Kidney Res Clin Pract 35 (2016) 182–186

Kidney Research and Clinical Practice

journal homepage: http://www.krcp-ksn.com
Contents lists available at ScienceDirect

Case Report

Rhabdomyolysis in a patient taking nebivolol

Ye Jin Kim, Hae Ri Kim, Hong Jae Jeon, Hyun Jun Ju, Sarah Chung, Dae Eun Choi, Kang Wook Lee, Ki Ryang Na*

Renal Division, Department of Internal Medicine, Chungnam National University Hospital, Daejeon, Korea

Article history:
Received 24 March 2015
Received in revised form
6 August 2015
Accepted 14 September 2015
Available online 22 January 2016

Keywords:
β-adrenergic blockers
Myopathies
Nebivolol
Rhabdomyolysis

Abstract

β Blockers such as propranolol and labetalol are known to induce toxic myopathy because of their partial β_2 adrenoceptor agonistic effect. Nebivolol has the highest β_1 receptor affinity among β blockers, and it has never been reported to induce rhabdomyolysis until now. We report a patient who developed rhabdomyolysis after changing medication to nebivolol. A 75-year-old woman was admitted to our hospital because of generalized weakness originating 2 weeks before visiting. Approximately 1 month before her admission, her medication was changed from carvedilol 12.5 mg to nebivolol 5 mg. Over this time span, she had no other lifestyle changes causing rhabdomyolysis. Her blood chemistry and whole body bone scan indicated rhabdomyolysis. We considered newly prescribed nebivolol as a causal agent. She was prescribed carvedilol 12.5 mg, which she was previously taking, instead of nebivolol. She was treated by hydration and urine alkalization. She had fully recovered and was discharged.

Introduction

There are various causes of rhabdomyolysis. Recently, many medicines and substances, including lipid-lowering drugs (fibrates and statins), alcohol, heroin, cocaine [1], diuretics, antibiotics, and antifungal agents [2], have been reported as causes of rhabdomyolysis.

Among antihypertensive agents, it has been reported that β blockers, such as propranolol [3], labetalol [4], pindolol [5,6], and xamoterol [6], can result in toxic myopathy, which induces muscle cramps, pain, and muscle enzyme elevation.

Nebivolol is a selective β_1-blocker with a nitric oxide–potentiating vasodilatory effect in comparison with other β blockers [7]. Nebivolol has a direct stimulatory effect on endothelial nitric oxide synthase, which results in increased levels of local nitric oxide [8,9]. It has been reported that nebivolol has an antioxidant effect [7,10]. In addition, there has been no published report of nebivolol-induced rhabdomyolysis. Although it is thought to have a more favorable side effect profile compared to other β blockers [11], nebivolol can possibly induce rhabdomyolysis. We treated a patient who developed rhabdomyolysis induced by nebivolol.

Case report

A 75-year-old woman was admitted to our hospital because of generalized weakness. The patient had been suffering from generalized weakness and anorexia for 2 weeks and remotely experienced symptom onset 1 month earlier. She had pain on the right knee and right thigh but no respiratory or cardiovascular symptoms suggesting infectious disease such as cough, sputum, rhinorrhea, sore throat, or fever. She had no other lifestyle changes, including trauma history, severe

* Corresponding author. Renal Division, Department of Internal Medicine, Chungnam National University Hospital, 282 Munwharo, Chung-gu, Daejeon 35015, Korea.
E-mail address: drgnr@cnu.ac.kr (KR Na).

http://dx.doi.org/10.1016/j.krcp.2015.09.003

exercise, burn, or diet, except for her change in medication from carvedilol 12.5 mg to nebivolol 5 mg 1 month before her admission. She visited a private clinic, and her serum levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were elevated markedly. She was transferred to an emergency room for further evaluation.

Previously, she was diagnosed with hypertension 11 years ago and severe cardiovascular disease (3-vessel disease) treated with a coronary artery bypass graft 4 years ago. She had taken fluvastatin 80 mg, valsartan 80 mg, aspirin 100 mg, and carvedilol 12.5 mg daily for 4 years. One month before her admission, carvedilol was changed to nebivolol 5 mg daily. She did not have diabetes mellitus, chronic hepatic disorder, or chronic kidney disease. She was a housekeeper without a history of smoking, alcohol intake, or herbal medication.

On physical examination, the patient was obese (body mass index, 26.57 kg/m^2). Initial blood pressure was 136/66 mmHg. The heart rate was 62 beats/min. The respiration rate was 20 breaths/min. Body temperature was 36.7°C. Her mental status was alert, and orientation was intact. She cannot stand up on her own strength because of generalized weakness and right knee pain. Muscle strength was decreased to Grade II on the right lower leg and Grade IV on the other extremities and trunk. No significant tender point was found. Her urine was a dark color when examined in the emergency room.

On the day of admission, her blood test disclosed the following: AST 1,091 IU/L, ALT 913 IU/L, blood urea nitrogen (BUN) 56.8 mg/dL, creatinine 1.3 mg/dL, lactate dehydrogenase (LDH) 6,541 IU/L, creatine kinase (CK) 37,399 U/L, CK-MB 399.7 ng/mL, troponin I 0.15 ng/mL, erythrocyte sedimentation rate 54 mm/h, and C-reactive protein 1.0 mg/dL. The serum myoglobin level was higher than the upper measurable range (> 3,000 ng/mL).

The levels of hemoglobin (13.3 g/dL), platelet (218,000/μL), white blood cells (8,700/μL), total bilirubin (0.7 mg/dL), alkaline phosphatase (106 IU/L), plasma sodium (141 mEq/L), potassium (5.0 mEq/L), chloride (108 mEq/L), phosphorus (4.8 mg/dL), and total calcium (9.4 mg/dL) remained in the normal range. An arterial blood gas analysis at this time revealed a pH of 7.37, PCO_2 37 mmHg, PO_2 87 mmHg, HCO_3 21.4 mmol/L, and O_2 saturation 96%.

The patient had the hepatitis B surface antibody. The results of the test for a hepatitis B surface antigen, hepatitis C antibody, reverse transcriptase-polymerase chain reaction of hepatitis C RNA, human immunodeficiency virus antibody, and rapid plasma reagin were all negative. The test for hepatitis A was not performed in consideration of low incidence of hepatitis A in her age.

The urine was strongly positive (+++) for blood in dipstick test, but only 3–5/hours postfertilization (HPF) red blood cells were present on microscopic examination. Other laboratory results include specific gravity 1.015, pH 5.5, protein (++), glucose (−), ketone (−), bilirubin (−), urobilinogen (trace), nitrite (−), many white blood cells, 2–3/HPF squamous epithelial cells.

There was no remarkable finding other than a simple cyst on the right kidney on an abdominal ultrasonogram and a cardiac echocardiogram. An electrocardiogram showed sinus rhythm with normal intervals.

Technetium-99m hydroxymethane diphosphonate bone scintigraphy showed increased tracer uptake in the abdominal wall, both thighs, both deltoid muscles, and the right teres muscles (Fig. 1).

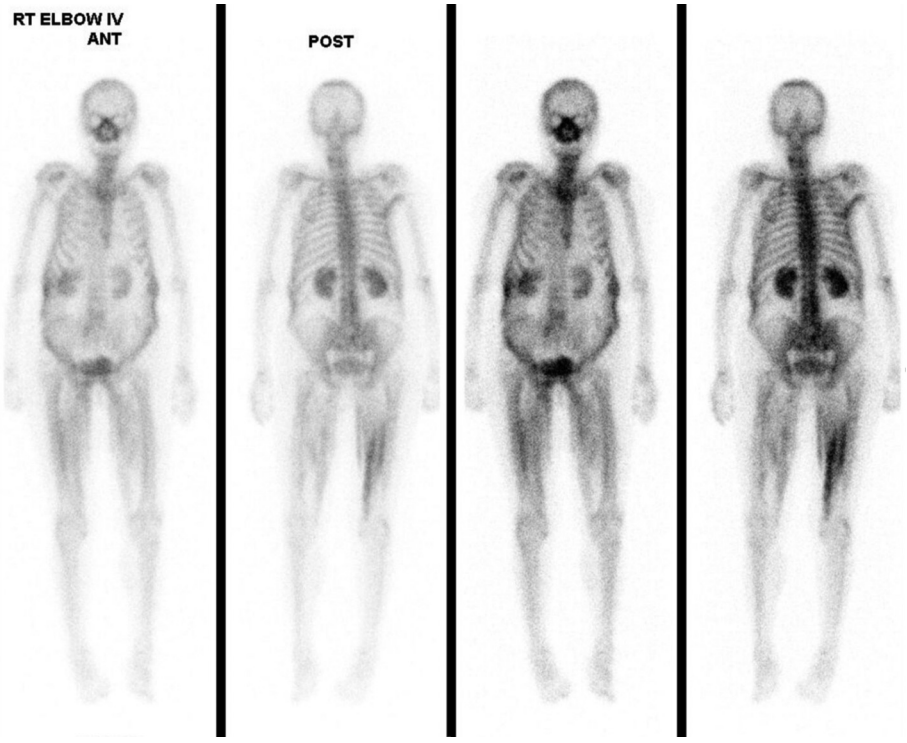

Figure 1. Tc-99m HDP bone scintigraphy. An increased tracer uptake was shown in the abdominal wall, both thighs, both deltoid muscles, and right teres muscles.
HDP, hydroxymethane diphosphonate.