

C-Reactive Protein Serum Levels In Rhabdomyolysis Patients

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Citation

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Abstract

Introduction: We hypothesized that Rhabdomyolysis might be associated with elevated C-reactive protein (CRP) serum levels. **Methods:** We reviewed the medical charts of five Rhabdomyolysis patients in whom CRP and creatine phosphokinase (CPK) serum levels had been measured together day by day, and in whom myocardial infarction and/or systemic infection had been excluded as well. **Results:** Mean age of Rhabdomyolysis patients was 41.8 ± 13.6 years. Rhabdomyolysis patients had mean maximal CPK and CRP serum levels of 14610 ± 14346 U/L and 57.7 ± 55.1 mg/L, respectively. CRP serum levels velocity paralleled CPK serum levels velocity among all patients. CRP serum levels significantly correlated with CPK serum levels ($r=0.53$, $p=0.005$). **Conclusions:** CRP serum levels are elevated in Rhabdomyolysis patients and are correlated with CPK serum levels. CRP serum levels may be measured together with CPK serum levels in order to monitor the inflammatory process associated with Rhabdomyolysis.

INTRODUCTION

Systemic inflammatory processes, such as systemic infections, might damage the membrane integrity of skeletal muscle cells and cause Rhabdomyolysis [1]. On the other hand, the release of toxic intracellular materials from damaged skeletal muscle cells into the circulation might cause systemic inflammation consistent with disseminated inflammatory coagulation [2]. Indeed, in the clinical practice we often see Rhabdomyolysis patients with fever and leukocytosis in which it is not clear what is the primary event: Inflammation-induced Rhabdomyolysis or Rhabdomyolysis-induced inflammation.

The inflammatory characteristics of Rhabdomyolysis per se have never been studied, to the best of our knowledge. Hence, we hypothesize that release of toxic intracellular materials from damaged skeletal muscle cells into systemic circulation might be associated with elevation of C-reactive protein (CRP) serum levels parallel to elevation of creatine phosphokinase (CPK) serum levels in Rhabdomyolysis patients.

METHODS

This was a retrospective study approved by the local ethics committee. The medical charts of consecutive Rhabdomyolysis patients admitted to the Department of Internal Medicine D, Sourasky Medical Center, Tel-Aviv,

between August, 2007 and October, 2008 were surveyed. CRP and CPK serum levels were measured day by day in these patients as part of the routine work-up. We excluded patients with evidence of systemic infection and/or myocardial infarction, since these conditions might have been associated with elevated CRP and/or CPK serum levels [3].

Increased CPK serum levels are the diagnostic hallmark of Rhabdomyolysis [1]. However, to the best of our knowledge, there is no consensus regarding CPK serum levels that define Rhabdomyolysis. Hence, we defined Rhabdomyolysis as CPK serum levels ten times higher the upper limit of normal range according to the local laboratory, i.e., CPK serum levels of 1740 U/L or more. CRP serum levels were analyzed by using the ADVIA 1650 chemistry system for wide-range-CRP [4]. CPK serum levels were analyzed routinely by the local laboratory.

All continuous variables (age, CRP serum levels, CPK serum levels, etc.) were expressed by means \pm standard deviation. Spearman's correlation coefficient was used in order to study the correlation between CRP serum levels and CPK serum levels. Two-tailed $p < 0.05$ was considered statistically significant. All statistical analysis was performed using the SPSS statistical package (SPSS Inc., Chicago, IL, USA).

RESULTS

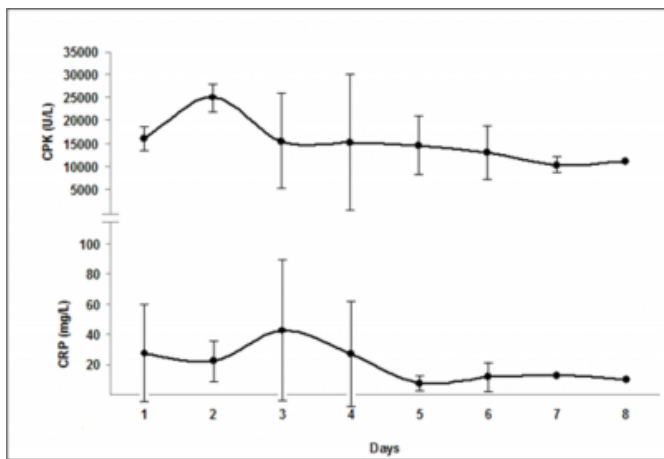
Included were five Rhabdomyolysis patients: four men and one woman. The clinical characteristics of the patients are presented in table 1:

Figure 1

Age	Sex	Major co-morbidities	Max CPK (U/L)	Max CRP (mg/L)	Etiology of Rhabdomyolysis
64	M	Bipolar disorder	14233	27.1	Fall
44	M	None	3190	143.5	Heat shock
38	M	Schizophrenia	39199	81.9	Crush injury
34	F	Bipolar disorder, hyperlipidemia	10001	24.1	Statins
29	M	Alcoholism	6430	11.7	Fall

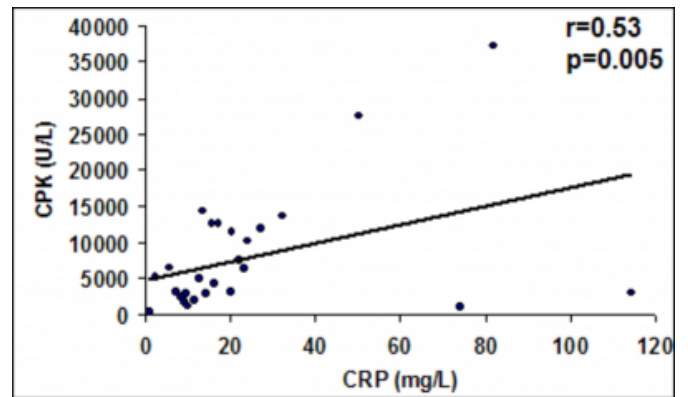
The mean age of Rhabdomyolysis patients was 41.8 ± 13.6 years. Rhabdomyolysis patients had mean maximal CPK and CRP serum levels of 14610 ± 14346 U/L and 57.7 ± 55.1 mg/L, respectively. CRP serum levels increased and decreased one day following and parallel to CPK serum levels. Mean CRP and mean CPK serum levels and velocities are presented in figure 1:

Figure 2



CRP serum levels significantly correlated with CPK serum levels as presented in figure 2:

Figure 3



DISCUSSION

Rhabdomyolysis is caused by skeletal muscle cell damage which leads to the release of toxic intracellular constituents into the circulation. Its main causes include trauma, ischemia, drugs, toxins, metabolic disorders, and infections. Rhabdomyolysis might be associated with severe acute renal failure, hypovolemic shock, and disseminated intravascular coagulation [1]. Although systemic inflammation has a role in these life-threatening complications, Rhabdomyolysis treatment has not been changed in the last few decades, and mainly includes hydration, diuretics and bicarbonate [2]. In the era of anti-inflammatory agents, there is probably a place to investigate their yield in treating Rhabdomyolysis, but the inflammatory properties of Rhabdomyolysis should be investigated first; the association between CPK serum levels and commonly used inflammatory biomarkers such as CRP serum levels has never been studied in Rhabdomyolysis patients, to the best of our knowledge, until now. In this study of Rhabdomyolysis patients, CRP serum levels were elevated and were correlated with CPK serum levels despite exclusion of patients with systemic infections. These findings confirm our hypothesis: release of toxic intracellular material from skeletal muscle cells into systemic circulation is associated with elevations of CPK serum levels as well as systemic inflammation consistent with elevations of CRP serum levels. CPK itself is not associated with inflammation, to the best of our knowledge, but other intracellular materials released together with CPK from the damaged skeletal muscle cells, such as free radicals [1], are probably the cause for the systemic inflammation observed.

According to our findings, CRP serum levels of 57.7 mg/L may be consistent with maximal CRP levels observed in Rhabdomyolysis patients without evidence of systemic infection, as compared with CRP serum levels of 100 mg/L

observed in patients with systemic bacterial infections [5]. Although the cohort described here was small, these findings may serve as reference range temporarily, until population-based reference ranges will be established derived from larger cohorts of Rhabdomyolysis patients.

Our findings are not of theoretical nature, what so ever; in the clinical practice, it is a clinical challenge to differentiate between infection-induced Rhabdomyolysis and Rhabdomyolysis-induced inflammation. In case of infection-induced Rhabdomyolysis, we sought to detect the infection and to treat it promptly and effectively. While in Rhabdomyolysis-induced inflammation, the straggle to detect infection might be uncalled for and expensive.

In conclusion, although our cohort was small, we demonstrated, for the first time, an inflammatory response in Rhabdomyolysis patients without evidence of systemic infection, and defined the mean peak CRP serum levels that were associated with this condition. We believe large-scale

studies are warranted in which CRP serum levels may be measured together with CPK serum levels in Rhabdomyolysis patients and address the prognostic value of these measurements.

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