

A RARE CASE OF QUADRIPARESIS

Dinesh Kumar¹, Prasanth Varghese², Percival Gilvaz³

¹Senior Resident, Department of Neurology, Jubilee Mission Medical College and Research Centre, Thrissur.

²Assistant Professor, Department of Neurology, Jubilee Mission Medical College and Research Centre, Thrissur.

³Professor and HOD, Department of Neurology, Jubilee Mission Medical College and Research Centre, Thrissur.

ABSTRACT

BACKGROUND

Proximal renal tubular acidosis is characterized by a defect in the ability to reabsorb bicarbonate in proximal tubule. It is usually associated with Fanconi syndrome. Isolated proximal RTA is a rare entity and it is mainly associated with drug intake like carbonic anhydrase inhibitors. Hereby, we describe a case of 46-year-old male presented with quadripareisis due to hypokalaemia accompanied with metabolic acidosis and other features suggested of type 2 RTA caused after intake of Acetazolamide for glaucoma.

KEYWORDS

Acetazolamide, Hypokalaemia.

HOW TO CITE THIS ARTICLE: Kumar D, Varghese P, Gilvaz P. A rare case of quadripareisis. J. Evolution Med. Dent. Sci. 2016;5(88): 6592-6593, DOI: 10.14260/Jemds/2016/1490

BACKGROUND

Renal Tubular Acidosis (RTA) is a constellation of syndromes arising from derangements of acid transport. Hypokalaemic periodic paralysis is a channelopathy causing recurrent episodic weakness. Renal Tubular Acidosis (RTA) is an uncommon secondary cause of Hypokalaemic periodic paralysis. Proximal renal tubular acidosis is characterised by a defect in the ability to reabsorb HCO₃ in the proximal tubule. Proximal RTA is more often associated with the Fanconi syndrome which is characterised by increased urinary excretion of solutes like phosphate, uric acid, glucose, amino acids, low-molecular weight proteins and bicarbonate. Many disorders may cause proximal renal tubular acidosis, but most commonly it is caused by drugs. Carbonic anhydrase inhibitors, acetazolamide which is used to manage conditions such as glaucoma or increased intracranial pressure is one such drug that causes isolated proximal RTA. Here, we describe such a case of hypokalaemic paralysis secondary to proximal RTA caused by acetazolamide used for glaucoma.

CASE REPORT

A 46-year-old male came with history of abrupt onset of proximal muscle weakness of all four limbs. No history of bowel and bladder involvement. No history of sensory symptoms. No history of any cranial nerve involvement. No h/o comorbidities in past. History revealed that patient was on acetazolamide for glaucoma for last 2 weeks. On examination, patient was conscious and well oriented. Tone was reduced in all the four limbs. Power was 1/5 in proximal group of muscles in all 4 limbs, while power was 3/5 distally. Deep tendon reflexes were 1+ in all limbs, bilateral plantar flexor, sensations were intact. Rest of systemic examination was within normal range.

Financial or Other, Competing Interest: None.

Submission 16-09-2016, Peer Review 22-10-2016,

Acceptance 28-10-2016, Published 03-11-2016.

Corresponding Author:

Dinesh Kumar,

F7/29 Mata Kaulan Marg,

Kashmir Avenue,

Amritsar-143001,

Punjab.

E-mail: manishksharma27@gmail.com

DOI: 10.14260/jemds/2016/1490



Blood pressure was normal. Considering history and clinical examination in view of the diagnosis of acute flaccid paralysis was entertained.

Laboratory findings showed normal haemogram, blood urea-18 mg/dL, serum creatinine 0.8 mg/dL, serum sodium 138 mEq/L, serum potassium - 2.2 mEq/L (low), serum chloride 105 mEq/L, serum calcium - 9.0 mg/dL, arterial blood gas showed pH 7.24 (Acidic pH), serum bicarbonate of 14 (low). Urinary pH done was < 5.5. Urine examination did not show any glucose, proteins or pus cells. Ultrasonography of kidney showed no renal parenchymal changes or evidence of renal lithiasis. ECG changes of hypokalaemia were found. Blood sugar, renal and liver function tests were within normal limits. Altogether, all the tests were consistent with features of proximal RTA.

Diagnosis of acetazolamide-induced proximal RTA presenting with hypokalaemic paralysis was entertained and acetazolamide was replaced with timolol. Repeat ABG was done after correction of hypokalaemia, which showed no evidence of metabolic acidosis. Repeat ABG pH was 7.38 (normal), bicarbonate was 26 (normal) and potassium was 3.9 mEq/L (normal). Patient's muscle weakness improved following removal of drug and potassium replacement. The patient was kept in hospital for next 5 days and no recurrence of symptoms was found and hence was discharged on timolol. The patient was followed in our OPD after 2 weeks and followup potassium was normal.

DISCUSSION

Patients with proximal RTA, however, have an intact ability to lower urinary pH to less than 5.5. Below a particular threshold, bicarbonate excretion in patients with proximal RTA ceases and the urine pH can fall to lower limits of normal. This is a distinctive feature from patients with distal RTA in whom the urine pH do not fall normally regardless of the degree of acidosis.

Unlike patients with distal RTA, urine PCO₂ measured should be normal in patients with proximal RTA indicating that their distal H⁺ secretion is intact and is absent or expressed weakly in most segments of the collecting duct and the distal segment of the proximal tubule. Both isoforms of carbonic anhydrase play an important role in acid-base transport throughout the nephron.

In the cytosol of tubular cells, carbonic anhydrase II favours the formation of bicarbonate and hydrogen ion from CO₂ and H₂O that enter the cell. Skeletal abnormalities and rickets are less common with proximal RTA than in classic distal RTA. Nephrocalcinosis and nephrolithiasis are usually absent in proximal RTA, but are prominent features of distal RTA. Hypokalaemia and renal potassium wasting are features of distal RTA. Proximal renal tubular acidosis is characterised by an inability to reabsorb bicarbonate in the proximal tubules. Most of the times, drug-induced proximal RTA is associated with Fanconi syndrome. Drugs that causes severe proximal RTA with Fanconi syndrome include ifosfamide, oxaliplatin, aminoglycosides, antiretroviral drugs, topiramate, valproic acid and others.^[1,2] Type 2 RTA is usually manifested as bicarbonate wastage in the urine reflecting that the defect in proximal tubular transport which is severe enough, so that the capacity for bicarbonate reabsorption in the thick ascending limb of Henle's loop and more distal nephron segments is overwhelmed.^[3] Most of times drug-induced proximal causes of isolated proximal RTA are: a) Genetic causes like NBCe1 mutation and CA II mutation (mixed RTA); b) Acquired causes include Carbonic anhydrase inhibitors-Acetazolamide, Topiramate, Dichlorphenamide and Brinzolamide.

The human kidney contains a membrane bound carbonic anhydrase protein that differs from cytoplasmic enzyme CA I, CA-II, CA-III and secretory form (CAVI) in saliva.^[4] The main isoform of carbonic anhydrase found in the kidney is the membrane-bound and cytoplasmic carbonic anhydrase isoform (CA-IV and CA II), respectively.^[5,6] CA II is more widespread and is present in almost all cells of the nephron, whereas CA IV has limited expression and is found mainly in the proximal tubule. CA inhibitors have been used in clinical practice, mainly to reduce elevated intraocular pressure in glaucoma or to treat mountain sickness.^[7] Three of them (acetazolamide, methazolamide and dichlorphenamide) can be administered systemically. All carbonic anhydrase inhibitors are sulfonamide derivatives and have the potential to cause proximal RTA.^[7] The defect in bicarbonate reabsorption with CA inhibitors is explained by inhibition of CA IV located in the apical membrane of the proximal tubule cells. It has been found that some CA inhibitors, such as acetazolamide and benzolamide, are less membrane-permeable and are not effective inhibitors of cytosolic CA as membrane-bound CA.^[8] Typically CA inhibitors, therefore, cause a pure proximal RTA as a result of inhibition of the membrane-bound CA IV isoform resulting in the isolated inhibition of bicarbonate reabsorption.^[9]

Likewise, our patient was on acetazolamide for glaucoma for 2 weeks subsequent to which he developed symptoms consistent with proximal RTA. Hypokalaemia and renal potassium wasting are characteristic of distal RTA.^[10] In proximal RTA, hypokalaemia can also occur particularly

during bicarbonate therapy or associated with Fanconi syndrome.^[11] Hypokalaemia results in muscle fatigability, weakness and electrical cardiac disturbances as in our patient, but ECG changes were not consistent with hypokalaemia. Drug-induced proximal RTA caused by CA inhibitors is usually mild and readily reversible. Our patient also recovered completely and shortly after stopping acetazolamide.

Ikeda et al also described a case of increased muscle weakness due to hypokalaemia secondary to proximal RTA caused by acetazolamide, but here patient was a known case of hypokalaemic periodic paralysis.^[12]

REFERENCES

1. Izzedine H, Launay-Vacher V, Isnard-Bagnis C, et al. Drug-induced fanconi's syndrome. *Am J Kidney Dis* 2003;41(2):292-309.
2. Schwartz GJ. Physiology and molecular biology of renal carbonic anhydrase. *J Nephrol* 2002;15(5):S61-74.
3. Moorthi K, Battle D. Renal tubular acidosis. In: Gennari J, Adrogue HJ, Galla JH, et al. (eds) *Acid-Base disorders and their treatment*. Boca Raton: Taylor and Francis 2005:417-59.
4. Karlmark B, Agerup B, Wistrand PJ. Renal proximal tubular acidification. Role of brush-border and cytoplasmic carbonic anhydrase. *Acta Physiol Scand* 1979;106(2):145-50.
5. Winum JY, Poulsen SA, Supuran CT. Therapeutic applications of glycosidic carbonic anhydrase inhibitors. *Med Res Rev* 2009;29(3):419-35.
6. Supuran CT, Scozzafava A. Benzolamide is not a membrane-impermeant carbonic anhydrase inhibitor. *J Enzyme Inhib Med Chem* 2004;19(3):269-73.
7. Keilani T, Segal R, Esparaz D, et al. Effect of dorzolamide, a novel topical carbonic anhydrase inhibitor, on urinary acidification in subjects with moderate renal impairment (clinical research meeting). *J Investig Med* 1995.
8. Battle D, Moorthi KM, Schlueter W, et al. Distal renal tubular acidosis and the potassium enigma. *Semin Nephrol* 2006;26(6):471-8.
9. Soriano RJ. Renal tubular acidosis: the clinical entity. *J Am Soc Nephrol* 2002;13(8):2160-70.
10. McSherry E, Sebastian A, Morris RC. Renal tubular acidosis in infants: the several kinds, including bicarbonate-wasting, classic renal tubular acidosis. *J Clin Invest* 1972;51(3):499-514.
11. Edelman CMJR, Rodriguez-Soriano J, Boichis H. An isolated defect in renal bicarbonate reabsorption as a cause of hyperchloremic acidosis. *J Pediatr* 1965;67:946.
12. Ken I, Yasuo I, Daisuke Y, et al. Acetazolamide-induced muscle weakness in hypokalemic periodic paralysis. *Internal Medicine* 2002;41(9):743-5.