Rhabdomyolysis as the first manifestation of human immunodeficiency virus infection

Rhea Bhargava¹ · Abdelrahman Abdallah Abohashem Aly¹ · Jim I. Mertz^{2,3,4} · Reem Mustafa^{1,5,6}

Received: 20 June 2015 / Accepted: 15 July 2015 / Published online: 12 August 2015
© Japanese Society of Nephrology 2015

Abstract Renal tubular acidosis (RTA) is a known complication of anti-retroviral medications. The presence of RTA in treatment naive-HIV patients is rare. A 49-year-old Caucasian woman presented with recurrent non-anion gap metabolic acidosis, AKI, rhabdomyolysis and hypokalemia on several occasions. Diagnosis of acquired distal RTA due to HIV was made given the history and laboratory data. To the best of our knowledge, this is the first case of HIV diagnosed with an initial presentation of rhabdomyolysis. We believe that acute renal failure was due to hypokalemia precipitating rhabdomyolysis caused by HIV-induced dRTA which was further exacerbated by amphetamine use.

Keywords Acidosis · dRTA · HIV · Rhabdomyolysis

Introduction

Renal complications in patients infected with human immunodeficiency virus (HIV) are usually secondary to the virus infectivity or toxicity from the HIV treatment. Renal tubular acidosis (RTA) is a known complication of some of the anti-retroviral medications. The presence of RTA in HIV patients without treatment is rare with very few cases reported. There is a clear association between hypergammaglobulinemia and distal RTA (dRTA). Even though HIV is commonly associated with hypergammaglobulinemia; human immunodeficiency virus is still not a commonly known cause of isolated dRTA. We report a case of recurrent severe hypokalemia in a patient with acquired distal RTA as a first manifestation of a new diagnosis of HIV.

Case

A 49-year-old Caucasian female with no significant past medical history presented to the emergency room with a 3-week history of muscle cramps, weakness and dark urine. She also complained of nausea, vomiting and decreased urine output in the preceding 3 days before admission. She was not taking any medications at home. Physical examination was unremarkable, except for diminished reflexes in the lower extremities. Initial laboratory data are shown in Table 1. ABG showed pH 7.38, PaCO₂ 27, PaO₂ 64.8 and bicarbonate of 9. The urine pH was inappropriately elevated at 6.5. Urine laboratory studies are shown in Table 2. Total protein was elevated at 8.1 g/dl with a reduced albumin of 2.6 g/dl. Lactic acid was measured at 1.6 mmol/L. The patient's urine drug screen (UDS) was positive for amphetamine. Her autoimmune workup

✉ Rhea Bhargava
bhargavar@umkc.edu

Reem Mustafa
ramustafa@gmail.com

¹ Department of Internal Medicine, University of Missouri-Kansas City, 2301 Holmes Street, Kansas City, MO 64108, USA

² Department of Nephrology and Hypertension, University of Missouri-Kansas City, Kansas City, USA

³ Saint Luke's Hospital, Kansas City, MO, USA

⁴ Kansas City Kidney Consultants, Kansas City, MO, USA

⁵ Department of Biomedical and Health Informatics, University of Missouri-Kansas City, Kansas City, MO, USA

⁶ Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Canada

Table 1 Serum laboratory values on admission

Sodium	124
Potassium	1.3
Chloride	83
Creatinine kinase	54,275
Bicarbonate	13
BUN	65
Creatinine	6.7

Table 2 Urine electrolyte values on admission

Sodium	59
Potassium	22.1
Chloride	20
Calcium	<0.5
Glucose	Negative
Urine anion gap	61.1
Urine pH	6.5
Urine screen for amino acids	Negative
Urine ketones	Negative

including ANA, ANCA, anti-dsDNA, SSA, SSB, RF came back negative. Her complement levels were within normal limits. The HIV antibody came back positive with a viral load of 172,828 copies/ml and CD4 count of 13. Kidney ultrasound did not show any signs of obstructive uropathy. Patient was admitted to the ICU and treatment was started with aggressive hydration, IV bicarbonate and potassium replacement along with temporary hemodialysis with a high potassium (K) bath. Even after resolution of her rhabdomyolysis, her electrolyte levels never fully corrected and she was discharged on bicarbonate and potassium supplements. Unfortunately, the patient was readmitted for severe hypokalemia 3 months later but without rhabdomyolysis or renal failure and was discharged with a higher dose potassium replacement. During the second admission she denied using amphetamines and her UDS was negative for illicit drugs. Diagnosis of acquired distal RTA was made in the follow-up visits due to the persistent hypokalemia, normal anion gap metabolic acidosis with an alkaline urine pH and in the absence of features suggestive of chronic RTA.

Discussion

We present above a case of new diagnosis of HIV with an initial presentation of rhabdomyolysis with hypokalemia and acquired distal RTA. To our knowledge, this is the first case of HIV diagnosed with an initial presentation of rhabdomyolysis. This case is also interesting given the

pathophysiology and the mechanism of the underlying disorder leading to the presentation of the patient. We concluded that the patient's renal failure was due to rhabdomyolysis which was precipitated by hypokalemia caused by HIV-induced distal RTA and was exacerbated by consumption of amphetamines.

Distal RTA is an uncommon disorder particularly in adults [1]. The most common causes include autoimmune disorders like Sjogrens syndrome and rheumatoid arthritis. Sometimes idiopathic distal RTA can be the first presentation of Sjogrens syndrome and should be ruled out first in these patients. In our patient, we found an alkaline urine pH along with hypokalemia despite non-anion gap systemic acidosis which is characteristic of distal renal tubular acidosis and further acidification testing was not performed. We also did not find any features like osteomalacia, short stature, nephrolithiasis or nephrocalcinosis suggesting chronic forms. No Fanconi syndrome-like features were present which solidified the diagnosis of distal RTA. With a negative autoimmune screen, we diagnosed HIV to be the cause of distal renal tubular acidosis.

HIV-associated renal injury is common and is known to be associated with several renal syndromes which include acute and chronic renal failure, HIV-associated thrombotic microangiopathy, immune-mediated glomerulonephritis and HIV-associated nephropathy or HIVAN (a focal segmental glomerulosclerosis associated with severe cystic tubular lesions) [1]. Most of these disorders involve the entire nephron and are generally not confined to the tubules. The presence of RTA in the present case without these factors is rare, with few cases reported in literature [13, 14]. There has been speculation and some evidence that renal injury by HIV can be either due to bystander injury or direct cytopathic injury caused by the virus [2]. The virus has been shown to cause nephropathy in infected infants of HIV-infected mothers [3]. In animal studies nephropathy was reproduced in transgenic mice and rats infected with the virus [4, 5]. This has also been shown in simian models of retroviral infection [6]. It has been suggested that the cytopathic effect of the virus could be caused by apoptosis that might be mediated by HIV proteins [1]. An adaptive cellular immune system can cause 'bystander injury' through hyperactive B-lymphocytes response [10]. A non-specific polyclonal plasma cell from B-lymphocyte differentiation may proliferate resulting in elevation of serum Ig levels and end up with hypergammaglobulinemic state [10]. There are some reports of reversal of renal abnormalities both histologically and biochemically in biopsy-proven HIV-associated nephropathy after treatment with highly active anti-retroviral therapy; however, some reports suggested that the kidney may remain a reservoir of the infection [7–9]. In this case it is difficult to differentiate hypergammaglobulinemia and cytotoxicity as the cause of the

disorder; however, given the new diagnosis of HIV the former would be favored.

A study by Chakraborty et al. in 2003 [11] investigated the prevalence of persistent renal metabolic acidosis in HIV-1-infected children and found that 18 out of the 34 children diagnosed with persistent metabolic acidosis were found to have distal RTA. The authors did note that the children were receiving anti-retroviral therapy and some were receiving *P. carinii* pneumonia prophylaxis with cotrimoxazole which is already known to affect renal tubular function. They also found that acidotic subjects were more immunocompromised [11]. This is similar to our patient who was severely immunocompromised with a very low CD4 count.

It is interesting that we did not identify any studies done to determine the prevalence of distal RTA in adults with HIV infection even though we did identify few cases reported of this disorder thought to be due to HIV infection itself in treatment-naïve patients [12, 13].

We believe clinicians should not only be alert to the development of tubular problems in HIV-infected patients, but that HIV testing can be considered in patients with unexplained secondary dRTA. This can sometimes manifest as a life-threatening condition as seen in our patient. We also believe that further studies need to be done to determine the incidence of hypokalemia and persistent non-GI-related acidosis in the HIV adult population. This could help in guiding therapy to prevent further tubular dysfunction due to anti-retroviral drugs in the patients who are treatment naïve. This case also highlights the severity of HIV-induced dRTA and hypokalemia and gives caution to identify such individuals early and treat them with anti-retroviral drugs that may spare renal function.

Compliance with ethical standards

Conflict of interest All the authors have declared no conflict of interest.

References

1. Battle D, Haque S. Genetic causes and mechanisms of distal renal tubular acidosis. *Nephrol Dial Transplant*. 2012;27(10):3691–704.
2. Kimmel PL, Barisoni L, Kopp JB. Pathogenesis and treatment of HIV-associated renal diseases: lessons from clinical and animal studies, molecular pathologic correlations, and genetic investigations. *Ann Int Med*. 2003;139:214–27.
3. Bruggeman L, Nelson P. Controversies in the pathogenesis of HIV-associated renal diseases. *Nat Rev Nephrol*. 2009;5(10):574–81.
4. Strauss J, Abitbol C, Zilleruelo G, Scott G, Paredes A, Malaga S, et al. Renal disease in children with the acquired immunodeficiency syndrome. *N Engl J Med*. 1989;321:625–30.
5. Kopp JB, Klotman ME, Adler SH, Bruggeman LA, Dickie P, Marinos NJ, et al. Progressive glomerulosclerosis and enhanced renal accumulation of basement membrane components in mice transgenic for human immunodeficiency virus type 1 genes. *Proc Natl Acad Sci USA*. 1992;89:1577–81.
6. Reid W, Sadowska M, Denaro F, Rao S, Foulke J Jr, Hayes N, et al. An HIV-1 transgenic rat that develops HIV-related pathology and immunologic dysfunction. *Proc Natl Acad Sci USA*. 2001;98:9271–6.
7. Stephens EB, Tian C, Dalton SB, Gattone VH 2nd. Simian-human immunodeficiency virus-associated nephropathy in macaques. *AIDS Res Hum Retroviruses*. 2000;16:1295–306.
8. Wali RK, Drachenberg CI, Papadimitritou JC, Keay S, Ramos E. HIV-1-associated nephropathy and response to highly-active antiretroviral therapy (Letter). *Lancet*. 1998;352:783–4.
9. Winston JA, Bruggeman LA, Ross MD, Jacobson J, Ross L, D'Agati D, et al. Nephropathy and establishment of a renal reservoir of HIV type 1 during primary infection. *N Engl J Med*. 2001;344:1979–84.
10. Ross MJ, Klotman PE. Recent progress in HIV-associated nephropathy. *J Am Soc Nephrol*. 2002;13:2997–3004.
11. Faulhaber J, Nelson P. Virus-induced cellular immune mechanisms of injury to the kidney. *CJASN*. 2007;2(Supplement 1):S2–5.
12. Chakraborty R, Uy CS, Oleske JM, Coen PG, McSherry G. Persistent non-gastrointestinal metabolic acidosis in pediatric HIV-1 infection. *AIDS*. 2003;17:673–7.
13. Laing CM, Roberts R, Summers S, Friedland J, Lightstone L, Unwin R. Distal renal tubular acidosis in association with HIV infection and AIDS. *Nephrol Dial Transplant*. 2006;21(7):2044.
14. Isa WY, Daud K. Distal renal tubular acidosis in HIV/AIDS patient. *Intern Med*. 2011;50(16):1765–8.