Case Report

Proximal renal tubular acidosis with primary Fanconi syndrome

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ABSTRACT

Renal tubular acidosis (RTA) is associated with normal or near normal glomerular filtration rate. Proximal RTA is associated with impaired bicarbonate reabsorption. This is manifested as bicarbonate wastage in the urine, and this reflects the defect in proximal tubular transport. Osteopenia or full-blown rickets may develop. Type 2 RTA is rare and occurs in association with conditions such as Fanconi syndrome. This is manifested as glycosuria, aminoaciduria, phosphate wasting and mild proteinuria. The basis of therapy is the continuous administration of appropriate amounts of alkali in the form of either bicarbonate or citrate, as well as the treatment of the cause.

Keywords: Bicarbonate wasting, Fanconi syndrome, Proximal RTA, Rickets

INTRODUCTION

Renal tubular acidosis (RTA) is a disease that is characterized by various features such as a normal anion-gap metabolic acidosis and this is seen to occur in the setting of a normal or near normal glomerular filtration rate (GFR). There are four main types of these disorders, namely:

• Proximal (Type 2 RTA)
• The classical distal (Type 1 RTA)
• Hyperkalemic (Type 4 RTA)
• Combined proximal and distal RTA (Type 3)

Proximal renal tubular acidosis is found to result from impaired bicarbonate reabsorption. Idiopathic or primary Fanconi syndrome (FS) is characterized by an important feature: the dysfunction of the proximal tubule. This finally leads to the loss of bicarbonate, phosphate, glucose, potassium, amino acids and other substances in urine. One very prominent clinical feature of FS is that there is a marked delay in body growth.

CASE REPORT

An eight-year-old female child, born of consanguous marriage, was brought to the Pediatric Outpatient Department with severe failure to thrive and a history of multiple fractures of bones and difficulty in walking since three years of age. She also had history suggestive of polyuria, along with a history of lethargy and anorexia. There was no history of fever, hematuria, diarrhoea, vomiting, jaundice. There was no history of any other significant drug intake for any other illnesses, apart from intake of Vitamin D supplements. Developmental milestones were normal. There was no history of any other similar illness in the family. On examination, the child appeared to be chronically malnourished, with a weight of 12 kilograms, as against an expected weight of 25 kilograms. Her height was 100.5 centimetres, as against an expected height of 133 centimetres, denoting severe retardation of growth (Figure 1).

She also had vitiligo, for which treatment was sought. She had a heart rate of 116 beats per minute and respiratory rate of 38 per minute. Blood pressure was
112/60 mm of mercury. She had widening of bones at the wrists. Examination of the abdomen revealed a palpable liver. Respiratory system and cardiovascular system were normal.

**Figure 1: Image depicting short stature and severe growth retardation.**

Slit lamp examination did not reveal any cystine crystals. There was also no evidence of KF rings. Laboratory work up showed Hemoglobin, total counts, platelets to be within normal limits. Serum levels of sodium was 125 mg/dl, potassium 2.9 meq/L, phosphate 2.3 mg/dl and chloride 105 mg/dl. Serum levels of calcium was 8.3 mg/dL and serum alkaline phosphate levels were 1723 mg/dl. Serum urea and creatinine levels were 15 mg/dL and 0.5 mg/dL respectively.

**Figure 2: Image depicting osteopenia and fracture malunion of femur.**

Further examination revealed a fracture malunion involving the left femur. Ultrasound of the abdomen did not show any evidence of nephrocalcinosis. The finding of severe growth retardation and Vitamin D resistant rickets, metabolic acidosis, glycosuria, with increased urinary excretion of sodium, potassium and phosphate, prompted the diagnosis of proximal RTA with Fanconi syndrome. The child was treated with sodamint tablets and Joulie's solution, along with vitamin D supplementation, after resolution of symptoms were noted.

**DISCUSSION**

The term renal tubular acidosis (RTA) is used to describe a specific group of transport defects in the reabsorption of bicarbonate (HCO₃⁻), the excretion of hydrogen ion (H⁺), or both. This particular condition was first described in the year 1935, followed by its confirmation as a renal tubular disorder in 1946, and later designated as “renal tubular acidosis” in 1951.

The RTA syndromes are characterized by certain features such as a relatively normal GFR and a metabolic acidosis that is accompanied by hyperchloremia and a normal plasma anion gap, with the absence of diarrhoea.² It must be noted that they can also be a part of a more generalized tubule defect, such as in the case of Fanconi syndrome. Proximal renal tubular acidosis (RTA) (Type II RTA) is one of the types of RTA, and it is characterized by a certain defect in the ability to reabsorb HCO in the proximal tubules.³ This is usually manifested as bicarbonate wastage in the urine, and this reflects the defect in proximal tubular transport. It indicates that the defect is severe enough that the capacity for bicarbonate reabsorption in the thick ascending limb of Henle’s loop and more distal nephron segments is significantly overwhelmed.³

It may occur as part of a generalized dysfunction of proximal tubules and patients can have increased urinary excretion of glucose, uric acid, phosphate, amino acids, citrate, Ca, K, and protein. Osteopenia (including rickets in children) may develop later. Type 2 RTA is very rare and most often occurs in patients who have one of the following: Fanconi syndrome. Light chain nephropathy due to multiple myeloma, or in case of various drug exposures (usually acetazolamide, sulfonamides, ifosfamide). It sometimes has been associated with other etiologies, including vitamin D deficiency, chronic hypocalcemia with secondary hyperparathyroidism, kidney transplantation, heavy metal exposure, and other inherited diseases (e.g., fructose intolerance, Wilson
Disease, oculo cerebrorenal syndrome (Lowe syndrome), cystinosis).

Idiopathic or primary Fanconi syndrome (FS) is characterized by an important feature - the global dysfunction of the proximal tubule. This finally leads to the loss of bicarbonate, phosphate, glucose, potassium, amino acids and other substances in urine. One very prominent clinical feature of FS is that there is a marked reduction in body growth. Different forms of Fanconi syndrome can affect different functions of the proximal tubule and result in different complications. The loss of bicarbonate results in type 2 or proximal renal tubular acidosis. The loss of phosphate ions results in causing rickets (even with adequate vitamin D and calcium), because phosphate is required for bone development.

A variety of genetically determined conditions, systemic disorders, or various exogenous toxins can produce this complex type of renal tubular abnormalities, or the syndrome may also be idiopathic, without any identifiable etiology. Although the syndrome is a relatively rare phenomenon, knowledge of its metabolic consequences is important for proper patient management. Important features, present in patients having Fanconi syndrome, include glucosuria, general aminoaciduria, and phosphaturia. Although features such as glycosuria and aminoaciduria appear to have few clinical consequences, renal phosphate wasting has been thought to play a very important role in the development of the metabolic bone disease which invariably develops in untreated cases and is also an important cause of morbidity. Development of renal tubular acidosis (RTA) may also contribute to bone disease, which is usually the Type II RTA. Children may present with vomiting, polyuria and failure to thrive. Deshpande et al have stated that although Primary Fanconi syndrome has not been reported in India, it must be remembered that there may be as yet unidentified metabolic causes that may be attributable. The diagnosis of primary Fanconi syndrome remains a diagnosis of exclusion.

The aim of treatment for RTA is to correct the biochemical abnormalities and also to improve growth in children and to prevent the progression of nephrocalcinosis and the development of chronic renal failure. The basis of therapy is the continuous administration of appropriate amounts of alkali in the form of either bicarbonate or citrate. In proximal RTA, the amount of alkali required is very large (up to 10 to 20 mmol/kg per 24 hours) due to the massive urinary losses of HCO₃⁻. A mixture of Na⁺ and K⁺ salts, preferably citrate, is tried. It is of importance to split the daily dosage in portions along day and night. Prognosis of proximal RTA would depend on the underlying etiology, especially in cases observed in the context of the Fanconi syndrome. However, in children with sporadic isolated proximal RTA the tubular defect improves over time, and therapy can be generally discontinued at about 3 to 5 years of age.

It must be borne in mind that replacement of the phosphate losses is mandatory, to prevent the progression of bone disease, which is an important reason for morbidity. Oral supplementation of 1-3 grams of neutral phosphate per day may be required. High doses of vitamin D or 1, 25-(OH)2 vitamin D3 must also be used in cases where there is documented rickets or osteopenia. Therapy with both phosphate and vitamin D has been proven to promote the growth in children and also improve symptoms as well as radiologic evidence of rickets in children.

CONCLUSION

The authors would like to sensitize readers to the diagnosis of Fanconi syndrome and Proximal RTA. As stated previously, this is a rare entity and requires greater knowledge and foresight in diagnosis and management. Early diagnosis prompts better management and a better overall prognosis.

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REFERENCES