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Acquired Distal Renal Tubular Acidosis Presenting with HypokalemicParalysis- A Rare Case Report

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ABSTRACT:
Acquired distal renal tubular acidosis is a rare disorder in adults. It usually presents with recurrent renal stones and metabolic acidosis, but extremely rarely distal RTA can present with sever hypokalemic paralysis. In this case report we discuss a case of distal RTA which is likely due to Sjogren's syndrome presented with severe hypokalemic paralysis. To confirm the diagnosis of distal RTA, an urinary acidification test is recommended using either the standard ammonium chloride test or furosemide-fludrocortisone combination test while the gold standard for the diagnosis of distal RTA is the conventional ammonium chloride test.Primary goal of treatment of distal RTA is to control the metabolic acidosis, whereby to reduce calciurea and hypocitraturia which can potentially mitigate the risk of osteoporosis, nephrocalcinosis and nephrolithiasis.

I. INTRODUCTION:

The kidneys and the lungs are the major organ systems which contribute to the maintenance of acid–base homeostasis in the body. This is accomplished by acid excretion by the kidneys, exhalation of carbon dioxide through the lungs and intracellular and extracellular buffering mechanisms. Sometimes distal renal tubular acidosis might be the first presentation of autoimmune diseases like primary Sjogren's syndrome, Systemic lupus erythematosus. It is considered to be due to renal tubulointerstitial involvement as a part of autoimmune process. Renal tubular acidosis occurs when the kidneys fail toadequately reclaim filtered bicarbonate ions or secrete sufficient hydrogen ions to maintain acid–base homeostasis, and it is characterized by normal anion gap metabolic acidosis.The term "distal renal tubular acidosis" is referred to the defective acidification by distal part of the nephron, namely the connecting tubule and the collecting duct.This is in contrast to the "proximal renal tubular acidosis" in which the reabsorption of bicarbonate by the proximal tubule is impaired. Acquired forms of distal renal tubular acidosis are commonly associated with autoimmune diseases such as primary Sjögren syndrome and systemic lupus erythematosus. Prevalence of distal renal tubular acidosis in primary Sjögren syndrome is estimated to be 5–25 % . Recurrent nephrolithiasis, nephrocalcinosis and chronic metabolic acidosis with high random urinary pH suggest the presence of distal renal tubular acidosis.

Confirmation of the diagnosis of distal renal tubular acidosis is done by a urinary acidification

test, either the well-known ammonium chloride test or lately proposed, less complicated furosemide – fludrocortisone test.

The patient we discuss in this case report, presented to emergency department with sever hypokalemia , non-anion gap metabolic acidosis and quadriparesis. The subsequent evaluation revealed distal renal tubular acidosis and the combination of clinical features and auto-immune markers were suggestive of primary Sjögren syndrome.

II. CASE REPORT:

61 yearold Chinese lady with past history of hypertension which is well controlled with amlodipine 2.5 mg once a day.She presented to emergency department with acute onset generalized weakness for one day duration associated with difficulty in walking.Vital signs were stable on admission, she was afebrile , blood pressure 141/74 mmHg, heart rate 73 bpm and oxygen saturation was 99% on room air. On examination her GCS was 15,upper limb and lower limb power was 3/5 both proximally and distally, and sensation was intact.

Initial lab tests showed severe hypokalemia and non-anion gap metabolic acidosis.

Serum potassium 2.0 mmol/l, serum bicarbonate 16.0 mmol/l, anion gap 10 and serum creatinine was 105 umol/l (eGFR 74 ml/min). CT scan of the brain showed no acute infarct or intracranial hemorrhage.

She was admitted to medical hi-dependency unit for cardiac monitoring, insertion of central line and potassium replacement with intravenous potassium chloride. The power of

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upper limbs and lower limbs improved to 5/5 after correction of hypokalemia.

Further investigations showed urine Ph 7.0, urine anion gap +13, urine potassium/creatinine ratio 7.5 and 24 hour total urine potassium was 36 mmol per day.Us kidneys and renal artery doppler showed normal size kidneys (right kidney 9.5 cm and left kidney 9.9 cm) with normal echogenicity, no evidence of nephrocalcinosis or renal artery stenosis. Serum renin and aldosterone ratio was within the reference range.

She was diagnosed with distal renal tubular acidosis and was discharged with oral potassium chloride SR 1200 mg twice a day and oral sodium bicarbonate 500 mg three times per day. She was supposed to follow up with outpatient renal clinic to monitor serum potassium, serum bicarbonate and renal function and to complete the work up for distal renal tubular acidosis. But she defaulted follow ups and medications for five years and presented with generalize weakness to outpatient renal clinic. During first clinic visit her serum potassium 2.4 mmol / l, serum bicarbonate 17 mmol/l, anion gap 9 and serum creatinine was 120 mol/l (eGFR 49 ml/min). She was advised to admit to the hospital for telemetry monitoring and intravenous replacement of potassium, but was not keen.She was started on 30% potassium citrate 7.5 ml twice daily, serum potassium improved to 4.0 to 4.5 mmol/l and renal function remained stable.

CT KUB without contrast was done and showed medullary nephrocalcinosis with bilateral non obstructive renal calculi.

Further history revealed she has dry eyes and dry mouth for many years, hence ENA screen was done which turned out to be positive for Anti SS-A and Anti SS-B antibodies.

Due to financial constrained patient refused further investigations and referral to rheumatologist to exclude likely diagnosis of underlying primarySjögrens syndrome. Hence the conclusion after second presentation was distal renal tubular acidosis due to possible underlying sjogrens syndrome complicated withnephrocalcinosis and renal calculi.

TABLE 1: Laboratory findings on admission

Parameter	Result	Reference range
Serum urea	6.5	2.8-7.7 mmol/l
Serum sodium	140	135-140 mmol/l
Serum potassium	2.0	3.5-5.3 mmol/l
Serum chloride	114	96-108 mmol/l
Serum bicarbonate	16	19-31 mmol/l
Serum creatinine	105	50-90 umol/l
Anion gap	10	
Serum phosphate	0.52	0.65-1.65 mmol/l
Serum Calcium	2.24	2.10-2.60 mmol/l
Serum Magnesium	1.01	0.65-0.95 mmol/l
Autoimmune profile	ANA-Positive Anti ds-DNA- negative Anti SS-A-positive Anti SS-B-positive	

TABLE 2:Urine studies

Parameter	Result
Urine Ph	7.0
Urine sodium	40 mmol/l
Urine Potassium	14 mmol/l
Urine Chloride	41 mmol/l
Urine anion gap	+13
24-hour urine potassium	36 mmol/Day
24-hour urine volume	2560 ml

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TABLE 3: Changes in serum potassium and bicarbonate in response to initiation of potassium citrate

Serum potassium (mmol/l)	2.4	3.1	3.2	4.9	3.7	2.9	3.2	4.3	4.2
Serum Bicarbonate(mmol/l)	20.5	19.3	17	29.7	20.7	22.2	19.1	24.8	23
30% Potassium citrate (ml)	-	-	10 ml twice a day	5 ml twice a day	5 ml twice a day	7.5 ml twice a day	7.5 ml twice a day	7.5 ml twice a day	7.5 ml twice a day

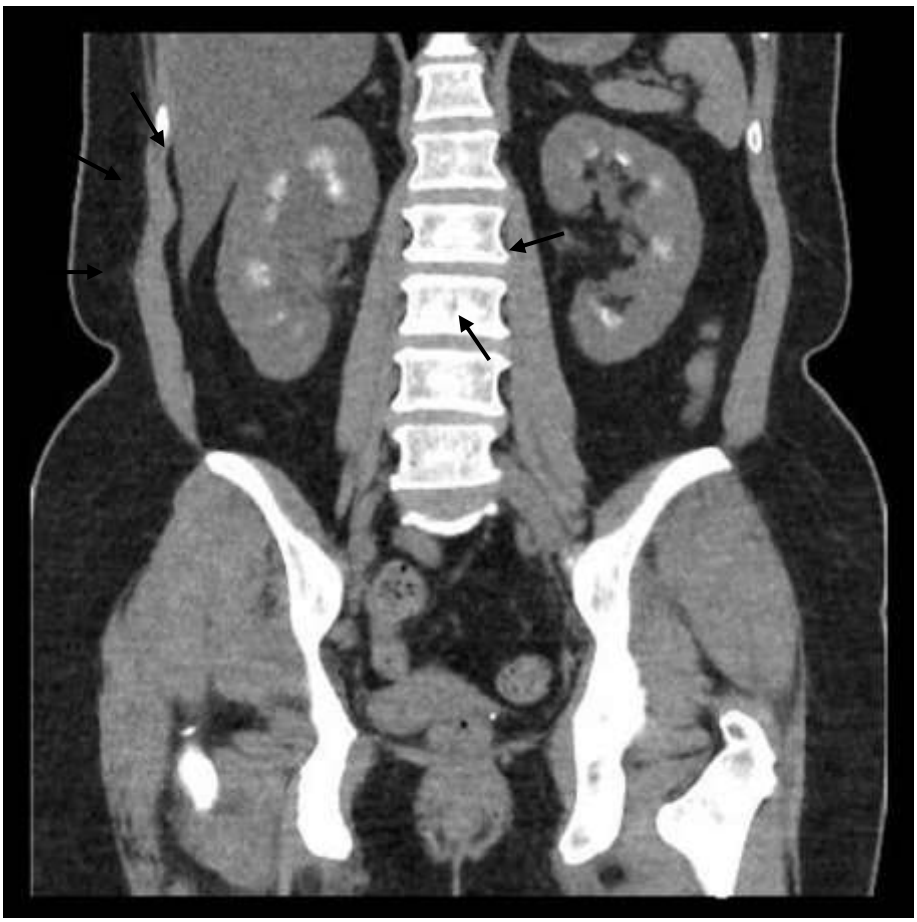

FIGURE 1:Non contrast CT KUB showing medullary nephrocalcinosis (Black arrows).

III. DISCUSSION:

Distal renal tubular acidosis is an uncommon disorder and the common causes for new-onset distal RTA in adults are autoimmune diseases (eg, Sjögren's syndrome and systemic lupus erythematosus). Sometimes distal RTA might be the first presentation of the autoimmune conditions like Sjögren's syndrome.Prevalence of distal renal tubular acidosis in primary Sjögren syndrome is around 5–25 %.

Hereditary distal RTA is commonly due to genetic mutations in the basolateral chloride-bicarbonate exchanger (SLC4A1 gene) and in the apical hydrogen-ATPase (ATP6V0A4 and ATP6V1B1 genes).

Distal RTA is a result of impaired acidification at the distal renal tubule and is characterized by the inability to lower urinary pH maximally (<5.5) in the presence of systemic acidemia. Meanwhile proximal HCO_3^- reabsorption generally remains normal.Recurrent nephrolithiasis and chronic metabolic acidosis are common presentations, while server hypokalemia with muscle paralysis is a very rare presentation of acquired form of distal RTA. About 5% of the patients with distal RTA develops

nephrolithiasis,meanwhile 56 % develops nephrocalcinosis.

To confirm the diagnosis of distal RTA, a urinary acidification test is recommended using either the standard ammonium chloride test or furosemide-fludrocortisone combination test.

Gold standard for the diagnosis of distal RTA is the conventional ammonium chloride test, however recently proposed furosemide and fludrocortisone combination test is becoming more popular due to its easy applicability and well tolerance by the patients.

Distal acidification

The α-intercalated and principal cells, located in the collecting tubule, are the majorcontributors for the secretion of hydrogen irons. The principle cells reabsorb sodium via epithelium sodium channels (eNac) creating luminal electronegativity, which facilitates the secretion of potassium or hydrogen irons.

The luminal electronegativity induces the expression of hydrogen ATPase pumps in α-intercalated cells leading to secretion of hydrogen ions.Hydrogen ions and bicarbonate irons are generated by the activity of intracellular carbonic anhydrase-II enzyme. The chloride-bicarbonate cotransporter (Ae-1) located at the basolateral membrane exchanges intracellular bicarbonate with extracellular chloride irons. The apical hydrogen H+ /K+ exchanger of α-intercalated cell is another ATPase which contributes to hydrogen ion section and potassium ion reabsorption. Pathophysiologically causes of distal RTA can be divided in to four main categories, (1) voltage defect, (2) H+ secretion defect, (3) H+ gradient defect and (4) ammonium generation defect.

Clinical presentation

Renal stones and metabolic acidosis are some of the common presentations of distal RTA.In the presence of chronic metabolic acidosis, bones exchange sodium, potassium and calcium for hydrogen iron, resulting in osteoporosis and hypercalciuria.Metabolic acidosis also leads to enhanced proximal tubular reabsorption of citrate, resulting in hypocitraturia. Hypercalcemia in combination of hypocitraturia and alkaline urine promote nephrocalcinosis and nephrolithiasis.Sometime patients with distal RTA develops hypokalemia due to potassium wasting triggered by hydrogen iron secretion defect.Despite potassium wasting, these patients usually maintain normal serum level, by potassium shift from intracellular compartment. However like the case we discussed above there are case reports which describe patients who present to the emergency department with hypokalemic paralysis, including respiratory arrest.

Treatment

Primary goal of treatment of distal RTA is to reveres the metabolic acidosis, whereby to reduce calciurea and hypocitraturiawhich might mitigate the risk of osteoporosis, nephrocalcinosis and nephrolithiasis.Current recommended drug of choice is potassium citrate (1–2 meq/kg/day) which provides both bicarbonate and potassium.

IV. CONCLUSIONS:

In this review, we discussed a case of acquired distal renal tubular acidosis presenting with sever hypokelmic paralysis possibly due to underlying primary Sjögrens syndrome. Clinicians should have high index of suspicion and exclude distal renal tubular acidosis in patientspresenting with recurrent calcium phosphate stones and metabolic acidosis with or without hypokalemia.The diagnosis of distal RTA is made using a urinary acidification test, in which the patient is unable to acidify the urine to pH <5.5. The treatment of distal RTA is based on restoring the acid–base balance, which can be achieved with potassium citrate.

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