Case Report

Distal renal tubular acidosis secondary to vesicoureteral reflex: A case report in a 14-year-old girl

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ABSTRACT

Vesicoureteric reflux (VUR) is the most common congenital anomaly of the urinary tract that occurs in 30–50% of children presenting with recurrent urinary tract infections. Long-standing untreated VUR results in renal scarring and hydronephrotic change ultimately leading to chronic renal failure and arterial hypertension. However, it may also result in diffuse tubulopathy compromising the concentrating capacity of tubules and urinary acidification defects. Renal tubular dysfunction should be considered in all children with VUR presenting with failure to thrive, rickets, bony deformity/pain, hypokalemia, and metabolic acidosis. We report such a case of a 14-year-old girl who presented with rickets, failure to gain weight and height, bony pains, and muscle weakness with a history of VUR. On investigation, she was found to have normal anion gap metabolic acidosis with hypokalemia suggestive of distal renal tubular acidosis. She responded well to oral alkali and potassium replacement therapy.

KEY WORDS: Distal renal tubular acidosis, Nephrocalcinosis, Vesicoureteral reflex

INTRODUCTION

Vesicoureteric reflux (VUR) is the retrograde flow of urine from the bladder into the ureter and is the most frequent malformation of the urinary tract. It occurs in 30–50% of children with recurrent urinary infections.[1] It predisposes the kidney to parenchymal infection, resultant scarring, and hydronephrotic changes by allowing ascent of bacteria from bladder to the upper urinary tract.

Reflux nephropathy develops in 30–60% of children with VUR. It predominates in girls at a proportion of 4:1, but its severity is greater in boys.[2] The most serious consequences are chronic renal failure and arterial hypertension.[3] Long-standing VUR can also lead to diffuse tubulopathy and urinary acidification defects.[4] Very few cases of distal renal tubular acidosis (dRTA) secondary to VUR have been reported in the literature. We report such a rare case of dRTA secondary to VUR in a 14-year-old girl.

The renal tubules play an important role in fluid, electrolyte, and acid-base homeostasis. In 1946, Albright and Burnett described dRTA as a distinct clinical entity.[5] dRTA is a nonuremic defect of urinary acidification characterized by normal anion gap hyperchloremic metabolic acidosis. It is characterized by an inability to lower urinary pH <5.5 even in the face of systemic acidosis and nephrocalcinosis. These patients have features of rickets/osteomalacia and stunted growth. It may be primary, due to various genetic mutations or secondary to systemic causes such as Sjogren's syndrome, lupus, sickle cell disease, or VUR/obstructive uropathy.

Access this article online	
Website: jprsolutions.info	ISSN: 0975-7619

CASE REPORT

A 14-year-old girl born of a non-consanguineous marriage presented to us with complaints of failure to gain weight, bony pains, and muscle weakness for the past 2 years. She had a significant history and was symptomatic for the age of 3 years when he had recurrent urinary tract infections, poor feeding, and poor growth. On workup, she was found to have Grade 4 VUR for which she was operated. Postoperatively, the reflux got corrected, but the hydronephrosis persisted, however, she was not symptomatic.

She was first by birth order and her younger sister was asymptomatic. On examination, her height was 143 cm (<2 standard deviation), weight: 43 kg,

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Received on: 14-05-2019; Revised on: 04-06-2019; Accepted on: 08-07-2019

pulse rate: 80/min, blood pressure: 110/70 mm Hg, standardized morbidity ratio = Tanner's stage 4, signs of rickets in the form of wrist widening, and waddling gait.

On systemic examination, proximal muscle weakness was present. On investigation, she was found to have hyperchloremic, normal anion gap metabolic acidosis with raised parathormone, and alkaline phosphatase. Simultaneous urinary pH was 6.5 despite systemic acidosis. Serum creatinine was normal. X-ray shows bilateral wrists showed widening and fraying of metaphysic.

With these investigations, a diagnosis of dRTA was made secondary to reflux nephropathy. He was started on alkali replacement in the form of sodium bicarbonate tablets, oral potassium supplements, oral calcium, and Vitamin D. With this treatment, his bone pains decreased and muscle weakness improved. Her alkaline phosphatase normalized, PTH nearly normalized, and acidosis got corrected.

Investigations

- Serum sodium – 136 mEq/L
- Serum potassium – 3 mEq/L
- Serum chloride – 110 mEq/L
- Serum calcium – 7.5 mEq/L
- Alkaline phosphatase – 2740 IU/L
- Paratharmone – 922 pg/ml
- Serum chloride – 0.9 mg/dl.

Arterial Blood Gas Analysis

- pH – 7.25
- PCO_2 – 56
- HCO_3 – 16
- Anion gap – 10
- Urine pH – 6.5.

DISCUSSION

dRTA is characterized by decreased proton excretion due to a proton pump defect or back diffusion of protons.[6] Tubular dysfunction should be considered in all children with failure to thrive, polyuria, refractory rickets, hypokalemia, and metabolic acidosis.

RNA and diarrhea are important causes of metabolic acidosis in children.[7] These disorders can be readily differentiated from most other causes of metabolic acidosis by estimation of the plasma anion gap. Normal anion gap in the presence of acidosis (hyperchloremic metabolic acidosis) suggests increased urinary (proximal RTA) or gastrointestinal loss (diarrhea) of bicarbonate or impaired excretion of H^+ ions (dRTA).[8] Hypokalemia is usually associated with metabolic alkalosis. The occurrence of metabolic acidosis and hypokalemia suggests RTA or gastrointestinal loss of bicarbonate (diarrhea and ureterosigmoidostomy).

In children, dRTA is almost always observed as a primary entity and rarely associated with autoimmune conditions. Pathogenically, dRTA can develop when there is a true failure of the distal nephron to secrete hydrogen ions (secretory defect or classic dRTA) or when such capacity is intrinsically intact, but secondarily impaired. The non-secretory defects are caused by either an inability to create a steep lumen-to-cell H^+ gradient due to increased back leak of secreted H^+ (gradient defect) or an inability to generate/maintain a distal lumen-negative transepithelial difference (voltage-dependent defect), as observed in patients with impaired distal Na^+ transport (obstructive uropathy and sickle cell disease).[9]

Investigations in children with distal (Type 1) RTA include estimation of urine calcium excretion, ultrasound for renal calcification, and workup for secondary causes (e.g., obstructive uropathy, reflux nephropathy, and chronic tubulointerstitial nephritis).

Treatment of RTA includes administration of alkali in the form of sodium bicarbonate 7.5% (1 mEq/mL) or tablets; Shohl's solution (1 mEq/mL); and polycitra solution (2 mEq/L). Alkali therapy is usually combined with potassium replacement to avoid severe hypokalemia. Potassium supplements in patients with acidosis are usually administered as citrate salts.

Although chronic renal failure and arterial hypertension are considered as the most important complications of VUR, urinary concentration and distal acidification defects are also important complications that may be seen in some children which should also be ruled out. The acidemia decreases bone collagen synthesis and determines end-organ resistance to growth hormone and insulin-like growth factor-1. This results in growth failure. If not timely treated with alkali replacement and potassium therapy, it results in varied symptoms of poor growth, muscle weakness, and bony pains. Hence, the physician should be aware of the clinical presentation and the correct management of this illness to prevent rickets/osteomalacia and growth retardation in patients with long-standing VUR.

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Source of support: Nil; Conflict of interest: None Declared