wks)	2	6	4	1½	10
Lethargy / Refusal to feed	X	-	-	-	-
Diarrhoea / Dehydration	-	X	-	-	-
Tachypnoea ± Apnoea	X	X	-	X	-
Failure to thrive	X	X	X	X	X
Urine pH	8.0	6.5	8.0	6.4	5.8
Urine pH after acid loading test	ND	ND	ND	ND	5.8
Serum HCO_3	15	ND	15	ND	1.8
Growth velocity (g/wk)					
Before treatment with $NaHCO_3$	-5	0	40	35	75
During treatment with $NaHCO_3$	260	650	200	245	875
Treatment stopped	-13	-170	ND	ND	ND
Treatment resumed	240	525	-	-	-

- = absent
X = present
ND = not done.

sodium bicarbonate supplement, at 10mmol/kg, was commenced with change in growth velocity to 875gm/week.

A summary of the major biochemical and anthropometric changes in the patients is shown in the Table.

Discussion

Under poor socio-economic conditions, maternal undernutrition is associated with a decreased birth weight and often an inadequate breast milk production.[3,4] Therefore, the infants are at risk for primary FTT, usually from about 4 months of age, when the rate of breast milk production has slowed down and nutritionally adequate weaning diet has not been introduced due to poverty or ignorance.[3,4] When growth failure begins in the neonatal or early infancy period, it is often a consequence of a wide range of underlying diseases. However, with an organ/system dysfunction, specific features provide clues to the likely aetiology. When there are no clues to specific organ/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 inborns errors of metabolism are the most likely aetiology. Metabolic acidosis, a common feature of several inborn errors of metabolism (IEM) presenting in the neonatal period is usually severe and progressive, and commonly has other findings in addition to FTT and acidosis. With primary renal tubular acidosis, there is no obvious systemic disorder and associated findings are related to the renal tubular dysfunction.[5]

Renal tubular acidosis (RTA) is a clinical state of hyperchloraemic metabolic acidosis with a normal anion gap, resulting from impaired urinary acidification in spite of a normal glomerular filtration rate.[5] There are four distinct types namely: distal or classic or type 1 RTA, type 3 RTA is a hybrid of types 1 and 2, and type 4 is accompanied by hyperkalaemia in contrast to the others. Although, the definitive diagnosis of RTA often requires doing a complete set of serum electrolytes to demonstrate the low serum bicarbonate and a normal anion gap and hence distal hydrogen ion secretion, the urine pH alone is considered a useful screening test of renal acidification. In the adult, urine obtained in the fasting state has a pH of 6.0; however infants (older than 2 weeks) who have a higher endogenous acid production generally have a urine pH less than 6.0. Therefore, if an infant is not

acidotic and urine pH is 6.0, RTA is unlikely. A urine pH of ≥5.5 despite acidosis is diagnostic of distal RTA.[6,7] As shown in the Table, the constant feature in our patients was FTT that persisted in the hospital in spite of caloric intakes of 130-150 kcal/kg/day. Four of the patients had urine pH ≥ 6.4 despite concomitant moderate to severe acidosis, thus confirming DRTA. Unfortunately, we could not measure the serum bicarbonate level in the second and fourth patients because they came in at periods when our laboratory did not have the required reagents for the test. The fifth patient had urine pH of 5.8 hence the need to confirm the diagnosis by the ammonium chloride loading test. The ability of the patient to further acidify the urine following ammonium chloride loading confirms the diagnosis of DRTA. Sepsis evaluation was negative in all cases and there were no findings suggestive of IEM. All the patients responded to 8-10mmol/kg/day of alkali (baking soda) therapy; growth velocity increased by 160 to 800 g/week during period of sodium bicarbonate therapy. Baking soda is readily available even in the open market and can be freshly prepared daily by dissolving a level teaspoonful (3.5grammes) in 30mls of water. This will create a 1mmol/ml solution of sodium bicarbonate.

Distal renal tubular acidosis if undiagnosed leads to continued growth retardation, rickets, polyuria and nephrocalcinosis. Although adequate treatment can improve most of the symptoms, the nephrocalcinosis appears irreversible and may lead to chronic renal failure.[8] Since DRTA can be treated cheaply and effectively, early recognition of primary DRTA is of foremost clinical importance. This is possible with attention to the non-specific symptoms of vomiting, polyuria, dehydration and particularly FTT, and a high index of suspicion.

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