A RARE CAUSE OF RHABDOMİYOLYSİS: SİLDENAFİL

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Abstract

Introduction: Rhabdomyolysis is a syndrome characterized by muscle necrosis and the release of intracellular muscle components into the bloodstream.

Case Report: A 29-year-old male patient presented to the emergency department complaining of nausea, vomiting and widespread body pain. Physical examination of the agitated patient who did not want to talk was as followed; Vitals: BP: 115/50, Pulse: 85, Sa02: 95. The patient was conscious, oriented, cooperative and his GCS was 15. Biochemical values in laboratory tests; AST: 224 U/Lt, ALT: 183 U/Lt, LDH: 1273 U/Lt, creatine kinase(CK): 33639 U/Lt, and drawn arterial blood gas were determined as follows: pH: 7.45, HCO3:18.7 meq/lt, lactate: 2.4mmol/lt. All other laboratory tests were normal. An ECG was performed and it showed sinus tachycardia. When anamnesis was deepened, he stated that he used Sildenafil and alcohol 24 hours before and just 3 hours before his admission to the hospital. Patient informed us that there was no coitus. In the follow-up, the patient who was given hydration and sodium bicarbonate treatment did not develop dialysis necessity, his biochemical values showed a rapid decrease of CK level 24000-11000-5000 and the patient was discharged because of the decline of all his complaints.

Conclusion: Even in patients with nonspecific symptoms, anamnesis (drug use, etc.) should be deepened. Physician awareness is important to prevent possible toxicities and systemic dysfunctions that may be caused by them.

Keywords: Rhabdomiyolysis, Sildenafil, Creatine Kinase

Introduction

Rhabdomyolysis is a syndrome characterized by musclenecrosis and the release of intracellular muscle components into the blood stream. The most common causes of rhabdomyolysis include drugs, toxins, infections, muscle trauma, convulsive seizures, hyperthermia, electrolyte imbalances, muscle enzyme defects, cocaine and alcohol use.(1,2)

Sildenafil is the first drug to be effective orally in the treatment of erectile dysfunction (ED).

In this article, we aimed to present a case of rhabdomyolysis due to Sildenafil.

Case Report

A 29-year-old male patient presented to the emergency department complaining of nausea, vomiting and widespread body pain. Physical examination of the agitated patient who did not want to talk was as followed; Vitals: Blood Pressure: 115/50mmHg, Pulse: 110/dk, Sa02: 95%. The patient was conscious, oriented, cooperative and his Glasgow Coma Scale was 15. No fever was observed and the entire systemic

examination was natural. Biochemical values in laboratory tests were; AST: 224 U/Lt, ALT: 183 U/Lt, total bilirubine:1.4 mg/dl, Crp: 1.4 mg/dl, LDH: 1273 U/lt, creatine kinase (CK): 33639 U/lt, blood urea nitrogen (BUN): 135 mg/dl Creatinine:1,7mg/dl and drawn arterial blood gase were determined as follows: pH: 7.45, hHCO3:18.7 meq/lt, lactate: 2.4mmol/lt. All other laboratory tests were normal. An ECG was performed and it showed sinus tachycardia. When anamnesis was deepened, he stated that he used Sildenafil and alcohol 24 hours before and just 3 hours before his admission to the hospital. The blood ethanol level was then requested. And 18 mg/dl. Laboratory values of the upper limit of 10 mg / dl considered induced intoxication provided. We thought that the patient's ethanollevel could also affect rhabdomyolysis but the main factor was sildenafil.

Patient informed us that there was no coitus. With no known additional medication use, trauma, seizure history, chronic disease, negative infective parameters, the patient was interned to internal medicine service to follow rhabdomyolysis. There was no change in liver renal function during follow - up, urine output was present. 1000 cc intravenous saline, 250 cc / hour was started. Urine output was also monitored and 3000 cc fluid treatment was given for 24 hours on the day of admission. 2000 cc treatment was continued for 2 days after hospitalization. Besides, 3 amp NaHCO3 was given on the day of admission. Urine output was 1500 cc / 24 hours on the first day, 1200 cc / 24 hours on the second day and 1300 cc / 24 hours on the third day. The patient was also asked to drink 2lt of water per day. The patient was admitted to the Internal Medicine Department and was followed up for 3 days; hydration and sodium bicarbonate treatment, no need for dialysis, biochemical values showed a rapid decrease. CK values obtained at the time of admission to emergency, 4th hour and 8th hour respectively: 24000 U/lt-11000 U/lt-5000 U/lt, On the 3rd day of hospitalization AST:55 U/Lt, ALT:75 U/Lt, BUN:95 mg/dl, Creatinine:1 mg/dl, CK:400 U/lt and the patient was discharged from the hospital because all of his complaints decreased.

Discussion

Rhabdomyolysis is a syndrome characterized by muscle necrosis and the release of intracellular muscle components into the blood stream. The most common causes of rhabdomyolysis include drugs, toxins, infections, muscle trauma, convulsive seizures, hyperthermia, electrolyte, imbalances, muscle enzyme defects, cocaine and alcohol use. (1,2)

Acute renal failure is probably the most important and most feared complication of rhabdomyolysis and occurs in about 30% of patients. Conversely, rhabdomyolysis has been reported to be a factor in 8% of acute renal failure cases.(3) However; acute renal failure has not developed in our case. Clinical findings -as in ourpatient -is muscle pain, muscle tension, fatigue, mildfever, dark urine (cola/tea color). Swelling and tenderness in the retained muscles and hemorrhagic color change on the skin is rarely seen. The retained muscles welling may not become as obvious until the patient is given i.v. fluids. Postural muscles, leg and calf muscles are most commonly involved. If there is no heart or brain damage, CK values above 5 folds of normal suggest rhabdomyolysis. CK> 5000 U/lt indicates severe muscle destruction. (4)

The physical examination is completely normal as in the classical presentation of the disease. The diagnosis is made with history, CK and Myoglobin. There is a clear relationship between the CK level and the severity of the disease and the amount of muscle retained, but the CK level in determining renal insufficiency is not the level yet CK> 16,000 U/lt is associated with the development of acute renal failure. In the treatment, aggressive fluid therapy should be regulated at 2.5 cc/kg/hour and urine output at 2 cc/kg/hour after correcting fluid clearance with 24-72 hours IV crystalloids. There is no prospective controlled study showing urine alkalinization and benefits of forced diuresis with mannitol until now.

Penile erection is caused by increased blood flow resulting in smooth muscle relaxation in corpus cavernosum sinusoids. The nitric oxide released by sexual stimulationin creases the activation of guanylate cyclase and causes the synthesis of cyclicguanosine monophosphate (cGMP). CGMP provides

smooth muscle relaxation, which results in increased arterial flow and corporal veno-occlusion. Intracellular cGMP is degraded by phosphodiesterase enzymes. Four phosphodiesterase isoforms (type 2,3,4,5) were detected in the human penile tissue, with predominant isoform type 5 in this tissue. Sildenafil is an oral, potent and selective inhibitor of cGMP-specific phosphodiesterase type 5 (PDE5).

In a study conducted by Mohey V et al in rats, it has been shown that Sildenafil has renoprotective effects. (5) According to this study, this characteristic of Sildenafil can be considered as the reason for not developing acute renal failure despite high levels of creatine kinase in our patient.

34 year old patient was found dead at his work place. An autopsy was performed and revealed desmethyl-carbodenaphil and it's hydroxy metabolite in his blood cromatography. (6) In this case, it is possible that the patient used the drug in toxic doses. As it is known that systemic and vascular side effects of the drug may occur; it is used for therapeutic purposes in erectile dysfunction and many other diseases related to vascular structures and smooth muscles.

In a study conducted in rats, it has been shown that low-dose Sildenafil can prevent carbontetrachloride-induced hepatotoxicity by inhibiting PDE5. (7).

There are many studies on the use of Sildenafil in Congenital Diaphragmatic Hernia and Pulmonary HT. In a case of rhabdomyolysis associated with the use of statin and Sildenafil, a 66-year-old male patient with DM and HT was reported to use Sildenafil for 5 months and to admit to the hospital with myalgia. (8)

A study in Korea reported that high doses of Sildenafil may cause rhabdomyolysis. (9) The true incidence of Sildenafil-related renal matters is unknown, since the post-marketing data are very limited. More cases can be detected as the number of prescription of Sildenafil increases.

Conclusion

Even in patients with nonspecific symptoms, anamnesis (druguse, etc.) should be deepened. Physician awareness is important to prevent possible toxicities and systemic dysfunctions that may be caused by them.

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