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Case Report

A Case of Rhabdomyolysis Associated with Peginterferon use in Chronic Hepatitis C

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ABSTRACT

Rhabdomyolysis is a serious clinical condition resulting from release of toxic intracellular materials into the systemic circulation. Multiple factors have been demonstrated to be responsible for this syndrome. However, currently medications and alcohol are considered to be the primary causative agents.

To the best of our knowledge there are few reported cases of rhabdomyolysis following prescription of peginterferon alfa-2b in patients with chronic hepatitis. Here, we have reported the case of a 46-year-old male with hepatitis C virus (HCV) infection who suffered an acute onset of generalized myalgia and weakness, with elevated serum creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) levels six months after administration of peginterferon alfa-2b. Considering the clinical picture and laboratory findings, we diagnosed the patient with rhabdomyolysis. Peginterferon alfa-2b and ribavirin were discontinued and intensive intravenous hydration commenced. Within ten days the patient improved significantly after which he was discharged in an appropriate physical condition.

Keywords: Rhabdomyolysis; Peginterferon alfa-2b; Chronic hepatitis C

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INTRODUCTION

The term rhabdomyolysis refers to a critical clinical condition resulting from release of toxic intracellular materials into the systemic circulation as a consequence of loss of the integrity of the skeletal muscle cell plasma membrane(1-3). The clinical presentation of rhabdomyolysis ranges from an asymptomatic rise in creatine phosphokinase (CPK) levels in the blood to severe complications such as acute kidney injury (AKI), heart arrhythmias and coagulopathies among which AKI is more common(1,4). Muscular pain and weakness associated with a reddish color change of the urine is considered as the characteristic clinical picture that may be accompanied by illness, high fever, tachycardia, nausea and vomiting in more severe cases(5). Although rhabdomyolysis is considered to be a fatal syndrome, full recovery is possible with timely diagnosis and intervention(6).

Multiple hereditary and acquired factors have been

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discovered to be responsible for rhabdomyolysis(4). The acquired forms of this disease are classified into two types, traumatic and non-traumatic. While traumatic injuries have previously comprised the majority of acquired types, currently non-traumatic etiologies that include medications and alcohol are ranked as the primary causative agents(7-10). Over 150 medications and toxins have been reported as etiologies for skeletal muscle injury among which cholesterol lowering agent myopathies are probably the most common cause for drug-related muscle pain(11,12).

To our knowledge there are few reported cases of rhabdomyolysis following prescription of interferon alfa in patients with chronic hepatitis. Here, we report the case of a 46-year-old male with chronic hepatitis C virus (HCV) infection who suffered from drug-induced rhabdomyolysis following administration of peginterferon alfa-2b.

CASE REPORT

A 46-year-old male who was being treated with peginterferon alfa-2b (1.5 µg/kg/week) and ribavirin (1000 mg daily) for HCV presented to our clinic due to acute onset of generalized myalgia and weakness since four days prior. Hepatitis C was diagnosed one year ago as confirmed by results of the polymerase chain reaction test; liver biopsy at that time was remarkable for chronic active hepatitis.

Treatment with peginterferon alfa-2b began six months prior to the current presentation. On physical examination we detected an evident decrease in muscle forces where the upper limb muscle forces were 2 out of 5 and the lower limb muscle forces were 4 out of 5. Deep tendon reflexes were normal and symmetric. There was no sensory dysfunction. The patient's vital signs were all normal.

Laboratory findings demonstrated marked increase in CPK at 56500 U/L (normal range for males: 24-190 U/L) and lactate dehydrogenase (LDH) at 5790 U/L (normal range: 207-414 U/L). His serum aldolase level was 14.2 U/L (normal range: ≤7.6 U/L).

The patient was admitted with a presumed diagnosis of drug-related inflammatory myopathy. Peginterferon alfa-2b and ribavirin were discontinued. In the meantime, we performed a biopsy of the striated muscle of the thigh, an electromyography (EMG) and nerve conduction velocity (NCV) tests, all of which were reported to be normal. Additionally, a sonography of the abdomen and pelvis revealed a normal-sized liver with coarse heterogeneous increased echo texture and no evidence of any solid or cystic mass. All other parameters were normal.

Further evaluations showed a number of pathological alterations in serum concentrations of creatinine, blood urea nitrogen (BUN), uric acid, alanine aminotransferase (ALT), aspartate aminotransferase (AST), calcium, phosphorus and urine analysis (U/A). In view of the clinical picture and laboratory results, the patient was diagnosed with rhabdomyolysis. He was subsequently treated with intravenous fluids.

Within ten days, his myalgia disappeared and there was significant improvement in his weakness. His laboratory changes returned to normal. The patient made a complete recovery and was discharged in an appropriate physical condition.

Table 1 shows laboratory values prior and post-treatment. The remaining laboratory values are shown in Table 2.

DISCUSSION

This case report described a patient with acute rhabdomyolysis associated with peginterferon alfa-2b. To our knowledge a limited number of cases linked to the occurrence of rhabdomyolysis due to administration of peginterferon have been reported.

Reinhold et al. provided a report of severe rhabdomyolysis leading to lethal complications that included multiple organ failure in a 56-year-old male previously under treatment with a high dose of peginterferon alfa-2a as an adjuvant treatment in malignant melanoma(13). Additionally, two cases of rhabdomyolysis following administration of high doses of interferon in patients with metastatic melanoma were reported by Van Londen(14) and Anderlini(15). Greenfield et al. described the appearance of rhabdomyolysis in a patient with chronic HCV ten weeks after initiation of interferon alfa at a dose of 5 million international units (MIU) ,three times per week(16). A case of acute rhabdomyolysis was reported in a 70-year-old male who was treated with interferon alfa-2b (3 MIU, three times week) for chronic HCV. The rhabdomyolysis began two weeks after initiation of the medication(17).

Rhabdomyolysis is a serious clinical syndrome that results from breakdown of skeletal muscles which is attributed to injury of myocyte membranes and leakage of intracellular materials into the systemic circulation. The clinical presentation of consists of a wide spectrum of symptoms that range from an asymptomatic rise in muscle enzymes to AKI, a mostly reversible condition that complicates 4%-33% of patients, and severe electrolyte imbalances(1,18-21). While a broad spectrum of etiologies including traumas, various diseases,

Table 1: **Critical laboratory results prior to and post-treatment.**

Variables		Prior to treatment	Post-treatment
Urea (mg/dl)		219	79
BUN (mg/dl)		102.3	36.9
Uric acid (mg/dl)		9.2	6.5
Creatinine (mg/dl)		5.58	1.15
AST (U/L)		1860	86
ALT(U/L)		406	151
CPK(U/L)		56500	189
Aldolase(U/L)		14.2	8.5
Calcium(mg/dl)		6.9	9.1
Phosphorus (mg/dl)		7.2	3.9
Urine analysis (U/A):	Proteins	Positive (++)	Negative
	Blood	Positive (+++)	Trace
	WBC/hpf*	6-8	6-8
	RBC/ hpf	45-50	3-4
	Cast/hpf	Granular	Not seen
24 hour U/A:	Urine protein (mg/24 h)	235	98
	Urine volume (ml/24 h)	2400	1000
	Urine creatinine (mg/24 h)	1029	1230

*: High power field

Table 2: **Additional paraclinical data.**

Complete blood count		**Liver function tests**		**Autoimmune markers**	
WBC (per mm^3)	6100	Alkaline hosphatase(IU/L)	243	C-reactive protein(mg/l)	16
Polymorphonuclear (%)	78	Albumin(g/dl)	2.5	Erythrocyte sedimentation rate (mm/h)	58
Lymphocyte (%)	19	Total protein(g/dl)	5.7	Rheumatoid factor(IU/L)	28
Hemoglobin (g/dl)	9.9	Total bilirubin(mg/dl)	1.2	Anti-nuclear antibody(titer)	1/100
Hematocrit (%)	31.3%	Direct bilirubin (mg/dl)	0.6	Anti DNA(IU/ml)	17.2
Mean corpuscular volume(MCV, fL)	106.5	Prothrombin time(second)	15.9	Anti-smooth muscle antibody	positive
Mean corpuscular hemoglobin(MCH, pg)	33.7	Partial thromboplastin time (second)	35	anti-liver-kidney microsome antibodies (AU/ml)	3.6
Platelet (per mL)	61000			Anti JO1	7.9
Biochemistry		**Viral markers**		Protein electrophoresis	
Na(mEq/L)	136	Hepatitis C virus(HCV) Antibody	positive	Albumin	42%
K(mEq/L)	5.1	HCV RNA:	Not detected	Alpha 1 globulin	2.6%
Alfa-feto protein(U/ml)	7.13			Alpha 2 globulin	6.3%
				Beta globulin	2.8%
				Gamma globulin	46.3%

infections and drugs are considered responsible for rhabdomyolysis, at the present time the vast majority are attributed to consumption of alcohol, illegal drugs and medications(9,18,19,21). Although the diagnosis is established by identifying elevated levels of serum CPK levels, further evaluations should be performed considering the probability of electrolyte abnormalities and AKI(18,19).

The main therapeutic intervention is hospitalization accompanied by early, aggressive intravenous fluid

resuscitation with the intent to maintain normal or high intravascular volume in order to prevent or treat AKI(1,18,19,21). Correction or prevention of electrolyte abnormalities and any upcoming complications should be considered. Although administration of bicarbonate-containing fluids, mannitol and loop diuretics can be considered, little evidence of their efficacy is available due to the lack of large randomized control studies. Thus it is difficult to make strong recommendations in this field. Overall, a favorable prognosis is anticipated in cases of early, prompt treatment(18,19,21).

Healthcare providers should be aware of the musculoskeletal side effects of peginterferon alfa-2b. The drug should be discontinued in cases of reported muscle aches or muscle weaknesses. Discontinuation leads to complete recovery from this disease. In addition, AKI is a probable complication for which physicians should be well informed and prepared to recognize the signs of this syndrome in order to provide immediate, proper treatment. Rhabdomyolysis seems to be a dose-dependent adverse effect of this drug(17). Thus, measurement of CPK activity should be considered after initiation of peginterferon alfa-2b treatment and after every dose increase in order to monitor for the onset rhabdomyolysis and prevent its irreversible complications.

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