Original Research Paper

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Internal Medicine

VITAMIN D DEFICIENCY ASSOCIATED SECONDARY HYPERPARATHYROIDISM PRESENTING AS HYPOKALEMIC PERIODIC PARALYSIS - A RARE CAUSE OF RTA II

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ABSTRACT A 24yr-old female with no known co-morbidities presented to casualty with complaints of acute weakness of bilateral lower limbs for 1 day which rapidly progressed to quadriparesis over few hours. On presentation, her vitals were normal. Neurological examination revealed acute flaccid paralysis and inability to hold neck (grade 0/5). Deep tendon reflexes were diminished. Initial labs showed profound hypokalemia 1.9 meq/l. ABG revealed hyperchloremic non-anion gap metabolic acidosis which with hypokalemia suggested a possibility of Renal Tubular Acidosis. A diagnosis of type II RTA was made secondary to vitamin D deficiency complicated by secondary hyperparathyroidism, severe hypokalemia leading to periodic paralysis. Patient was managed conservatively with electrolyte and vit D deficiency correction to which patient responded well and was discharged with restoration of normal power and resolution of quadriparesis.

KEYWORDS : RTA/VIT D/ PARALYSIS/HYPOKALEMIA

BACKGROUND

Renal tubular acidosis (RTA) is group of disorders having proximal renal tubular defect in the reabsorption of bicarbonate ($HCO3^-$) or the distal excretion of hydrogen ion (H^+). Proximal RTA may have a hereditary origin or may be secondary to administration of carbonic anhydrase inhibitors. Low levels of Vitamin D lead to secondary rise in blood PTH levels which has a significant role in bicarbonate wastage.1 Hypokalaemia usually accompanies both distal and proximal RTA.2 Hypokalemic periodic paralysis is mostly observed in distal RTA. It is very rarely seen in proximal RTA. This case presents a rare case of VDD induced pRTA presenting with hypokalemia severe enough to cause periodic paralysis. VDD remains mostly underdiagnosed. A delay in comprehending its association with pRTA could lead to complication like electrolyte imbalance, poor growth in children, osteomalacia.

CASE PRESENTATION

A 24yr-old female with no known co-morbidities presented to the emergency department with complaints of acute onset weakness of bilateral lower limbs for 1 day which rapidly progressed to quadriparesis over few hours. No sensory complaints were reported by patient. Bladder and bowel habits were intact. She denied any history of vomiting, diarrhea, blood in urine or similar illness in the past. Family history was non-contributory. Patient denied history of any medication or drugs or metal or toxin exposure.

On presentation, her vitals were within normal limits. Neurological examination revealed generalised flaccid paralysis with diminished power in bilateral upper limbs (grade 1/5), lower limb (grade 1/5) and inability to hold neck (grade 0/5). Deep tendon reflexes were diminished. Sensory examination was normal. Following history and examination, a possibility of Guillain-Barre syndrome and periodic paralysis was kept.Initial lab investigation in the ED showed profound hypokalemia 1.9 meq/l. Venous blood analysis revealed hyperchloremic non-anion gap metabolic acidosis (pH 7.16, bicarbonate 12meq/l, chloride 116meq/l, pCO_2 26mmHg). (Table 1)

A hyperchloremic normal anion gap metabolic acidosis with hypokalemia suggested a possibility of Renal Tubular Acidosis(RTA). ECG showed mild ST depression with U waves. (Figure 1) On further evaluation, patient was found to have vitamin D deficiency, hypocalcemia and secondary hyperparathyroidism. Urinalysis showed pH 7.2, positive urine anion gap and an elevated fractional excretion of bicarbonate (>15%). Thyroid function test and ultrasound KUB was normal.

Frusemide- fludrocortisone stress test performed and urine got acidified post administration. Urine tested positive for amino-acids. Serum protein electrophoresis performed and found to be normal. Tmp/GFR was calculated and found to be 1 indicative of phosphaturia. Opthalmological examination was unremarkable. A diagnosis of type II RTA was made secondary to vitamin D deficiency complicated by secondary hyperparathyroidism, severe hypokalemia leading to periodic paralysis.

Table 1. Metabolic Profile

Basic chemistry		Reference values
pH	7.16	
Bicarbonate	12 mEq/L	22–26 mEq/L
Sodium	138 mEq/L	135–145 mEq/L
Potassium	1.9 mEq/L	3.5–5.0 mEq/L
Chloride	116 mEq/L	98–107 mEq/L
Magnesium	2 mEq/L	1.5-2.5 mEq/L
Protein	5.3 g/dl	6-8g/dl
Albumin	2.6 g/dl	3.7-5.3 g/dl
Blood urea	24 mg/dl	10-40 mg/dl
Uric acid	3.5mg/dl	2.5-7 mg/dl
Creatinine	0.9 mg/dl	0.7-1.3 mg/dl
Calcium	6.7 mg/dl	8.5-11 mg/dl
Phosphorus	1 mg/dl	2.5-5.5 mg/dl
Parathyroid hormone	88 ng/L	10–65 ng/L
Vitamin D (25-OH D)	15 nmol/L	62–200 nmol/L
Urinary creatinine	20 mg/dl	For adult women, 0.59 to 1.04 mg/dl
Urinary phosphate	10mg/g	58-846mg/g (female)
TMP/GFR	1	2.6- 3.8 mg/dL

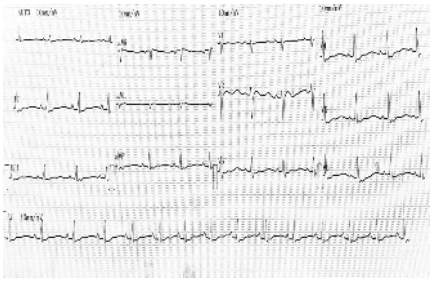

Figure 1. ECG of the patient showing hypokalemic changes

Patient was admitted to intensive care unit in view of severe hypokalemia and other metabolic derangements. Patient was managed with intravenous potassium, calcium replacement and bicarbonate correction. Vitamin D supplements were given. The weakness resolved after 3 days of therapy. She reported improvement in her symptoms in follow up visits.

DISCUSSION

Secondary hypokalemic periodic paralysis has been seen previously in pRTA.3 Patients with proximal RTA develops hypokalemia due to failure of proximal bicarbonate reabsorption.4 Bicarbonaturia results in fall in intravascular volume, which triggers RAAS activation. There is also increased Na+ delivery to distal tubule due to compromised proximal HCO3–reabsorption. Stimulation in RAAS along with increased distal Na+ delivery, cause an upsurge in potassium loss in urine manifesting as hypokalemia.[4]

Acid base homeostasis is mainly regulated by the kidneys. It mainly involves two processes, first is bicarbonate reabsorption in the proximal tubule and the second is excretion of hydrogen ion(H^+) in the distal nephron. Impaired reabsorption of filtered HCO3- in the proximal tubule is the hallmark of proximal RTA. It can either present as an isolated defect of bicarbonate reabsorption or as Fanconi syndrome.[5,6] Vitamin D deficiency has been known to cause Type II RTA with or without Fanconi syndrome.7,8 VDD is one of the most common nutritional deficiency. It is highly prevalent in adult female.[9]

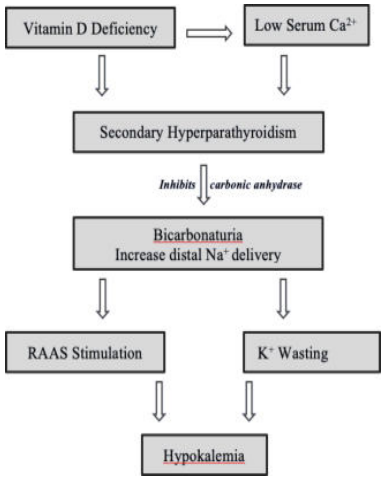

Figure 2. Vitamin D deficiency leading to hypokalemia causing hypokalemic periodic paralysis

In our patient, the diagnosis of proximal RTA was made owing to VDD. Vitamin D plays a significant role in intestinal absorption of calcium and phosphorus. Low levels of calcium and phosphorus were seen in our patient in the background of vitamin D deficiency. Both VDD and hypocalcemia lead to secondary hyperparathyroidism. Hyperparathyroidism is associated with both proximal and distal RTA10. Excess of parathyroid hormone affects renal tubular functions. Parathyroid hormone hampers activity of carbonic anhydrase in proximal tubule, which impairs proximal bicarbonate reabsorption leading to metabolic acidosis.11 Chronic metabolic acidosis has been identified to cause osteomalacia in adults due to loss of calcium salts from bone and hypophosphatemia.12 Failure to identify the relationship between VDD and proximal RTA can lead to under diagnosis and inadequate management of complications associated with it.

Due to coexistent hypocalcemia, hypophophatemia, phosphaturia and elevated PTH levels, vitamin D deficiency resulting in secondary hyperparathyroidism was suspected as most likely explanation.

TAKE HOME MESSAGES

- Vitamin D deficiency associated secondary hyperparathyroidism can cause proximal renal tubular acidosis.
- RTA should be kept as a possibility in the evaluation of hypokalemic periodic paralysis.

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