ORIGINAL RESEARCH PAPER

Paediatrics

KEY WORDS: Rickets , Distal renal tubular acidosis , hyperchloremic metabolic acidosis

REFRACTORY RICKETS SECONDARY TO DISTAL RENAL TUBULAR ACIDOSIS: A RARE CASE REPORT.

Dr Gajanan Yelme Consultant pediatrician, Department of pediatrics, Shri Balaji Institute of medical science and research, Raipur, Chhattisgarh.

Dr Sainath Pattewar Consultant nephrologist, Department of nephrology, Shri Balaji Institute of medical science and research, Raipur, Chhattisgarh.

ABSTRACT

Type I (distal) renal tubular acidosis (RTA) is a disorder associated with inability of distal tubule to secrete H+ ion which causes hyperchloremic metabolic acidosis. It is also characterized by an abnormal increase in urine pH, reduced urinary excretion of ammonium and bicarbonate ions, and mild or no deterioration in renal function. The children suffering from rickets secondary to distal RTA may not respond to usual doses of calcium and vitamin D. Thorough workup and cautious management is required in these cases. Here we present a case of 2-year-old male child who presented to us with pneumonia, failure to thrive, developmental delay, features of rickets, nephrocalcinosis and acidosis. The patient was diagnosed as refractory rickets and managed for the same.

INTRODUCTION:

Rickets is caused by defective mineralization or calcification of bones before epiphyseal closure in children (1). Vitamin D deficiency is the most common cause of rickets (2,3), but other conditions that affects bone mineralization, including renal tubular acidosis (RTA), can cause rickets (4,5). Renal tubular acidosis (RTA) is a group of transport defects secondary to reduced proximal tubular reabsorption of bicarbonate (HCO3 -), the distal secretion of protons (hydrogen ion, H+) or both. The characteristic features of renal tubular acidosis include normal anion gap and hypercholeramic metabolic acidosis [6].There are 3 types of renal tubular acidosis. type 1 (distal) RTA; type 2 (proximal) RTA; and type 4 RTA secondary to true or apparent hypoaldosteronism. Distal RTA is caused by failure of H+ secretion from distal nephron. [7] This failure to secrete H+ ions is primarily responsible for inability to acidify the urine and leads to acidosis. Associated impaired reabsorption of potassium leads to metabolic derangement like acidosis and hypokalemia. Rickets in children with distal renal tubular acidosis is caused by bone resorption due to chronic acidosis and reduced absorption of calcium from renal tubules. [8]

CASE REPORT:

A 2 year old severely malnourished boy was admitted in our hospital with lower respiratory tract infection. He had a history of cough cold and fever since 15 days. The signs and symptoms gradually worsened and the patient developed rapid breathing and inability to take proper food since 3-4 days. On admission the baby was having respiratory distress in the form of intercostal and subcostal retractions, nasal flaring and grunting. For these complaints he was admitted in pediatric intensive care unit. He was 2nd by order of birth. He was born at 37 weeks' gestation by normal vaginal delivery and weighed 2.5 kg. He was immunised appropriate for his age. There was a significant history of delayed developmental milestones, failure to thrive and received vitamin D injections (3 lac unit) twice in last 1 year. Baby had not started walking yet. According to mother he lagged behind his elder sister in achieving developmental milestones specially the gross motor milestones. He was short in stature, measuring 75 cm (<3rd percentile) and weighing 6.5 kg (<3rd percentile).

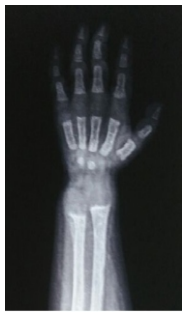
His investigations showed anaemia with neutrophilic leucocytosis with positive CRP test. Chest X-ray was suggestive of right middle lobe pneumonitis with obscuration of right heart border.USG abdomen showed bilateral nephrolithiasis. He was initially kept Nil per orally and oxygen inhalation was started along with IV antibiotics and IV fluids. Baby's condition stared to improve with treatment and his respiratory distress settled down and baby started taking oral feeds well. By Day 5 of admission he was shifted to ward.

During general examination he was found to have widened wrists, frontal bossing, open anterior fontanelle, ricketic rosary and double malleoli (Marfan's sign). In view of these features X-Ray of both wrists was taken which showed signs of rickets including osteopenia and splaying of metaphysic. He was worked up for refractory rickets and the laboratory findings were found to be suggestive of rickets secondary to distal renal tubular acidosis [Table 1].

Table 1: Investigations showing hypokalemia and hyperchloraemic metabolic acidosis.

Serum Sodium (meq/L)	142
Serum Potassium (meq/L)	2.6
Serum Chloride (meq/L)	120
Calcium (mg/dl)	8.8
Phosporus (mg/dl)	1.2
Alkaline Phosphatase (IU/lit)	379
Urine PH	7.0
25-OH vitamin D (n g/ml)	94
Blood urea (mg/dl)	22
Serum creatinine (mg/dl)	0.3
Arterial blood pH	7.1
Urine pH	7.0

Fig 1: Skeletal X-ray showing diffuse osteopenia, fraying in the both distal radius and ulna,



Urine PH more than 5.5 in presence of hyperchloraemic metabolic acidosis is almost diagnostic of distal renal tubular acidosis. Since our patient had all the classical features of distal renal tubular acidosis a diagnosis of rickets secondary to distal renal tubular acidosis was made and the patient was treated with calcium supplementation, potassium chloride and sodium bicarbonate replacement was given to correct hypokalemia and acidosis . After correction of hypokalemia and metabolic acidosis he was discharged with an advice to remain under regular follow up.

DISCUSSION:

Rickets is one of the common disorders seen in growing children. It

is usually caused by deficiency of vitamin D and calcium. The various causes of rickets include conditions with decreased intake of calcium; malabsorption; and/or increased excretion of calcium, phosphate, or vitamin D. The prevalence of rickets more in dark skinned children.(9) Rickets refractory to vitamin D supplementation are mostly secondary to condition affecting kidneys like renal tubular acidosis. (10)

The primary mechanism responsible for acidification of urine includes: a) H+ and HCO3- ions from H2O and CO2 by cytosolic carbonic anhydrase II (CA II), b) excretion of H+ ions into the collecting tubule by vacuolar H^+-ATPase, and c) excretion of HCO3- ions into the blood by the HCO3-/Cl- anion exchanger (AE1)(11). Defect of any of these components can cause a functional defect in urine acidifica-tion. (12) The main defect in distal tubular acidosis is inability of distal tubule to secrete H+ ion which causes hyperchloremic metabolic acidosis. The most common cause of distal renal tubular acidosis is mutations in the gene that encodes AE1.(13) Another mutations that causes inherited distal RTA and sensorineural hearing loss is mutation in gene *ATP6V0A4 and ATP6V1B1* encoding the a4 and B1 subunits of vacuolar H+-ATPase (14-16). The patient usually presented with chronic hyperchloremic metabolic acidosis, a normal anion gap, alkaline urine with a positive urine anion gap, hypokalemia, and nephrocalcinosis.

The treatment of distal renal tubular acidosis is not only correction of primary metabolic abnormalities ie hyperchloremic metabolic acidosis and hypokalemia but also for prevention of rickets , growth retardation and nephrolithiasis. The treatment of metabolic acidosis involves supplementation of potassium citrate or sodium citrate The hypokalemia should be managed by potassium supplementation and a potassium sparing diuretic like spironolactone, triametrene or amiloride.[10] Rickets due to distal tubular acidosis can be treated by calcium and vitamin D supplementation along with correction of primary metabolic abnormality (acidosis and hypokalemia). Phosphate supplementation can be given to the patients with vitamin D-resistant rickets with RTA. (18)

1. Hochberg Z. Rickets: past and present. Introduction. Endocr Dev. 2003;6:1–13.
2. Pettifor JM. Rickets and vitamin D deficiency in children and adolescents. Endocrinol Metab Clin North Am. 2005;34:537–553. vii.
3. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357:266–281.
4. Kooh SW, Fraser D, Reilly BJ, Hamilton JR, Gall DG, Bell L. Rickets due to calcium deficiency. N Engl J Med. 1977;297:1264–1266.
5. Albright F, Burnett CH, Parson W, Reifenstein EC, Roos A. Osteomalacia and late rickets: Various etiologies met on United States with emphasis on that resulting from specific forms of renal acidosis, therapeutic implications for each etiological subgroup, and relationship between osteomalacia and Milkman's syndrome. Medicine. 1946;25:399–479.
6. Chan JC. Acid-base disorders and the kidney. Adv Pediatr. 1983;30:401-71.
7. Pereira PC., Miranda D., Oliveira E., Silva ACS e. Molecular Pathophysiology of Renal Tubular Acidosis. Current Genomics. 2009;10(1):51-59.
8. Sahay M, Sahay R. Renal rickets-practical approach. Indian Journal of Endocrinology and Metabolism. 2013;17(Suppl1):S35-S44.
9. Pettifor JM. Nutritional rickets: deficiency of vitamin D, calcium, or both?Am J Clin Nutr. 2004 Dec;80(6 Suppl):1725S-9S.
10. Litman NN, Ulstrom RA, Westin WW. VITAMIN D RESISTANT RICKETS. California Medicine. 1957;86(4):248-253.
11. Rodríguez Soriano J. Renal tubular acidosis: the clinical entity. J Am Soc Nephrol. 2002;13:2160–2170.
12. Batlle D, Haque SK. Genetic causes and mechanisms of distal renal tubular acidosis. Nephrol Dial Transplant. 2012;27:3691–3704.
13. Shayakul C, Alper SL. Inherited renal tubular acidosis. Curr Opin Nephrol Hypertens. 2000 Sep;9(5):541-6. Escobar LI, Simian C, Treard C, et al.
14. Stover EH, Borthwick KJ, Bavalia C, Eady N, Fritz DM, Rungroj N, et al. Novel ATP6V1B1 and ATP6V0A4 mutations in autosomal recessive distal renal tubular acidosis with new evidence for hearing loss. J Med Genet. 2002;39:796–803.
15. Smith AN, Skaug J, Choate KA, Nayir A, Bakkaloglu A, Ozen S, et al. Mutations in ATP6N1B, encoding a new kidney vacuolar proton pump 116-kD subunit, cause recessive distal renal tubular acidosis with preserved hearing. Nat Genet. 2000;26:71–75.
16. Karet FE, Finberg KE, Nelson RD, Nayir A, Mocan H, Sanjad SA, et al. Mutations in the gene encoding B1 subunit of H+-ATPase cause renal tubular acidosis with sensorineural deafness. Nat Genet. 1999;21:84–90.
17. Oguejiofor P, Chow R, Yim K, Jaar BG. Successful Management of Refractory Type 1 Renal Tubular Acidosis with Amiloride. Case Reports in Nephrology. 2017;2017:8596169.
18. Minari M, Castellani A, Garella S. Renal tubular acidosis associated with vitamin D-resistant rickets. Role of phosphate depletion. Miner Electrolyte Metab. 1984;10:371–374.