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A Surviving Patient with Record High Creatinine

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ABSTRACT

Creatinine is a product of muscle protein breakdown cleared by the kidneys at a constant rate. The glomerular filtration rate is estimated based on serum creatinine. There is no definitive level of serum creatinine which is itself incompatible with human survival. We present the highest serum creatinine associated with survival based on a thorough review of the literature. A 34-year-old male patient with baseline serum creatinine of 1.2 mg/dl presented our emergency department with a six week history of new onset of uremic symptoms. His past medical history was unremarkable. On exam, he was in no distress. His BMI was 28. His exam was significant only for elevated blood pressure and asterixis. His peak serum creatinine was 53.9 mg/dl. The patient subsequently required maintenance hemodialysis and later changed to long-term peritoneal dialysis. To our knowledge, based on a thorough review of the literature using PubMed, Cochrane Database and the United States Renal Data System (USRDS), this is the highest level of serum creatinine ever reported. We conclude that serum creatinine itself is non-lethal. It is more likely that other electrolyte and retained metabolic abnormalities of renal failure frequently cause symptoms or death before creatinine toxicity, if such a level exists, creatinine has reached.

Keywords: Survival; Outcome; Uremia; Mortality; Creatinine

1. Introduction

Creatinine is the product of dephosphorylation of creatine phosphate during muscle contraction and is freely filtered and normally also secreted via the proximal tubules and excreted by the kidneys [1-4]. Thus, creatinine clearance exceeds glomerular filtration rate by the amount or percent of creatinine secretion. The serum creatinine level is relatively constant and its value is used to estimate glomerular filtration rate (eGFR) [5]. The normal reference range for serum creatinine is 0.7 to 1.3 mg/dL (62 - 115 umol/L) for men and 0.6 to 1.1 mg/dL (53 - 97 umol/L) for women [3]. Although creatinine is often assumed to be one of the uremic toxins, very little data are available on its adverse effects on human physiology [6]. One animal study reported that creatinine injection reduced survival time in anephric rats [7]. A canine study showed gastrointestinal side effects of chronic creatinine intoxication [8]. The authors did not receive funding or support for this case study.

2. Case Presentation

A 34-year-old man with a baseline creatinine 1.2 mg/dl in 2003 and no significant past medical history presented to the Lankenau Medical Center Emergency Department with complaints of nausea, vomiting and diarrhea over the prior six weeks. These symptoms, in addition to 30-pound weight loss, led to the patient's hospital admission. He also reported intermittent ankle swelling and nocturia two to three times nightly. He denied dysuria, hematuria, foamy urine or seizure.

Past medical history included cervical radiculopathy in the distant past. He denied any childhood kidney disease or recurrent urinary tract infections. There was no history of hypertension. He did not take non-steroidal anti-inflammation drugs. He occasionally used mail-order herbal colonic cleansers. The patient denied tobacco, alcohol, and drug abuse. Family history was significant for diabetes, hypertension and COPD in his mother. His

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father died of prostate cancer. He denied any family history of kidney disease or autoimmune disease.

On exam he appeared to be in no acute distress. His body mass index was 28. His vital signs were normal except blood pressure 184/93. His oxygen saturation was 100% on room air. Neurological exam revealed asterixis. There was no uremic frost and the remainder of the physical examination was unremarkable.

The urinalysis showed a specific gravity of 1.016, pH 6.5, with 3 plus proteinuria and positive for red blood cells and leukocytes, too numerous to count. No casts or crystals were detected. His urine protein to creatinine ratio showed 6.2 grams of proteinuria. The serum potassium was 5.6 mEq/L, BUN 135 mg/dL and creatinine 51 mg/dL. The latter was confirmed by dilution method and rose to 53 mg/dl prior to initiation of hemodialysis. Calculated eGFR was 1 ml/min. Further tests showed microcytic iron deficiency anemia, hyperphosphatemia, hypocalcaemia and secondary hyperparathyroidism. His arterial pH was 7.33. He had a weakly positive cANCA, which was likely not clinically significant. Detailed laboratory values are shown in **Table 1**.

Renal ultrasound showed an atrophic right kidney (6.8 cm) and a normal to slightly small sized left kidney (9.8 cm) with cortical hyper echogenicity. There was no hydronephrosis, cystic kidney disease or nephrocalcinosis. His chest X-ray was unremarkable.

An internal jugular venous hemodialysis catheter was placed and hemodialysis was initiated on the day of admission. He was discharged 9 days later after being set up for outpatient maintenance hemodialysis. At the time of hospital discharge, his creatinine was down to 12.7 mg/dl with the help of hemodialysis. The patient subsequently changed modality to long term peritoneal dialysis and was doing well on follow up examination 6 months after discharge.

Table 1. Extended Laboratory Data.

Lab	Reference	Patient Value
Sodium	136 - 144 mEq/l	136
Potassium	3.6 - 5.1 mEq/l	**5.6**
Chloride	98 - 109 mEq/l	**96**
Carbon Dioxide	22 - 32 mEq/l	**17**
Glucose	70 - 99 mEq/l	96
BUN	8 - 20 mg/dl	**135**
Creatinine	0.8 - 1.3 mg/dl	**51.0**
Calcium	8.9 - 10.3 mg/dl	**7.7**
Phosphorous	2.4 - 4.7 mg/dl	**15.7**
Protein, total	6.0 - 8.2 g/dl	8.2
Albumin	3.4 - 5.0 g/dl	3.7
AST	15 - 41 u/l	6
ALT	16 - 63 u/l	8
CPK	16 - 300 u/l	**431**
PTH, intact 2	12 - 88 pg/ml	**1187.2**
pH	7.35 - 7.45	**7.33**
PCO2	35 - 48 mmHg	**31.0**
PO2	83 - 100 mmHg	114
WBC count	4.5 - 10.8 K/ul	7.7
Hemoglobin	14.0 - 17.5 g/dl	**5.6**
MCV	83 - 97 fl	**80.9**
Platelet	150 - 400 k/ul	343
PT	12.3 - 14.9 sec	17.5
PTT	24 - 36 sec	38
Glomerular BM Ab	<1.0	<1.0
Antistreptolysin O	<117 IU/ml	30
Hep B Surface Ag		Nonreactive
ANA	<1:40	Nonreactive
C-ANCA	Negative	**Positive, 1:20**
P-ANCA	Negative	Negative
HIV 1&2	Negative	Negative

3. Discussion

Creatine is a dietary non-essential amino acid which is phosphorylated by the enzyme creatine kinase in the liver, pancreas and kidney. Creatine phosphate is then released into the blood stream and is stored by organs such as the brain and muscle for growth, tissue repair and other energy dependent activities [1,3]. In muscle, dephosphorylation of creatine releases energy required for muscle contraction [3,4]. Approximately 1 to 2 percent of free creatine in muscle irreversibly and spontaneously converts to creatinine which in turn is released into the blood stream and freely filtered, secreted and excreted by the kidneys [2,3].

Serum creatinine level is commonly used as an indicator of the kidney function. Although it is a marker of uremic toxicity, the actual effect of creatinine on homeostasis in humans is unresolved. In fact, higher creatinine values at presentation with end stage renal disease have been shown in a study of over 5000 patients to correlate with increased survival possibly because it is a marker of functional status and muscle mass in a given patient [9]. Animal studies generally conclude that createnine toxicity in and of itself is not a major factor in uremic toxicity. However, Levine, *et al*. reported creatinine injections to the nephrectomized rats reduced lifespan by two days when compared to nephrectomized rats injected with water alone. This study concluded that creatinine reduced survival dose-dependently [7]. Canines chronically "intoxicated" with creatinine to an average serum concentration of 38 mg/dl, was associated with gastroduodenitis and mild anemia [8].

A literature search of PubMed, Cochrane Reviews, and the United States Renal Data System (USRDS) failed to reveal case reports or data sets with a creatinine level as high as our patient. The USRDS records show that over the past 15 years, less than only 1.28% of all new ESRD cases have a reported initial creatinine over 20 mg/dl [10]. Their data also include no values over 30 mg/dl indicating that the reported case herein could be the highest createnine (53 mg/dl) in the literature. Despite this recording the high level, the patient's functional status and clinical outcome were remarkably stable out of proportion to the chemical evidence of his azotemia. It is possible that this patient has a chronic single functioning kidney which was affected by either essential hypertension or chronic glomerulopathy. More likely, he may have focal and segmental glomerulosclerosis related to a small kidney and chronic hyperfiltration. However, renal biopsy was contraindicated due to advanced and irreversible nature of the kidney disease and the presence of a single functioning kidney.

In summary, we report what appears to be the highest recorded serum creatinine in a surviving uremic patient. This finding implies that creatinine itself may have a minimally pathophysiologic effect on uremic patients.

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Abbreviations

eGFR: estimate glomerular filtration rate.
COPD: chronic obstructive pulmonary disease.
USRDS: United States Renal Data System.
ESRD: End stage renal disease.
BUN: Blood urea nitrogen.
AST and ALT: liver enzymes.
CPK: creatinine kinase.
PTH: parathyroid hormone.
ANA: anti-nuclear antibody.
ANCA: anti-neutrophil cytoplasmic antibodies.
BMI: body mass index.