RESEARCH PAPER | Medical Science | Volume : 4 | Issue : 8 | August 2014 | ISSN - 2249-555X

Recurrent Hypokalaemia, Osteomalacia, Distal Renal Tubular Acidosis, Secondary To Mixed Connective Tissue Disorder (Mctd) - A Case Report

KEYWORDS: Hypokalemia, overlap syndrome(MCTD), distal renal tubular acidosis.

Vidyasagar Kekathi
Associate Professor of General Medicine, Government General Hospital Kurnool

Abdur Rahim
Associate Professor of General Medicine, Government General Hospital Kurnool

Sudhakar Penumadu
Professor of General Medicine, Government General Hospital Kurnool

Harish
Resident in General Medicine, Government General Hospital Kurnool

ABSTRACT *Recurrent hypokalaemia with osteomalacia with distal renal tubular acidosis secondary to serologically positive over lap syndrome is a rare entity. A female patient aged 29 years presented with sudden onset of weakness of all four limbs, on evaluation hypokalemia was evident and treated accordingly after which she recovered, but complained of generalized myalgias and was having waddling gait. X-ray pelvis with femur showed fracture, on further evaluation investigations revealed distal renal tubular acidosis. Serologically there was evidence of overlap syndrome (MCTD) which was the cause for renal tubular acidosis.*

INTRODUCTION:

Recurrent hypokalaemic period paralysis may be primary or secondary. Primary hypokalaemic periodic paralysis is inherited and manifest in younger age group below <25 years. Secondary hypokalaemic periodic paralysis may be secondary to diuretic abuse, hyperthyroidism, gastroenteritis, renal tubular acidosis, villous adenoma of colon. Renal tubular acidosis is of two types proximal (type-2), distal (type-1) which can be differentiated by ability to acidify urine PH <5.5. Distal RTA may be secondary to tolune toxicity, Amphotericin toxicity, overlap syndromes.

Mixed connective tissue disorder (MCTD) is an overlap syndrome that embraces features of SLE, Scleroderma, polymyosistis /dermatomyositis. People with MCTD will be having high titers of antibodies to nuclear RNP-anti UIRNP. Renal involvement in MCTD is seen in 25% cases, presenting as either glomerulonephritis or tubulointerstitial disorders, of which glomerulonephritis is common. Tubulointerstitial nephritis can present as fanconi syndrome, renal tubular acidosis. MCTD presenting as renal tubular acidosis is rare.

CASE REPORT

A 29 year old female presented with sudden onset of weakness of all four limbs and on nervous system examination higher mental functions were normal with hypotonia and grade 1 power of all four limbs. Similar complaints of 2 to 3 episodes per year since 2 years, diagnosed as recurrent hypokalaemia. Patient had Routine investigations - complete blood picture, random blood sugar, blood urea, serum creatinine, complete urine examination, liver function tests were within normal limits. Serum electrolytes initially showed K^{+} 3.0 mmol/l, Na^{+1} 142mmol/l, CL^{-1} 120mmol/l, ca^{+2} 6.5mmol/l. Treated with potassium infusion. After recovery on ambulation we noticed waddling gait, for which x-ray pelvis was taken showing fracture femur. We considered possibility of association of hypokalaemia with osteomalacia secondary to renal tubular acidosis and investigated. Urinary potassium levels were 33.4 mmol/l (normal <15 mmol.l) with sodium 158 mmol/l and chloride 190mmol /l with acidic urine ph of 6.5 and urine electrophoresis negative for bence jones protein. Arterial blood gas analysis initially s/o metabolic acidosis, serum proteins were showing hypoproteinemia with proteins 5.7g/dl and low albumin 2.2g/dl with normal serum globulin. Chest X-ray and ultrasound abdomen were normal, while HRCT chest was showing ground glass haziness in both lungs suggestive of early stage of interstitial lung disease. Spirometry and 2Decho were normal. X-ray pelvis was showing fracture left upper 1/3rd of femur(figure1). Thyroid profile and parathyroid hormones were normal with CPK-212u/l. With low serum potassium, increased urinary potassium, urinary ph-6.5 the diagnosis of renal tubular acidosis type-1(distal) considered and further evaluated for the cause. Serology was positive for RA factor, ANA, U1RNP, RO-52, SS-B/LA suggesting MCTD as cause for RTA.

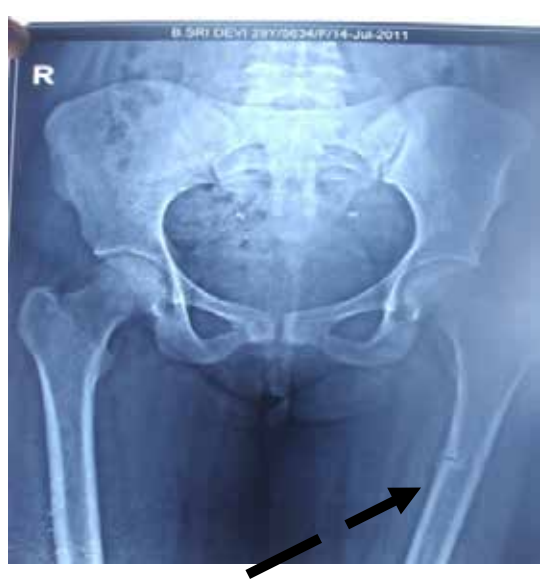

Figure 1: X-ray pelvis with upper 1/3 of femur – fracture upper 1/3 of left femur, osteoporosis

Volume : 4 | Issue : 8 | August 2014 | ISSN - 2249-555X

Investigations
* Hb – 9.8 mg/dl
* TLC – 4700 cells/Cmm
* RBS – 94 mg/dL
* Blood urea – 18 mg/dL

Serum Electrolytes:
Na^+ - 142 mmol/L (135 – 155mmol/L)

K^+ - 3.0 mmol/L (3.5 – 5.5)

Cl^+ 120 mmol/L (98 – 107)
* Ca++ - 6.5 mmol/L (8.5 – 10.5)
* Phosphours - 4.6 mg/dL (2.5 – 5)mg/dL
* Magnesium – 1.9 mg/dL (1.5 – 2)

Liver function test-
Total bilirubin-0.7mg/dl

Direct bilirubin-0.2mg/dl

Indirect bilirubin-0.5mg/dl

SGPT-29 U/L

SGOT-31U/L

Alkaline phosphatase-156U/L

Serum total proteins – 5.7 grms/dL (6-8)

Serum albumin - 2.2grms/dL (3.5)

Serum globulin – 3.5 grms/dL

* Serum parathyroid hormone – 19.2 pg/ml (15 – 65 pg/ml)
* Regular Thyroid profile – Normal
* Serum CPK -80u/l

ABG Analysis:	**on 28/07/2011**	**on 19/08/2011**
p^H -------→	7.25	7.376
Pco_2 ------→	2.4mmHg	28.1mmHg
Hco_3 -------→	12.8mmol/L	16.1mmol/L
Po_2 --------→	102mmHg	116mmHg

Table1: Extractable Nuclear Antigens Qualitative profile

Auto Antibody	Result
U1-nRNP	Positive
RO-52	Strong Positive
SS-B/La	strong Positive
Sm	Negative
SS-A	Negative
SCl-70	Negative
PM-SCl	Negative
Jo-1	Negative
ds-DNA	Negative
PCNA	Negative
CENP-B	Negative
Histones	Negative
Nucleosomes	Negative
Rib-P Protein	Negative
AMA - M2	Negative

Urine Analysis:
Specific gravity – 1.010
Albumin – Nil
Sugar – Nil
Deposits – 2-4 puscells/hpf
Phosphates - absent
Potassium – 33.4 mmol/day (<15mmol/L)
Sodium – 158mmol/day
Chlorides – 180mmol/day
Calcium – 190mg/day

Urine pH – 6.5 (acidic)
* **ECG** –within normal limits – no u waves
* **U/s abdomen** – Normal
* **Chest X-ray – PA view** – Normal study
* **CT Scan abdomen** – Normal study
* **HRCT Chest** :
  Ground Glass Haziness Posterior in both lungs.
  Early stage of interstitial lung disease

TREATMENT ADVISED
* Syrup Potklor - 15ml in glass of water BD
* Tab: Calcium - 500mg BD
* Tab: Soda mint - 1 tablet TID
* Tab: Azaroan – 50mg BD
* Tab:Pantop–40mg
  Tab: Bio D3 – 1 tablet OD
* Patient improved clinically with treatment. Patient is stable for the past 2 years.

DISCUSSION:
Hypokalemic periodic paralysis may be primary or secondary type[4]. Primary hypokalemic paralysis is autosomal dominant occurs <25 years age group and is exacerbated by strenuous exercise, high carbohydrate diet, cold exposure, excitement[4].

Secondary hypokalemic periodic paralysis associated with gastroenteritis, diuretic abuse, renal tubular acidosis, Bartter syndrome, hyperthyroidism, villous adenoma of colon[1,6].

In the present case the age of onset is > 25 years which rules out possibility of inherited (primary) form of hypokalemic periodic paralysis hence secondary hypokalemic periodic paralysis was considered. There was no history of diarrhea, vomiting, or diuretic abuse in the present case. The absence of polyuria, polydipsia, nausea, vomiting, constipation, hypochloremia, and hyponatremia ruled out Bartter syndrome. Normal serum magnesium and urinary calcium excretion ruled out the possibility of Gitelman's syndrome. Acidic urinary PH of 6.5 but >5.5, high urinary potassium levels with ABG analysis suggesting metabolic acidosis suggested distal RTA (type1) in this case (Table-2).

Table-2 Distinguishing features of the different RTAs.

	Proximal RTA	Distal RTA	RTA IV
Type of Acidosis	Hyperchloremic metabolic acidosis	Hyperchloremic metabolic acidosis	Hyperchloremic metabolic acidosis
Serum Potassium	lo	low	high
Urine pH	< 5.5	>5.5	< 5.5
Urine bicarbonate loss	↑↑↑	↑↑	↑↑

Volume : 4 | Issue : 8 | August 2014 | ISSN - 2249-555X

RTA type-1 is either inherited or acquired. Inherited RTA type I can be either autosomal-dominant or autosomal-recessive. In the acquired form, the disorder can be caused by drugs, autoimmune diseases, or by infection(2). Some of the more common acquired forms are caused by Sjögren syndrome, lupus, hepatitis, treatment with amphotericin B, toluene toxicity, and chronic pyelonephritis[7,8]. In present case no h/o drug intake, infection, gluesniffing, chronic pyelonephritis are present. Serology was positive for RA factor, ANA, U1RNP, RO-52, SS-B/LA suggest overlap syndrome that is MCTD as cause for RTA.

MCTD is an overlap syndrome that embraces features of SLE, scleroderma, polymyositis/dermatomyositis. It usually takes several years before enough overlapping features have appeared to be confident that MCTD is the most appropriate diagnosis. Raynauds phenomena is the commonest problem and one of the earliest manifestation of MCTD.

Initially renal involvement was considered rare. After 4 decades of trials renal involvement was thought to be present in about 25%. RTA is a disorder of renal tubule acidification characterized by hyperchloremic acidosis and hypokalemia and inability to lower urinary Ph < 5.5. In this disorder distal nephron does not lower urinary Ph because collecting duct permits back diffusion of H^+ from lumen to blood or inadequate transport of H^+ions. Chronic acidosis impairs absorption of calcium causing renal hypercalciurea and mild secondary hyperparathyroidism. Osteomalacia occurs because of acidosis induced loss of bone material and inadequate production of 1,25 (OH)2D3,and may present with pseudofractures which occurred in this case. .[5]

Majority of cases of type 1 RTA result from sjogren syndrome, SLE, scleroderma which are part of mixed connective tissue overlap syndrome. In present case the serology was positive for ANA, U1RNP, RO-52, SS-B/LA along with, recurrent hypokalaemia, low urinary ph, low serum calcium, fracture femur suggesting recurrent hypokalemia with ostomalacia secondary distal RTA (type 1) secondary to MCTD (Serological positive)[9].

ALORCON-SEGOVA Diagnostic criteria: for MCTD
Serologic: high titers of U1-nRNP

Clinical Criteria: 3/5 (must have synovitis or myositis)
Edema of the hands
Synovitis
Myositis
Raynaud's phenomenon
Acrosclerosis

Conclusions:
* Recurrent Hypokalemia + Osteomalacia = RTA
* Recurrent hypokalaemia+osteomalacia+high titres of antibodies= overlap syndromes
* Recurrent Hypokalemia + Hypertension = 1. Liddle Syndrome

2. Mineralocorticoid excess
* Recurrent Hypokalemia + Age <25yrs = Channelopathy
* Recurrent Hypokalemia + Hypomagnesaemia = R/O Bartter Syndrome or Gitlesmans Syndrome
* Recurrent Hypokalemia + Fine tremors = Thyrotoxic periodic paralysis

REFERENCE
1. Stedwell RE, Allen KM, Binder LS: Hypokalemic paralyses: a review of the etiologies, pathophysiology, presentation, and therapy. | 2. Rodríguez Soriano J. Renal tubular acidosis: the clinical entity. J Am Soc Nephrol 2002. Aug;13(8):2160-2170 10.1097/01.ASN.0000023430.92674.E5 [PubMed] [Cross Ref] | 3. Am J Emerg Med 1992, 10(2):143-148. PubMed Abstract | Publisher Full Text | 4. Soule BR, Simone NL. Hypokalemic periodic paralysis: A case report and review of the literature. Cases J. 2008;1:256–61. [PMC free article] [PubMed] | 5. Batlle D, Moorthi KM, Schlueter W, Kurtzman NSemin Nephrol. 2006 Nov; 26(6):471-[PubMed] [Ref list] | 6. Bagga A, Dutta S. Hypokalemic muscle paralysis. Indian Pediatr. 1994;31:1297–8. [PubMed] | 7. McCurdy DK, Frederic M, Elkinton JR. Renal tubular acidosis due to amphotericin B. N Engl J Med 1968. Jan; 278(3):124-130 10.1056/NEJM196801182780302 [PubMed] [Cross Ref] | 8. Carlisle EJ, Donnelly SM, Vasuvattakul S, Kamel KS, Tobe S, Halperin ML. Glue-sniffing and distal renal tubular acidosis: sticking to the facts. J Am Soc Nephrol 1991. Feb;1(8):1019-1027 [PubMed] | 9. Bagga A, Bajpai A, Gulati S, Singh A Indian Pediatr. 2001 Nov; 38(11):1301-5. | 10. Srivastava RN, Bagga A. Pediatric Nephrology. 2nd ed. Delhi: Cambridge Press; 1997. Renal tubular disorder; pp. 203–7. |