RENAL TUBULAR ACIDOSIS IN KELANTAN, MALAYSIA – A CASE REVIEW

D Zainal

ABSTRACT

Renal tubular acidosis (RTA) is a defect in urinary acidification in the absence of renal failure. All records of patients admitted to adult medical wards at the University Hospital USM (HUSM), Kelantan between 1986 to 1990 with the diagnosis of renal tubular acidosis were reviewed.

Sixteen (16) patients were identified and fulfilled the diagnostic criteria. Their mean age at presentation was 28.9±0.74 years. The triad of muscle weakness, hypokalaemia and systemic metabolic acidosis were the characteristic features at presentation. Normal serum alkaline phosphatase and skeletal X-rays were noted.

Their prognosis were generally good. Their mean serum bicarbonate and potassium on follow up were 17.84±0.35 and 3.82±0.05 mmol/L respectively.

The importance of regular follow-up and long-term management is emphasised.

Keywords: *renal tubular acidosis, case review, Kelantan.*

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INTRODUCTION

Renal tubular acidosis is a clinical syndrome characterised by a defect in urinary acidification in the absence of nephron loss resulting in systemic metabolic acidosis and other metabolic abnormalities[1].

There are two major types of renal tubular acidosis:

(a) Type 1 formerly known as classical or distal renal tubular acidosis. The most common of these syndromes, this is characterised by inability of the kidneys to lower the urine pH to less than 5.3 in the presence of metabolic acidosis[2,3]. Fractional excretion of bicarbonate is low and is commonly associated with nephrocalcinosis and nephrolithiais.

(b) Type 2 renal tubular acidosis is due to a defect in the proximal tubules; a less common type, this is characterised by glycosuria, aminoaciduria, phosphaturia, uricosuria, abnormal increase of fractional urinary excretion of bicarbonate in the face of normal or near normal plasma bicarbonate and the ability to lower urine pH in severe acidosis.

Thus far there is no review of renal tubular acidosis from this part of Malaysia and this paper is meant to highlight this clinical problem and guide us in the future management of these cases.

MATERIALS AND METHODS

Patients and definition

This is a retrospective study. All records of patients diagnosed as renal tubular acidosis (RTA) in University Hospital USM (HUSM) between 1986 and December 1990 were reviewed. Only 16 patients were identified and fulfilled the criteria of renal tubular acidosis.

Type 1 renal tubular acidosis was diagnosed on the basis of the patient's inability to lower the urine pH below 5.3 in the presence of systemic acidosis (defined by serum $HCO_3 < 15$ mmol/L). An acid loading test, as described by Wrong and Davies, was performed in patients with a serum HCO_3 of 15 – 20 mmol/L; distal renal tubular acidosis was diagnosed when patients were unable to lower urine pH below 5.3 after oral ingestion of 0.1 gm/kg of ammonium chloride. The test was considered positive only when there was a reduction of serum bicarbonate of more than 2 mmol/L.

Type 2 RTA is ideally diagnosed when there is massive bicarbonaturia with fractional excretion of bicarbonate exceeding 15% in the face of normal serum bicarbonate after sufficient oral or intravenous bicarbonate is given to normalise the serum bicarbonate. Unfortunately due to inadequate facilities at that time, urine bicarbonate estimation was not done. Hence the diagnosis of type 2 RTA was made after excluding other possible causes of hypokalaemia with metabolic acidosis and the ability of the kidneys to acidify urine (pH below 5.3) in the presence of severe systemic metabolic acidosis defined as serum bicarbonate less than 15 mmol/L.

Biochemistry

Freshly voided urine was examined for pH (by pH meter), sugar, albumin (Uristix Ames Victoria, Australia) and sediment. Blood urea nitrogen (BUN), serum creatinine, electrolytes, calcium, phosphate, albumin and globulin were performed using conventional methods.

Serum alkaline phosphatase was assayed by the technique described by Babson et al.

Antinuclear antibodies and dsDNA were assayed by indirect immunofluorescence, using mouse tissues as substrates and a serum dilution of 1:10.

Twenty-four hours urine collection for measurement of uric acid, phosphate and calcium were done in all cases.

Roentgenographic study

Chest and plain KUB X-rays were performed in all patients except those who were pregnant. Ultrasound of kidneys were not routinely done in all these cases during this period.

Statistical analysis

The biochemistry results were analysed using mean ± 1SEM.

RESULTS

Patients

Sixteen (16) patients fulfilled the diagnostic criteria of RTA. All of them were female. Mean age at presentation was 28.90±0.74 years. Malay to Chinese ratio was 9:1. The average number of newly diagnosed RTA was 3.5 per year. The presenting features are shown in Tables I and II.

Department of Medicine
Hospital University USM
16150 Kubang Kerian
Kelantan
Malaysia

D Zainal, MRCP (UK)
Lecturer

Table I – The presenting symptoms of patients with RTA in HUSM, Kelantan.

Symptoms	No	%
Generalised muscle weakness	12	66.6
Anorexia	8	50.0
Vomiting	4	25.0
Constipation	3	18.75
Tetany	3	18.75

Table II – The associated factors identified in RTA patients diagnosed in HUSM

	No	%
Urinary tract infection	3	18.75
Pregnancy	3	18.75
Unknown	10	62.50

Table III – The serum biochemistry results of patients with RTA on admission

	Mean±SEM	Range
Blood urea (mmol/L)	4.01 ± 0.47	1.90 – 6.20
Sodium (mmol/L)	138.10 ± 0.85	134.00 – 141.00
Potassium (mmol/L)	2.38 ± 0.29	1.30 – 4.10
Bicarbonate* (mmol/L)	11.09 ± 1.19	6.90 – 18.30
Chloride (mmol/L)	106.90 ± 3.27	97.00 – 133.00
Creatinine (umol/L)	76.40 ± 5.38	44.00 – 97.00
Calcium (mmol/L)	2.05 ± 0.06	1.70 – 2.27
Phosphate (mmol/L)	1.12 ± 0.07	0.80 – 1.50
Albumin (gm/L)	43.20 ± 0.81	40.00 – 48.00
Alkaline phosphatase (IU/L)	137.90 ± 3.54	127.00 – 161.00
Uric acid (umol/L)	262.80 ± 26.12	150.00 – 390.00
Urine pH#	6.88 ± 0.27	5.00 – 8.00

Corrected to 2 decimal places.
* arterial blood samples
# Early morning urine pH

Biochemistry

The laboratory investigation results were reviewed: liver function test, random blood glucose, HbsAg, serology test for connective tissue disease and the X-rays were normal. The biochemistry results on admission are detailed in Table III.

The 24 hours urinary excretion of calcium, phosphate, uric acid were assayed and were within normal limits.

Quantitative measurement of amino-acid in the urine was not performed.

Short acid load tests were carried out in six of the patients (Table IV).

In patients no. 3 and 5, their kidneys were able to acidify urine below pH 5.3.

In the remaining patients this test was not carried out because they had severe metabolic acidosis. They were labelled as having distal RTA as they were unable to acidify urine to pH below 5.3.

Table IV – Results of acid loading test

Patients	Arterial bicarbonate Mean±1 SEM	Urine pH Mean±1 SEM
1. CBS	9.90 ± 0.19	6.61 ± 0.03
2. FBS	15.15 ± 0.47	7.20 ± 0.04
3. ZBM*	13.87 ± 0.27	5.16 ± 0.03
4. RBM	14.78 ± 0.54	7.23 ± 0.04
5. NBM*	17.58 ± 0.36	5.54 ± 0.08
6. ZBH	11.26 ± 0.56	6.83 ± 0.02

Units in mmol/L
*Two of the patients were able to acidify urine to pH below 5.3

OUTCOME

All of the patients responded to the treatment given. All were alive at discharge. The three pregnant patients gave birth to normal babies. Upon discharge, 9 out of the 16 patients came back for regular follow-up but the rest defaulted treatment. Their mean arterial bicarbonate and serum potassium on follow-up were 17.84±0.35 and 3.82±0.05 mmol/L respectively.

DISCUSSION

From this review the incidence of RTA in our hospital (HUSM) is 3.5 per year.

This cannot be taken as the true incidence of RTA in this state as patients could have been admitted to other surrounding hospitals. All of our patients were young females and distal RTA was the commonest type as previously reported[1,2].

The exact cause in our patients was not known as most of the known secondary causes were excluded by history and laboratory investigations. They probably inherited the disease from their parents[3-5]; and this should be proven later on by tracing the immediate relatives.

However 37.5% of them were noted to have associated factors. Perhaps RTA is common and most are subclinical and become prominent when there is associated stress.

This condition is characterised by the triad of generalised muscle weakness, hypokalaemia and systemic metabolic acidosis.

This is further confirmed by inability of the kidneys to acidify urine in the presence of metabolic acidosis.

Classically the serum chloride in these patients is higher than normal. In our patients, some of their serum chloride were found to be normal. Perhaps this was due to some technical errors in the measurement of chloride.

The acid loading test done in our patients revealed that 66.7% of them were unable to acidify urine, hence were labelled as distal RTA. The remaining two patients were able to acidify urine to below pH5.3, hence were labelled as proximal RTA. Since their urinary calcium, phosphate and uric acid excretion were within normal limits, it is possible that both these patients have incomplete distal RTA.

Batlle et al[6] reported a small number of adult patients who had normal capacity to maximally lower urine pH in metabolic acidosis and inability to normally increase the urine minus PCO_2 gradient. According to their hypothesis, these patients had a decrease in distal H+ secretion that could only be determined during bicarbonate loading. In their view, assessment of PCO_2 in highly alkaline urine may represent the most sensitive test to investigate distal acidification.

There were also conditions that had been diagnosed as distal RTA based on pH of urine[7-9] but was challenged by Carlisle[10] who emphasised that the rate of excretion of NH_4 was not uniformly low in these patients. Low rate of NH_4 excretion is crucial to diagnose distal RTA[10]. From all these experiences it is clear that distal RTA confirmation should not be dependent on only one test.

All of our patients had normal levels of serum alkaline phosphatase and normal skeletal X-rays. This was in contrast to that reported by the Thai workers[4]. Perhaps our patients were younger, had shorter duration of illness and sought treatment earlier.

Nephrocalcinosis with or without nephrolithiasis has been radiologically demonstrated in 63% of 43 patients having distal RTA[11]. The incidence of nephrocalcinosis could even be higher through the use of renal ultrasound, a method reported to be more sensitive than abdominal radiograph for detecting renal parenchymal calcification[12]. We could not comment on the incidence of nephrocalcinosis in our cases as not all of our patients were routinely screened for this at presentation. Perhaps with the presence of more ultrasonographists in our hospital now, the detection rate could be as stated in previous studies.

The main objective in treating distal RTA is correction of metabolic acidosis. The other abnormal metabolic changes will revert to normal upon correction of the acidosis[13-15]. Furthermore, correction of acidosis will prevent bone abnormalities, nephrocalcinosis and nephrolithiasis.

Once nephrocalcinosis is established, it does not revert even though appropriate alkali supplementation is instituted[16]. The outcome in our patients was generally good. Upon discharge, only 56.25% of them came back for regular follow-up. Those on follow-up remained asymptomatic. Their mean serum bicarbonate and serum potassium were 17.84±0.35 and 3.82±0.05 respectively. All of them have normal renal function. From our study it is clear that RTA in our patients seem to be relatively benign compared to recent report[4]. Early recognition and prompt treatment is important.

Attempt to improve our laboratory facilities is important based on previous report. Variants of RTA may be missed if one depended on one method for diagnosis. Urine examination for pH, bicarbonate, ammonium ions, titrable acid and urine PCO_2 should be done in every case of RTA in future.

Patients who default treatment should be traced and given proper education on the disease process. The long-term objective is not only to keep them asymptomatic but to preserve normal renal function. Although sporadic cases of transient RTA have been reported[17] it should be pointed out that distal RTA is a permanent disorders. Therefore alkali therapy must be continued throughout the patients' lifetime.

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