Case Report:

Rhabdomyolysis secondary to diarrhoea induced hypokalemia in a human immunodeficiency virus-seropositive patient

K. Swaroopa,[1] M. Murali Krishna,[1] Y.S.N.Raju,[1] M.V.S. Subbalaxmi,[1] Naval Chandra,[1] Siraj Ahmed Khan[2]
Departments of [1]Medicine, [2]Biochemistry, Nizam's Institute of Medical Sciences, Hyderabad

ABSTRACT

Hypokalemia with rhabdomyolysis caused by diarrhoea is uncommon in human immunodeficiency virus (HIV) infected patients. We report the case of a patient with HIV1 infection who presented with chronic diarrhoea that led to hypokalemia induced rhabdomyolysis and acute kidney injury (AKI). A 32 -year-old man, known to be HIV-1 seropositive who was on treatment with tenofovir, lamivudine, lopinavirand ritonavir, presented to the emergency department with 6 months history of diarrhoea and sudden onset of weakness of all 4 limbs of two days duration. On examination limb power was grade 3/5 with hypotonia and diminished reflexes. Laboratory investigations showed severe hypokalemia, low urinary potassium, normal anion-gap metabolic acidosis, markedly increased creatine kinase and mildly increased serum creatinine. He was diagnosed as having diarrhoea induced hypokalemic myopathy leading to rhabdomyolysis and AKI. With potassium supplements, antiprotozoal treatment and adequate hydration he improved significantly and is on regular follow-up. Patients presenting with hypokalemia should be closely monitored for rhabdomyolysis, because outcome is good with early treatment.

Key words: *HIV, Diarrhoea, Hypokalemia, Rhabdomyolysis*

Swaroopa K, Murali Krishna M, Raju YSN, Subbalaxmi MVS, Chandra N, Khan SA. Rhabdomyolysis secondary to diarrhoea induced hypokalemia in a human immunodeficiency virus-seropositive patient. J Clin Sci Res 2015;4:164-8. DOI: http://dx.doi.org/10.15380/2277-5706.JCSR.14.006

INTRODUCTION

Rhabdomyolysis refers to the disintegration of striated muscle resulting in release and circulation of muscle cell constituents into the extracellular fluid.[1] When hypokalemia develops rapidly and becomes severe, muscle injury and rhabdomyolysis may occur.[2] Hypokalemia induced rhabdomyolysis is a rare condition that can be caused by gastrointestinal or renal loss of potassium or due to drugs like diuretics, laxatives, among others. There are few reports in literature about chronic diarrhoea leading to secondary rhabdomyolysis in a human immunodeficiency virus (HIV) - seropositive patient and we report one such case.

CASE REPORT

A 32-year-old male patient with HIV1 Infection from 2001 who was non-compliant with antiretroviral treatment (ART), came to our institute with chief complaints of chronic intermittent diarrhoea of 6 months duration, sudden onset progressive weakness of lower limbs of 2 days duration in the form of inability to hold objects, get up from squatting position and walk without support. There was no history of fever, trauma, vomiting or backache prior to the illness. There was no history of sensory symptoms, cranial nerve involvement, and bladder or bowel incontinence. He was receiving antiretroviral treatment with ritonavir/lopinavir, tenofovir and lamivudine

Received: 11 February 2014; Revised manuscript: 10 July 2014; Accepted: 18 July 2014.

Corresponding author: Dr K. Swaroopa, Assistant Professor, Department of General Medicine, Nizam's Institute of Medical Sciences, Hyderabad, India.
e-mail: swarooparedymd@gmail.com

Online access
http://svimstpt.ap.nic.in/jcsr/apr-jun15_files/2cr215.pdf
DOI: http://dx.doi.org/10.15380/2277-5706.JCSR.14.006

from last one-and-half year. At admission his vital parameters were stable. Neurological examination showed hypotonia with diminished deep tendon reflexes and decreased power (3/5) in all limbs, more pronounced in lower limbs. Rest of the neurological examination, including sensory system examination was normal. Other systems examination was also normal.

The differential diagnosis we considered initially were (i) weakness secondary to hypokalaemia (as he had history of diarrhoea); (ii) HIV-associated neuropathy in the back ground of longer duration of HIV infection which usually manifests with paresthesias and pain in the extremeties and (iii) possibility of acute inflammatory demyelinating polyneuropathy was also considered in view of weakness of limbs and associated hypotonia and its higher incidence in HIV-infected patients. Laboratory investigations showed cluster differentiation (CD4+) T-lymphocyte count of 191 cells/mm^3, haemoglobin 13.3 g/dL, total leucocyte count 4,500/mm^3, platelet count 3.2 lakhs/$mm.^3$ Serum alkaline phosphatase was normal. There was a mild elevation in hepatics transaminases [aspartate aminotransferase (AST) 198 IU/L, alanine aminotransferase (ALT) 65 IU/L].

Other investigations included total proteins 6.9 g/dL and albumin 3g/dL; blood urea 18mg/dL; serum creatinine 0.6 mg/dL and serum electrolytes showed sodium 133meq/ L, potassium 1.5 meq/L, calcium 8.6 meq/ L, phosphorous 3.5 meq/L, magnesium 2.1 mg/ dL, and bicarbonate 14meq/L. Urine microscopy was normal. Spot urine examination showed a low potassium of 9 meq/L (normal 6-20 meq/L) which is near the lower normal limit. Arterial blood gas analysis showed normal anion-gap metabolic acidosis. Stool culture had grown normal flora and no evidence of cysts or ova of parasites. Electrocardiogram (ECG) showed broad flat T waves and QT prolongation QT_C interval 0.49 second (Figure 1).

Nerve conduction studies showed significant reduction in compound muscle action potential (CMAP) amplitudes of all motor nerves with normal sensory nerve action potential (SNAP) amplitudes, distal latencies, conduction

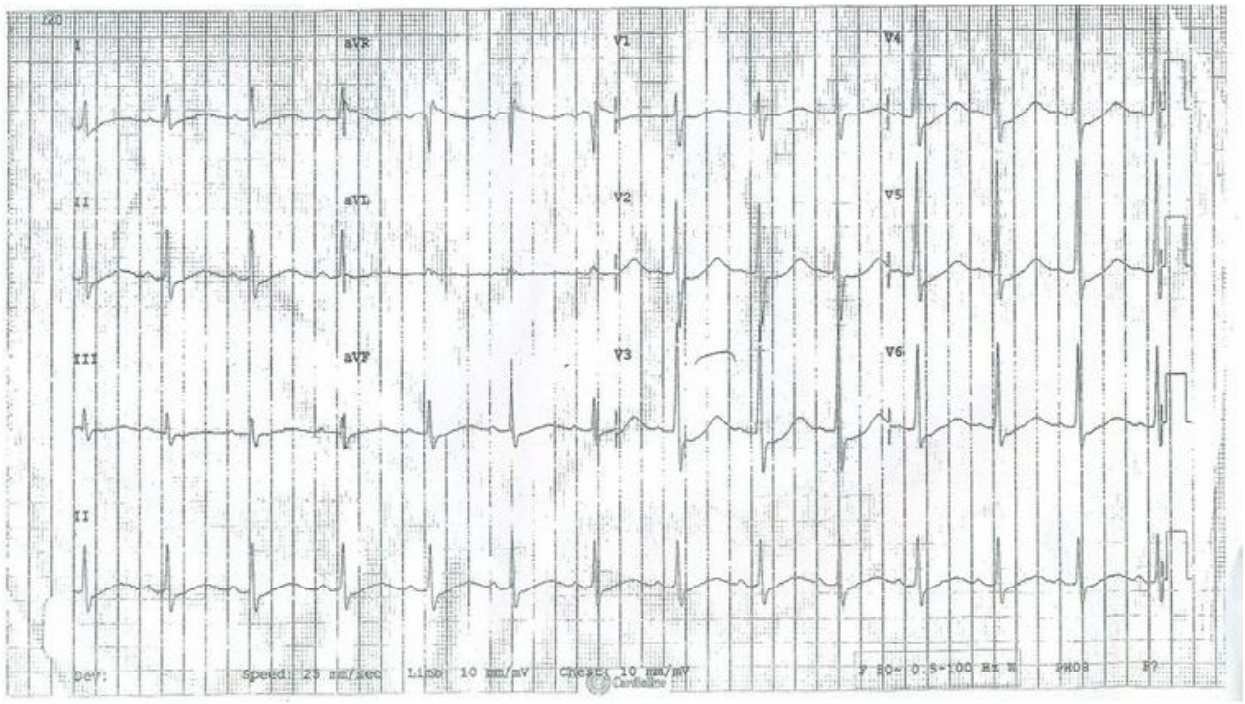

Figure 1: Electrocardiogram showing QT - prolongation and broad flat T - waves

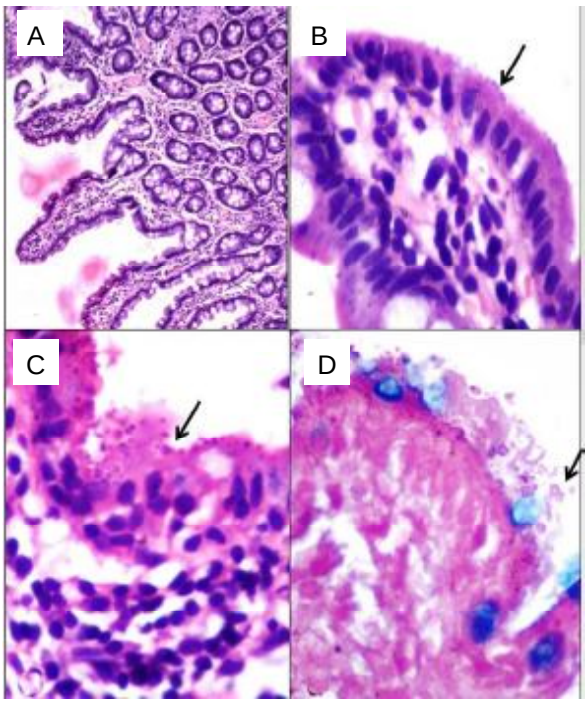

Figure 2: Duodenal biopsy photomicrograph showing duodenal mucosa with sub-epithelial tissue (Haematoxylin and eosin, × 40) (**A**). Photomicrograph showing tiny round basophilic organisms (Haematoxylin and eosin, × 400) in the superficial component (arrow) (**B** and **C**). Photomicrograph showing cryptosporidia (arrow) (Periodic acid Schiff, × 100) (**D**).

velocities and F-wave latencies. The differential diagnosis considered for paralysis were acute motor axonal neuropathy (AMAN), Guillain-Barre syndrome, hypokalaemic paralysis. Causes for diarrhoea that were considered were parasitic infections with giardia, cryptosporidium, isospora and HIV infection itself. Colonoscopy was normal. Upper gastrointestinal endoscopy and duodenal biopsy (from D2) showed cryptosporidium (Figure 2). He was treated with antiprotozoal, nitazoxanide 500 mg and ofloxacin 200 mg twice daily along with parenteral potassium 120 meq/day in normal saline and oral potassium (potklor syrup) 20 meq 6 hourly for 5 days. Two days after admission his power of limbs and reflexes improved, but he complained pain and spasm in both lower limbs. Deep vein thrombosis was ruled out. Rhabdomyolysis was suspected; serum creatine kinase (CK) was 9323 IU/L (normal 20-200 IU/L); creatine kinase muscle brain (CK-MB) fraction was normal. As there was no evidence of renal loss of potassium, and no history of diuretic or laxative usage, hypokalaemia was considered to be due to diarrhoea and it was concluded rhabdomyolysis was due to hypokalemia. He was continued treatment with intravenous fluids along with potassium supplementation and adequate urine output was maintained. Antiretroviral therapy was continued with ritonavir/lopinavir, tenofovir and lamivudine. During hospital stay, his serum creatinine had risen from 0.6 mg/ dL to 1.4 mg/dL in 48 hours. Liver function tests, serum creatinine, potassium and creatine kinase values during the hospital course are shown in Table1. General condition of the patient improved and diarrhoea responded to nitazoxanide treatment. The patient is on regular follow-up in the out patient department and is doing well at 6 months follow up.

DISCUSSION

Chronic diarrhoea is a common gastrointestinal manifestation in patients with acquired immune deficiency syndrome (AIDS). This is commonly caused by opportunistic infections commonly, parasitic infections but can also be

Table 1: Laboratory abnormalities during in-hospital stay

Parameter	Day1	Day 3	Day 6	Day of discharge	At 2 weeks follow-up
Serum potassium (meq/L)	1.5	2.4	3.2	4	4.4
Creatine kinase (IU/L)	ND	9323	3990	1560	80
Serum creatinine (mg/dL)	0.6	1.4	0.8	0.6	1.0
AST (IU/L)	68	198	134	106	35
ALT (IU/L)	65	112	124	74	20

AST = aspartate aminotransferase; ALT = alanine aminotransferase ND = not done

caused by the HIV infection itself.[3] Hypokalemia is one of the complication due to chronic diarrhoea which can lead to various complications like arrhythmias, glucose intolerance, muscular weakness, rhabdomyolysis and paralysis.[4]

Hypokalemia is responsible for 14%-28% for the total cases of rhabdomyolysis. However, often hypokalemia is not recognized as the cause of rhabdomylosis due to the compensatory increase in serum potassium levels caused by rhabdomyolysis itself.[4] The proposed mechanism is that, normally, during exercise, muscles release intracellular potassium causing local rise in potassium which causes vasodilation and increases perfusion to the active muscle cells. Hypokalemia decrease local hyperkalemia preventing the vasodilation which results in tissue hypoxia and rhabdomyolysis.[5]

There are mainly three categories of patients with rhabdomyolysis: i) pure exercise-induced rhabdomyolysis; ii) patients with genetically acquired defects in adenosine triposphate (ATP) generation; and iii) patients with one or more precipitating causes like infections, drugs or toxins e.g., cocaine, amphetamines, snake venom toxin (especially of sea snakes), injuries (direct and ischaemic) and situations with long-standing muscular contraction or rigor (status epilepticus, malignant hyperthermia) etc., leading to rhabdomyolysis.[4,6] In our patient rhabdomyolysis was possibly due to hypokalemia secondary to diarrhoea. Tenofovir induced hypokalemia was also considered in differential diagnosis, but it was ruled out as there was no evidence of proteinuria, renal dysfunction or other evidence of Fanconi syndrome.

Rhabdomyolysis is a syndrome characterized by skeletal muscle breakdown, myoglobinuria, and creatine phosphokinase (CPK) elevation and may commonly lead to renal dysfunction.[6] The most common symptoms of rhabdomyolysis are fatigue, weakness, muscular pain and swelling, tea-coloured urine, sometimes life-threatening disease process with multiple organ dysfunction syndrome disseminated intravascular coagulation (DIC) and cardiac arrest.[7] It is possible for some patients to remain asymptomatic.[7] About 10%-50% of patients with rhabdomyolysis develop acute kidney injury (AKI) which accounts for 8% to 15% of total cases of AKI and associated with mortality rate of 5%.[1,7] Our patient had AKI as there was greater than two-fold rise in serum creatinine from baseline in 48 hours suggestive of stage II AKI.[8] AKI improved by day 6 in our patient (Table 1).

A five-fold or greater increase in serum CK, the most sensitive enzyme marker of muscle injury without cardiac or brain injury is sufficient to diagnose rhabdomyolysis.[9] The CK rises within 12 hours of muscle injury, peaks in 1-3 days, and declines 3-5 days after the cessation of muscle injury as seen in our patient. A peak CK level of 5000 U/L or greater is predictive of development of AKI. Myoglobin has a short half-life of 2-3 hours and returns to normal within 6-8 hours. Estimation of myoglobin in serum and urine is useful, only in the early phases of the disease.[7] Hence, many workers do not recommend measurement of myoglobin for diagnosis of rhabdomyolysis.[7] In the present report rhabdomyolysis was diagnosed on the basis of serum CK levels and monitored by its serial measurement.

Rhabdomyolysis is a rare manifestation, and can occur at any stage of HIV infection and is usually multifactorial.[6] Risk factors for rhabdomyolysis among the HIV positive patients include lower CD4+ T-cell count, use of lipid lowering drugs like statins, HIV ribonucleic acid (RNA) levels greater than 500 copies / mL, alcohol or drug use, black race, longer duration of HIV infection, acquisition

of HIV through male-to-male sexual contact.[3] Our patient was at a high risk to develop rhabdomyolysis due to long duration of HIV infection and low CD4+ T-lymphocyte count.

Despite the frequent occurrence of diar- rhoeal disorders among patients with HIV/ AIDS, rhabdomyolysis secondary to diarrhoea induced hypokalemia is under reported. Therefore, it is important for clinicians to be aware of this association. Early diagnosis, along with aggressive treatment of complications, decreases the morbidity and mortality due to rhabdomyolysis. In conclusion, our case highlights that chronic diarrhoea with resultant hypokalemia should be included as one of the causes of rhabdomyolysis.

ACKNOWLEDGEMENTS

We acknowledge Dr Shanthiveer Uppin Associate Professor, Department of Pathology for help with expert opinion on the duodenal biopsy report of the patient.

REFERENCES

1. Walter LA, Catenacci MH. Rhabdomyolysis. Hospital Physician 2008;44:25 -31.
2. Pena Porta JM, Calvo Beguería E, de Vera Floristán CV, Oncins Torres R. Hypokalemic rhabdomyolysis and tetany as a presentation of celiac disease in an adult. Nefrologia 2008;28:343-6.
3. Lu SK, Jamaludin AZF, Rajendran N, Chong VH. Hypokalemic paralysis and rhabdomyolysis secondary to acquired immunodeficiency syndrome enteropathy. Infect Dis Clin Pract 2009;17:395.
4. Antoniadis DJ, Vavouranakis EM, Tsioufis KP, Toutouzas PK. Rhabdomyolysis due to diuretic treatment. Hellenic J Cardiol 2003;44:80-2.
5. Merrill ER. Acute HIV, rhabdomyolysis, renal failure, and hepatitis: a case report. The Med Forum 2010;12:28-9.
6. Moanna A, Skarbinski J, Kalokhe AS, Rimland D, Rouphael NG. Primary human immunodeficiency virus infection and rhabdomyolysis. J AIDS Clin Res 2011;2:1-3.
7. Huerta-Alardin AL, Varon J, Marik PE. Bench-to-bedside review: rhabdomyolysis–an oveview for clinicians. Crit Care 2005;9:158-69.
8. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Criti Care 2007;11:R 31.
9. Wig N, Handa R, Aggar wal P, Wali JP. Acute rhabdomyolysis following acute gas troenteritis. J Indian Acad Clin Med 2001;2:205 -6.
10. Straus SM, Kors JA, De Bruin ML, van der Hooft CS, Hofman A, Heeringa J, et al. Prolonged QTc interval and risk of sudden cardiac death in a population of older adults. J Am Coll Cardiol 2006;47:362-7.