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Recurrent Hypokalemic Paralysis - An Interesting Cause

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Abstract : Recurrent hypokalemic paralysis is caused y either channelopathies or by conditions associated with recurrent or persistent renal or non renal losses of potassium. Distal renal tubular acidosis (dRTA) is one of the causes of renal potassium loss leading to hyokalemia. One of the important presentations of dRTA is recurrent hypokalemic weakness, which can be life threatening.a We would like to present one such case of recurrent hypokalemic paralysis with respiratory weakness secondary to dRTA. Type 1 or dRTA involves impaired distal acidification of urine. dRTA often presents as renal stone disease with nephrocalcinosis in adults, rickets and growth retardation in children with ultimate short stature in adulthood. Our case is a 19-year-old male who had features of dRTA like recurrent hypokalemic paralysis, metabolic acidosis, stunted growth, rickets and nephrocalcinosis.

Keyword : Recurrent hypokalemic paralysis, Metabolic acidosis, Abnormal urine pH, Short stature,Rickets, Nephrocalcinosis, Distal Renal Tubular Acidosis.

Case Report:
19-year-old male presented to our hospital with acute onset progressive weakness of all four limbs. On admission, there was neither neck muscle weakness nor speech, swallowing, and breathing difficulty. He did not give any history of seizures or altered sensorium .There was no history suggestive of cranial nerve involvement. No history of fever or recent gastrointestinal or respiratory illness. He had no history of any sensory or sphincter control disturbances. No history of trauma or headache. There was no history of recent vaccination or intake of diuretic, laxative or any other drug .He gave history of similar weakness thrice in the past from which he had recovered with treatment. His first attack was at the age of 10 years. He had been advised to be on regular treatment, which he has been taking irregularly.There was no positive family history. He does not smoke or drink alcohol. On examination, he was short for his age (ht:147 cms) and also had genu valgum (see Figures 1 and 2).

Figure1

His basic investigations were as follows:
Complete blood count: Hb% – 9.8 gm%; TC – 9000 cells/cu.mm; DC – P61% L36% E3%; platelets – 2.20 lakh cells/cu.mm
Urine examination: nil albumin and sugar; occasional epithelial cells; no pus cells.
Random blood sugar: 121 mg%; Urea – 18 mg%; Creatinine – 0.5 mg%
Liver function tests: Serum bilirubin – 0.9mg/dl; AST – 31 IU/L; ALT – 22 IU/L
Chest X ray: normal;
Xray both knees: Metaphysial lucency and metaphysial (valgus) deformity (see Figure2)

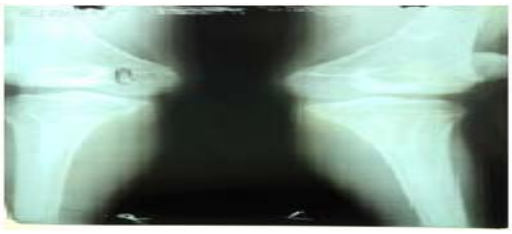

Figure 2

ECG: u waves in v2 to v6
Serum electrolytes:
Day1: Sodium – 139 meq/l; Potassium – **2.6 meq/l**; Chloride – 110 meq/l; Calcium – 8.9 mg/dl; Phosphorus – 2.2 mg/dl; magnesium – 2.0 mg/dl.
Within few hours of admission, patient developed neck muscle weakness, difficulty in swallowing and difficulty in breathing. He was immediately shifted
to IMCU and under careful observation, he was started on intravenous potassium chloride 20 mmol/hr. His symptoms improved gradually and he
regained normal muscle power over a period of 12 hours. Once he was able to swallow and speak well, oral syrup potassium chloride was given.
We proceeded with further urine analysis:
Urine specific gravity – 1.012, urine osmolality – 600 mosm/kg, Urine sodium – 102 meq/L, Potassium – 37.4 meq/L, chloride – 104 meq/L. 24 hrs urine potassium: **72 meq/d** (normal – <15 meq/d) which revealed increased urine potassium excretion.The Transtubular potassium gradient TTKG calculated as (P_{osmol} x $U_{Potassium}$)/($P_{Potassium}$ x U_{osmol}) was 5.9 indicating increased potassium secretion (plasma osmol – 280 mosm/kg).We moved with arterial blood gas analysis: serum pH – 7.1, Pco_2 – 29.5mm hg, Hco_3^-– 18.2 mmol/l, Serum Anion gap: $Na^+(Cl+Hco_3)$ =10.8, Impression: non anion gap metabolic acidosis.We proceeded with urine pH after ruling out urinary tract infection. His serial early morning urine pH was >5.5 (day 1: 5.8, day 2: 6.2, day 3: 6.0) and his urine anion gap $(Na^+ + K^+)Cl$ was positive (35.4) . Based on hypokalemic paralysis, non anion gap metabolic acidosis, renal potassium loss, positive urine anion gap, failure of urine acidification in the presence of systemic metabolic acidosis and the absence of other proximal tubular defect, we diagnosed him as a case of dRTA.

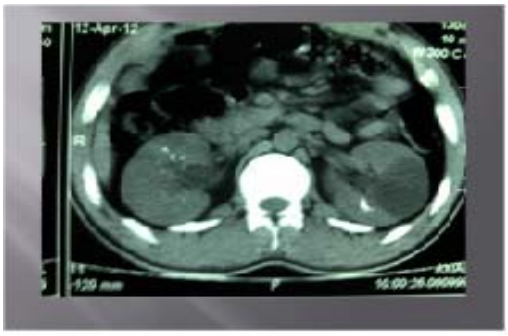

Figure3

His audiogram and thyroid function tests were normal. On further history taking and examination, we could not find features suggestive of any secondary cause of dRTA. Also since the patient has presented since childhood with recurrent hypokalemic paralysis and has features of rickets and short stature, we arrived at the probable diagnosis of primary dRTA.
After our patient regained full muscle power and after serum potassium reached normal values, we started him on oral sodium bicarbonate 30 mmol/d in divided doses.

Discussion:

Hypokalemia is defined as plasma K^+ concentration <3.6 meq/L.[1] It can be asymptomatic or can manifest as fatiguability, limb weakness and paralytic ileus. It can also cause serious complications like cardiac arrhythmias or respiratory paralysis. Distal renal tubular acidosis has been reported as an occasional cause of hypokalemic paralysis.[2] Renal tubular acidosis (RTA) was first described by Lightwood et al., in 1935[3]and Butler et al., in 1936 in children[4] and by Baines in 1945 in adults. Renal tubular acidosis defines a group of disorders in which tubular hydrogen ion secretion is impaired out of proportion to the prevailing glomerular

filtration rate (GFR). The defects responsible for impaired acidification are localized either to the proximal or the distal nephron. Albright et al. described dRTA as a distinct entity in 1946.[7] Type 1 RTA (dRTA) involves impaired distal acidification of urine. In contrast to proximal RTA, patients with dRTA cannot normally acidify the urine whether the bicarbonate is normal or markedly reduced.[8] Hence the classic feature of distal RTA is an inability to acidify the urine maximally (to pH <5.5) in the face of systemic acidosis,[9,10] provided other causes of low pH like urinary tract infection are ruled out. Further urine ammonia NH_4 excretion rate helps to differentiate dRTA from other forms of chronic hyperchloremic metabolic acidosis. A positive urine anion gap ($UNa^+ + UK^+ - Ucl$) indicates low ammonium excretion ,thus favouring dRTA.[8] In summary, dRTA is generally confirmed by systemic acidemia, a relatively high urine pH and a low ammonium excretion rate.[8] Distal RTA can be either primary or secondary to other causes. Primary dRTA may be hereditary or sporadic with autosomal recessive and autosomal dominant forms.[1] The clinical manifestations of dRTA depend upon the disease type, severity and whether it is acquired or inherited. The inherited form 7
of dRTA causes similar metabolic abnormalities, but it is more likely to result in decreased bone mineralization and growth retardation.In inherited forms of dRTA, the transport defects in alpha intercalated cells of the medullary collecting duct are responsible pathogenetically.[8] Autosomal dominant dRTA (type 1a) is caused by heterozygous mutations of gene SLC4A1 coding anion exchanger protein, AE-1 situated basolaterally.[8] Lack of basolateral exit of HCO_3^- leads to intracellular alkalinisation which inhibits apical proton secretion. AE-1 mutations cause late-onset and milder diseases. [11] Familial cases are mostly autosomal dominant.[12,13] Autosomal recessive dRTA I is genetically heterogenous and occurs with or without sensorineural deafness. Mutations involve the apical vacuolar H^+-ATPase and affect the a4 or B1 subunit of the proton pump.[11] Its onset is early and severe with nephrocalcinosis, growth delay and bone problems. In autosomally recessive dRTA with sensorineural deafness (type 1b), various mutations of ATP6V1B1 gene coding for the B1 subunit occur. Mutations in the a4 subunit of the proton pump manifest in adulthood with milder sensorineural deafness.[8] Autosomal recessive dRTA with normal hearing (type 1c) is caused by mutations in the ATP6N1B gene coding a non catalytic accessory subunit of the proton pump.[8]
The hallmark of distal RTA has been the inability to acidify the urine appropriately during spontaneous or chemically induced metabolic acidosis.[9] Reduction in the net H+ secretion in the distal nephron, together with continuous urinary bicarbonate losses, prevents urinary acidification which in turn impairs NH4+ and titratable acid excretion and results in positive acid balance, hyperchloremic metabolic acidosis and volume depletion.[9] Hypokalemia and hypercalcinuria

are typically present.[9,10] The development of systemic acidosis tends to diminish net proximal fluid reabsorption with an increase in distal delivery, resulting in volume contraction and activation of renin aldosterone system. Increased distal sodium delivery coupled with increased circulating aldosterone leads to increased renal k^+ secretion.[8] Hence urinary potassium losses lead to hypokalemia.

Calcium released from bone in the process of buffering of acid results in hypercalciuria.[1] In addition, metabolic acidosis impairs the hydroxylation of 25 (OH) vitamin D_3 to 1, 25 $(OH)_2$ vitamin D_3, thus decreasing intestinal calcium absorption as well as tubular reabsorption of calcium. The end result is hypercalciuria, negative calcium balance and secondary hyperparathyroidism with an additive deleterious effect on the skeleton.[6] Enhanced proximal citrate absorption accounts for hypocitraturia.[1]Since chronic metabolic acidosis also decreases renal production of citrate,[9,10]the resulting hypocitraturia in combination with hypercalciuria creates an environment favorable for urinary stone formation and nephrocalcinosis. Nephrocalcinosis appears to be a reliable marker for dRTA, because nephrocalcinosis does not occur in proximal RTA.[9,10]

Correction of metabolic acidosis in dRTA is achieved by administration of alkali in an amount only slightly greater than daily acid production. In adult patients with dRTA, this is may be equal to no more than1 to 3 mEq/kg/day.[14] In growing children, endogenous acid production is usually between 2 and 3 mEq/kg/day but may, on occasion, exceeds 5 mEq/kg/day. Larger amounts of bicarbonate must be administered to correct the acidosis and maintain normal growth.[9,10]

In adult patients with dRTA, correction of acidosis with alkali therapy reduces urinary K^+ excretion, and prevents hypokalemia and Na^+ depletion.[9] Therefore, in most adult patients with distal RTA, K^+ supplementation is not necessary.[9] However, patients with severe potassium deficits need K^+ correction prior to bicarbonate correction to prevent lowering of potassium levels to dangerous levels. Maintenance of a normal serum bicarbonate with alkali therapy also raises urinary citrate, reduces urinary calcium, lowers the frequency of nephrolithiasis and tends to correct bone disease and restore normal growth in children.[14,15] Therefore, every attempt should be made to correct and maintain near-normal serum bicarbonate in all patients with dRTA.

Either sodium bicarbonate tablets or Shohl's solution are used for bicarbonate correction. Citrate is generally tolerated better than sodium bicarbonate 1and can be given as the potassium or sodium salt, depending on the severity of hypokalemia.

Conclusion

Distal RTA has been reported as an occasional cause of recurrent hypokalemic paralysis, which can be life threatening. It is not only important to do potassium correction in a given case of hypokalemic paralysis, but also to find the underlying cause in each case, because early detection and appropriate treatment of the underlying disorder like dRTA can not only cure recurrent hypokalemic paralysis but can also help to achieve adequate growth velocity, adult height and prevent the development of other complications like rickets and nephrocalcinosis.

Bibliography

1. Dan L Longo, Dennis L Kasper, J Larry Jameson, Anthony S Fauci, Stephen L Hauser, Joseph Loscalzo, *Harrison's Principals of Internal Medicine*
,18th edition, volume 2, chapter 284.
2. Koul PA, Salcem SM, chronic active hepatitis with renal tubular acidosis presenting as hypokalemic paralysis with respiratory failure, *Ada Paediatr*
1992;31:662–665.
3. Lightwood R. Calcium infarction of kidney in infants. *Arch Dis Child* 1935;10:205–210.
4. Butler AM, Wilson JL, Farber S. Dehydration and acidosis with calcification of renal tubules. *J Pediatr* 1936;8:489–499.
5. Baines GH, Barclay JA, Cooke WT. Nephrocalcinosis
associated with hyperchloremia and low plasma bicarbonate. *Q J Med* 1945;14:113–122.
6. Horacio J. Adrogu, Nicolaos E. Madias, Renal tubular acidosis, Davison, Alex M.; Cameron, J. Stewart, Grunfeld, Jean-Pierre, Ponticelli, Claudio,
Ritz, Eberhard, Winearls, Christopher G., Ypersele, Charles van (Eds.), *Oxford Textbook of Clinical Nephrology*, 2005, 3rd edition, chapter 5.4.
7. Basak RC, Sharkawi KM, Rahman MM, Swar MM. Distal renal tubular acidosis, hypokalemic paralysis, nephrocalcinosis, primary hypothyroidism,
growth retardation, osteomalacia and osteoporosis leading to pathological fracture: a case report. *Oman Med J* 2011 Jul;26(4):271–274.
8. Seldin and Gieisch. Clinical syndromes of metabolic acidosis. *The Kidney*, 4th edition, volume 2.
9. DuBose TD, Jr. Disorders of acid base balance. Barry M. Brenner, *Brenner and Rector's The Kidney*, Philadelphia: WB Saunders, 8th edition, volume
1, chapter 14.
10. DuBose TD, McDonald GA, Renal tubular acidosis. DuBose TD, Hamm LL (Eds), *Acid-Base and Electrolyte Disorders: A Companion to Brenner and*
Rector's The Kidney, Philadelphia: WB Saunders; 2002:189 –206.
11. Troels Ring. Renal tubular acidosis. Ronco, Bellomo, Kellum (Eds.). *Critical Care Nephrology* 2nd edition.
12. DuBose TD. Autosomal dominant distal renal tubular acidosis and the AE1 gene. *Am J Kid Dis* 1999;33: 1190–1197.
13. Chaabani H, Hadj-Khlil A, Ben-Dhia N, Braham H. The primary hereditary form of distal renal tubular acidosis: clinical and genetic studies in 60-
member kindred. *Clin Genet* 1994;45:194–199.
14. Morris, Jr, RC, Sebastian A: Alkali therapy in renal tubular acidosis: Who needs it?. *J Am Soc Nephrol* 2002; 13:2186–2188.
15. Wrong O, Henderson JE, Kaye M: Distal renal tubular acidosis: Alkali heals osteomalacia and increases net production of 1,25-dihydroxyvitamin D. *Nephron Physiol* 2005; 101:72–76.