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Erythromelalgia accompanying rosuvastatin-associated myopathy

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Abstract

Background: Secondary erythromelalgia can occur due to various underlying medical disorders or drug toxicity.

Main observations: A 75-year old male developed acute secondary erythromelalgia following the onset of rosuvastatin use and associated myopathy. The illness was reversible after discontinuation of the pharmacological agent.

Conclusion: Secondary erythromelalgia may occur after rosuvastatin use, but this and other dermatological toxicities are rare.

Introduction

Rosuvastatin and other statin lipid lowering agents are largely known for their potential myopathic toxicity. Other highly studied toxicities of these agents include effects on the liver and kidney.[1,2] During the course of rosuvastatin use for an elderly gentleman, myopathy evolved and was accompanied by skin manifestations. The patient's illness is detailed, and the spectrum of reported dermatological manifestations of rosuvastatin toxicity are reviewed.

Case report

A 75-year old male developed angina and transient ischemic attacks over the previous two years. As a consequence, he received a paclitaxel-eluting coronary artery stent in the left anterior descending artery. He also had stents placed in both the right and left carotid arteries. He had suffered from hypertension, but it was controlled. He had been a past smoker and was also suffering from occasional bilateral leg claudication. In 2007, he had been prescribed atorvastatin (40 mg./day) while also receiving ramipril and clopidogrel. Over a month, he developed fatigue and myalgias. A dose reduction to 20 mg. daily was not accompanied by a change in symptoms, and the creatine phosphokinase (CPK) level was 300-400 U/L. Atorvastatin was discontinued, and fenofibrate (100 mg./day) was initiated. The fatigue and myalgias disappeared shortly thereafter, and the CPK decreased to 241 U/L.

In follow-up of his lipid profile, the following were reported: cholesterol 6.0 mmol/L., LDL cholesterol 3.8 mmol/L., HDL cholesterol 3.8 mmol/L., and triglycerides 1.2 mmol/L. In order to improve on the cholesterol profile, a trial of rosuvastatin (10 mg./day) was initiated and fenofibrate was discontinued. Other medications were unchanged and included ongoing use of ramipril, acetylsalicylic acid, and clopidogrel. Within the following week,

the patient complained of dizziness and mild chest tightness. The musculature of his distal limbs was painful. The hands especially towards the fingers showed pronounced erythema and warmth. The hands were mildly swollen, and he experienced persistent pulsating pain and dysesthesias. There was mild variation with temperature change but mainly benefit with cold, and there was little relief with elevation. Both feet were mildly affected. The CPK was 697 U/L., but the electrocardiogram and troponin levels were normal. Rosuvastatin was discontinued within two days, the discolouration of the extremities diminished considerably, and the discomfort faded. During the latter, blood counts, liver and kidney function studies, and blood pressure were unchanged and normal. Fenofibrate was recommenced without complications, and ezetimibe was added at a later date.

Discussion

This patient developed acute rosuvastatin toxicity which was manifest by myopathy and erythromelalgia. Although the myopathic events occurring after statin toxicity are considerably detailed in the medical literature, it is unclear what pathologic mechanisms led to this patient's skin manifestations. This pharmacological agent is capable of numerous physiological and biochemical effects.[3]

Erythromelalgia can occur in primary or secondary forms. Primary erythromelalgia is a genetic and inheritable disorder which is chronic.[4] Secondary erythromelalgia, however, as in our patient, can arise as a consequence of various underlying medical disorders or drug toxicities, and in this form can be reversible. Pharmacological agents previously implicated include calcium channel blockers (e.g., verapamil, nifedipine, nicardipine), ergot derivatives (e.g., bromocriptine, pergolide), norephedrine, ticlopidine, iodide in contrast solution, mercury, and some vaccines (e.g., hepatitis B and influenza). Some have postulated that erythromelalgia is a syndrome of disturbed microvascular dynamics.[5,6] Whereas the illness may lead to acute symptoms necessitating urgent review, the manifestations in themselves are not ones that pose immediate danger. As such, the toxicity reported herein is best described in the Common Terminology Criteria for Adverse Events v3.0 as 'flushing - grade 2'. Such a description contrasts hand-foot reactions such as palmar plantar erythrodysesthesia (hand-foot syndrome) which is a dose-dependent cutaneous rather than vascular skin toxicity due to cytotoxic chemotherapy.

Dermatological toxicity from rosuvastatin use is rarely published. A recent report indicated such toxicity (cited as a single case of possible Stevens-Johnson syndrome) in 1/2285 patients from a randomized trial.[7] Some studies have cited jaundice, but the latter is a consequence of direct hepatotoxicity.[8] Other studies find dermatological side-effects in consistently less than 2%, although details are uncommonly given.[9-15] Certainly, there is a lack of consistent side effects reported from the latter assessments which now include hundreds of thousands of patients. This infrequency mirrors that of other statins,[16] although unusual and rare reports of dermatological toxicity may emerge after the pharmacological agents have been consumed in larger numbers of patients over many years.[17,18]

Overall, it appears as if rosuvastatin and other statins have a remarkably low tendency to induce toxic skin manifestations.

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