SciMedCentral

Journal of Clinical Nephrology and Research

Case Report

Rhabdomyolysis in a Kidney Transplant Due to Excessive Weight Lifting: A Case Report

Lum EL[2], Sisk A[1]*, and Lassman C[1]

[1]*Department of Pathology, University of California, USA*
[2]*Department of Medicine, UCLA David Geffen School of Medicine, USA*

***Corresponding author**
Anthony Sisk, Department of Pathology, David Geffen School of Medicine, University of California, 10833 Le Conte Ave, CHS AS-306, Los Angeles, California, USA, Tel: 310-794-6424; Email: asisk@mednet.ucla.edu

Submitted: 09 November 2016

Accepted: 10 January 2017

Published: 12 January 2017

ISSN: 2379-0652

Keywords
- Rhabdomyolysis
- Acute kidney injury in rhabdomyolysis
- Rhabdomyolysis in kidney transplant
- ATN and kidney transplant

Abstract

Rhabdomyolysis, which refers to the breakdown of skeletal muscle tissue, can result in myoglobinuria and acute kidney injury. Injury can occur through multiple mechanisms, including: trauma, burns, and as a result of medication side effects. More recently, exercise programs utilizing intensive interval strength training sessions to rapidly build muscle mass have been shown to result in rhabdomyolysis. We present a case of rhabdomyolysis in a 30 year-old kidney transplant recipient who developed rhabdomyolysis and acute kidney injury after engaging in a strength training program.

INTRODUCTION

Rhabdomyolysis is a clinical diseasereferring to the breakdown of muscle tissue. The first clinical description of rhabdomyolysis was during World War II, when British physicians reported the link between crush injuries among air-raid casualties and acute kidney injury [1,2]. In the modern medical era most cases of rhabdomyolysis are non-traumatic, and usually the result of medications to treat another medical disease [1].

Most cases of rhabdomyolysis are mild, consisting of a combination of muscle soreness and elevations increatinine kinase (CK) and serum phosphorous. One of the major intracellularproteins released during rhabdomyolysis is myoglobin. Myoglobin contains a porphyrin ring and is primarily responsible for binding oxygen within muscle tissue. Myoglobin is freely filtered by the glomerulus and is absorbed by the renal tubular epithelial cells. Lysosomal breakdown of myoglobin results in the release of free ironwhich can beoxidized generating free radicals, which is toxic to renal epithelial cells [3]. Excessive exposure to myoglobin results in renal tubular dysfunction and acute kidney injury. Renal involvement occurs in up to one quarter of rhabdomyolysis cases, and when present indicates a worse prognosis [4]. Renal biopsy typically reveals a pattern of acute tubular necrosis (ATN) with concurrent positivestaining for myoglobin.

More recently several cases of exercise induced rhabdomyolysis have been reported, usually in the setting of intensive interval strength training [2]. Herein, we describe a case of rhabdomyolysis with acute kidney injury in a kidney transplant recipient who was actively participating in a strength training program.

CASE REPORT

A 30 year old 5'10" Caucasian male presented to our kidney transplant clinic for routine follow up and was found to have an elevated serum creatinine at 2.5 mg/dL.

The patient was initially diagnosed with kidney disease at age 15 after presenting with hearing impairment detected on a school physical examination. Further work up revealed microscopic hematuria and he underwent native kidney biopsy revealing Alport's Syndrome. A review of his family history revealed no other kindred with the disorder. He received treatment with prednisone and lisinopril.

Ten years later the patient's renal disease progressed and he was initiated on hemodialysis. He remained on hemodialysis for two years before receiving an HLA incompatible kidney transplant from a friend. Prior to transplantation he had a donor-specific antibody (DSA) to HLA A24 with a median fluorescence intensity (MFI) of 1551. No other HLA antibodies were detected on single bead antigen testing (Luminex). He received anti-thymocyte globulin and IVIG at the time of transplantation and his initial hospital course was uncomplicated. He was discharged on post-operative day 4 with a serum creatinine of 1.7 mg/dL. Repeat HLA antibody testing showed resolution of his pre-existing DSA. He was maintained on a regimen of prednisone, tacrolimus (a calcineurin inhibitor), and mycophenolate mofetil. At six months his serum creatinine was 1.4 mg/dL, repeat single antigen testing showed no HLA antibodies and a protocol biopsy showed no evidence of rejection. The patient continued to follow up every 3 months with a creatinine baseline between 1.4-1.7 mg/dL for the next two years.

One year prior to presentation the patient was seen in clinic with a serum creatinine of 1.5 mg/dL. He had recently started community college to complete pre-requisites to enroll in a master's program in exercise science and had started working as a personal trainer. Three months prior to presentation he was seen in clinic with a serum creatinine of 1.7 mg/dL and had a reported 10 lbs. weight gain (190 lbs.), which was attributed to weight lifting. He admitted to missing immunosuppressive medications about once or twice a month.

On presentation the patient reported severe fatigue, which he related to an increase in weight lifting in preparation for a competition. He reported intense daily weight lifting to the limit of exhaustion. He denied use of supplements and did admit to missing doses of nighttime tacrolimus and mycophenolate approximately once or twice a week due to fatigue. He was noted to be 25 lbs. (215 lbs.) heavier than his prior visit. His last work out was one week ago due to noted fatigue.

On examination the patient had a temperature of 36.9°C, a pulse of 65 beats per minute, blood pressure of 134/81 mmHg, and respiratory rate of 10 breaths per minute with a pulse oximetry reading of 98% on room air. His examination was notable for mild diffuse muscle tenderness that was rated a 2/10. The remainder of the physical examination was unremarkable.

Laboratory data one week prior to presentation was notable for an increased serum creatinine of 2.5 mg/dL, hyperphosphatemia a 5.5 mg/dL, 3+ blood and 2 RBCs perhpf on urinalysis, and a tacrolimus three-hour post dose level of 18.5 ng/dL. He was asked to repeat his blood testing to obtain a 12-hour trough level of tacrolimus. Repeat lab testing showed a persistently elevated serum creatinine of 2.3 mg/dL (see table 1), a 13-hourtacrolimus drug level of 6.5 ng/mL (normal level 5-8 ng/mL), and a creatinine kinase of 1000 U/L.

Given his persistently elevated serum creatinine the patient underwent percutaneous kidney transplant biopsy. Light microscopic examination showed acute tubular epithelial injury (ATN) characterized by patchy attenuation of tubules associated with loss of brush border staining and rare mitotic figures. There was very focal dense granular eosinophilic cast material suggestive of myoglobin (Figure 1) and prominent protein reabsorption droplets within proximal tubular epithelial cells. The tubulointerstitium showed no significant chronic changes. There was no tubulitis or interstitial inflammation to suggest ACR. Glomeruli were unremarkable. Arteries and arterioles were also unremarkable.A myoglobin immunohistochemical stain was performed and showed diffuse and strong granular to globular cytoplasmic staining (Figure 2) correlating to the prominent protein reabsorption droplets. Cast material was no longer present to evaluate on the myoglobin stain. Immunofluorescence microscopy was non-contributory. By electron microscopy, there was no obvious cast material suggestive of rhabdomyolysis/myoglobinuria. There were however, abundant secondary lysosomes and (Figure 3).

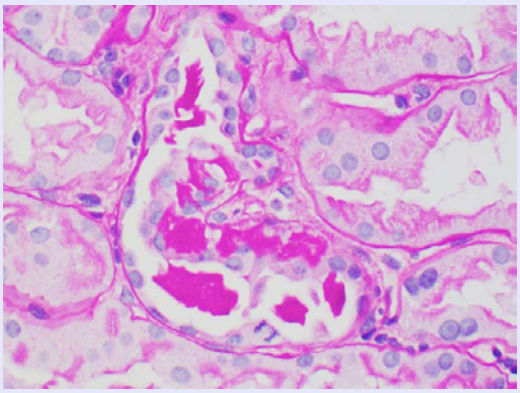

Figure 1 Dense eosinophilic granular cast material within an injured tubule. Note the mitotic figure at the bottom, arrow. (magnification x400; PASstain).

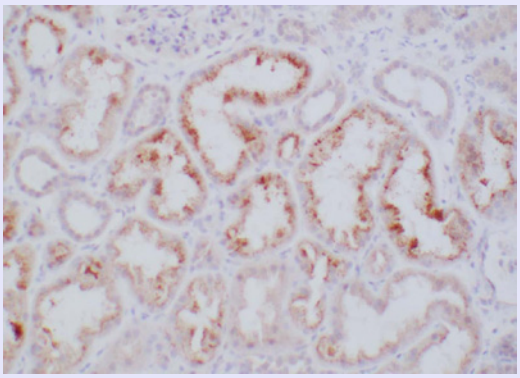

Figure 2 Diffuse granular to globular staining within the cytoplasm of many attenuated tubules. (magnification x200; myoglobin stain).

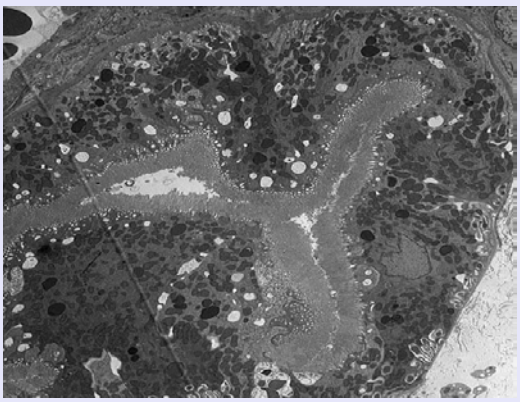

Figure 3 Electron microscopy of a proximal tubule showing many secondary lysosomes and protein reabsorption droplets. There was no globular or cast material that is consistent with myoglobin. (magnification x5,470).

DISCUSSION

Beyond the first year of kidney transplantation the most common cause of increased creatinine is chronic rejection, sometimes referred to as chronic allograft nephropathy. This process is not completely understood and typically presents with a gradual increase in serum creatinine with varying degrees of proteinuria and hypertension. There is currently no therapy for chronic rejection and renal transplant biopsy is often deferred in patients in whom chronic rejection is highly suspected. However,

Table 1: Patient Laboratory Results.

	One year prior	1 week prior to presentation	At presentation	3 months following presentation	Reference values
Serum					
Sodium (mmol/L)	142	146	141	140	135-146 mmol/L
Potassium (mmol/L)	4.2	4.9	4.3	4.3	3.5-5.3 mmol/L
Chloride (mmol/L)	103	107	104	104	98-110 mmol/L
Bicarbonate (mmol/L)	22	22	25	26	19-30 mmol/L
BUN (mg/dL)	25	23	23	25	7-25 mg/dL
Creatinine (mg/dL)	1.5	2.5	2.3	1.7 mg/dL	0.6-1.35 mg/dL
Calcium (mg/dL)	9.8	9.8	9.5	10	8.6-10.3 mg/dL
Phosphorous (mg/dL)	3.0	5.5	5.3	3.8	2.5-4.5 mg/dL
CK (U/L)	N/A	N/A	1000	102	63-473 U/L
Tacrolimus (ng/dL)	6.7	18.5	6.5	7.3	5-8 ng/mL (12 hour trough level)
Urine					
Urine pH	6.3	< 5	< 5	6.0	5.0-8.0
Blood	Negative	3+	2+	Negative	Negative
Protein	Negative	trace	Negative	Negative	Negative
RBCs	Negative	2	Negative	Negative	Negative

there are other potential causes of renal allograft insufficiency which maybe amendable to therapy, thus necessitating kidney transplant biopsy in selected patients.

The patient presented with an elevation in serum creatinine five years after an HLA incompatible living donor kidney transplant. Clinically, there was high suspicion for rhabdomyolysis given his history of strength training with muscle weight gain and diffuse muscle soreness and weakness on examination. The subsequent laboratory studies confirmed the diagnosis of rhabdomyolysis with myoglobinuria. The serum phosphorous and CK were both elevated. The mild elevation in CK, which is not consistent with severe rhabdomyolysis, were likely the results of the patient lack of exercise for one week prior to laboratory testing. One of the hallmarks of renal involvement is the discordanceof a positive urine dipstick for blood and the absence of blood under urine microscopy. This finding is the result of myoglobin in the urine cross-reacting with the urine dipstick, resulting in a false positive urine dipstick test [5,6].

Despite the clear evidence of rhabdomyolysis and myoglobinuria he underwent kidney transplant biopsy to evaluate for concurrent acute rejection or the presence of calcineurin inhibitor toxicity, both of which were absent on the performed biopsy. Late acute rejection in a kidney transplant recipient is the result of immunosuppression non-adherence or exposure to low drug levels. The development of late acute rejection carries a poor prognosis compared to rejection earlier in the course of transplantation. The patient in our case reported missed medications and had undergone desensitization with and HLA incompatible kidney transplant. HLA incompatible transplants have a much higher risk of antibody mediated rejection, with one center reporting a greater than 30% risk of rejection in the first year. These patients require higher doses of immunosuppression and missing medications, even a single dose, may be detrimental to the allograft.

In the setting of kidney transplantation there may also be an increased susceptibility towards developing AKI from rhabdomyolysis due to concurrent calcineurin inhibitor (CNI) use.The patient above was on tacrolimus. Most cases of CNI induced rhabdomyolysis are the result of drug-drug interactions with medications known to cause rhabdomyolysis, usually statins [2,4,7]. CNIs are also known to cause renal tubular dysfunction, which may increase the risk of kidney injury in the setting of myoglobinuria. The classic pathologicalfinding of CNI induced kidney injury is isometric vacuolization and/or medial hyalinosis, which our patient did not have. The patient's biopsy was consistent with myoglobinuria mediated injury of the kidney transplant without concurrent rejection, CNI toxicity, or chronic allograft nephropathy. The patient was instructed to reduce his exercise activity and drop out of his weight lifting competition. On follow up 3 months later he reported continued exercise, but at a reduced level. He weighed 210 lbs. and his creatinine had improved to 1.7 mg/dL.Current guidelines for kidney transplant recipients only specify the importance of exercise in improving overall health. Consideration on the type of exercise should be considered when counseling kidney transplant recipients, as they may be more susceptible to rhabdomyolysis and acute kidney injury.

REFERENCES

1. Vanholder R, Sever MS, Erek E, Lameire N. Rhabdomyolysis. J Am Soc Nephrol. 2000; 11: 1553-1561.
2. Keltz E, Khan FY, Mann G. Rhabdomyolysis. The role of diagnostic and prognostic factors. Muscles Ligaments Tendons J. 2014; 3: 303-312.
3. Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. N Engl J Med. 2009; 361: 62-72.

4. Walid MS. Blood urea nitrogen/creatinine ratio in rhabdomyolysis. Indian J Nephrol. 2008; 18: 173-174.

5. Iida S, Ishida H, Miyamoto N, Shirakawa H, Shimizu T, Setoguchi K, et al. Mild rhabdomyolysis after renal transplantation. Saudi J Kidney Dis Transpl. 2011; 22: 521-524.

6. Mittal T, Kohli HS. Post renal transplant acute kidney injury. Indian J Nephrol. 2014; 8: S33-S36.

7. Miller ML. Causes of rhabdomyolysis. UpToDate. 2016.

Cite this article

Lum EL, Sisk A, Lassman C (2017) Rhabdomyolysis in a Kidney Transplant Due to Excessive Weight Lifting: A Case Report. J Clin Nephrol Res 4(1): 1055.