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CASE REPORT

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Lovastatin-Erythromycin Induced Myositis: Case Report and Possible Mechanism

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Abstract

Lovastatin and erythromycin when used concurrently may cause myositis. Lovastatin is metabolized by the cytochrome CYP450 system, mainly using the CYP3A4 pathway. Drugs that inhibit or compete for the CYP450 pathway can cause elevations in lovastatin blood levels and resulting in possibility of increased side effects. Erythromycin is one of the agents known as one of the potent CYP450 pathway inhibitor, which can cause an acute increase of lovastatin concentration. We present a case of lovastatin-erythromycin induced myositis occurring in a 73-year-old female patient who was admitted to the intensive care unit for acute pulmonary oedema.

Key words: Lovastatin, Erythromycin, Myositis, Mechanism.

INTRODUCTION

Myositis is a human autoimmune disease characterized by weakness and wasting of muscles.[1] Lovastatin lowers total cholesterol and low-density lipoprotein cholesterol, reducing the cardiovascular-related morbidity and mortality in patients with hypercholesterolemia.[2,3] Erythromycin has excellent activity against most of the common streptococcal bacteria and an alternative to penicillin in penicillin-allergic patients.[4] Here we present an unusual case of lovastatin-erythromycin induced myositis when treated for acute pulmonary oedema.

CASE REPORT

Reason for visit: 73 year old Chinese female having complaint of heavy breathing was brought to Accident and Emergency unit (A&E).

The patient had past medical history reported diabetes mellitus type 2, chronic renal failure, hypertension, ischemic heart disease and congestive cardiac failure (CCF). The patient was using T. Furosemide 40 mg OD, T. Aspirin 150mg, T. Trimetazidine 20 mg TDS, T. Lovastatin 20 mg ON, T. Amlodopine 10 mg OD, T. Prazosin 3 mg TDS, T. Bisoprolol l5 mg OD, T. Ferrous Fumarate 400 mg OD, T.B. Complex 1 OD, T. Vitamin C 100 mg OD, T. Folic Acid 5 mg OD, S/C Mixtard 18 unit PM/14 units PM and T. Calcium Carbonate 500 mg TDS. Her care takers informed that the patient was compliant to her medications.

The physical examinations reported bi-lateral crepitation in both lungs. Apex beat was displaced with no murmur heard, jugular venous pressure was raised and bilateral pitted oedema was visible on both legs. X-ray showed cardiomegaly and echocardiogram reported ejection fraction of 32%. The post intubation atrial blood gases (ABG) concentration was pCO_2: 35.0%; pO_2: 225.2%; HCO^{3-}: 21.0%, SO_2: 99.6% with pH of 7.38. The baseline blood investigation revealed; Urea 20.7mmol/l; Creatinine 352µmol/l, Serum Sodium 138 mmol/l, Serum Potassium 4.1mmol/l, Total Protein 67g/l, Albumin 33 g/l, Alanine Amino Transferase (ALT) 21u/l, Aspartate Amino Transferase (AST) 28u/l, Alkaline Phosphatase (ALP) 62u/l and Creatine Kinase (CK) 380

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u/l. In addition, the baseline lipid profile reported Total Cholesterol 3.5 mmol/l, Triglycerides 1.1 mmol/l, LDL 1.5 mmol/l and HDL 1.5 mmol/l.

The 73 year old Chinese female patient was diagnosed with Acute Pulmonary Oedema (APO), was intubated and admitted to intensive care unit (ICU) due to tachypneic and prolonged gasping.

Initially, the patient was treated with IV Furosemide 10mg/hour, IV Ampicillin/Sulbactam (UNASYN) 1.5g BD, IV Omeprazole 40mg OD, S/C Actrapid 6 units TDS, S/C Insulatard 6 units ON and Dexmedetomidine 0.5mcg/kg/hour. T. Lovastatin and her other previous home medications except T. Bisoprolol, S/C Mixtard, were started during this admission. On the third day of admission T. Erythromycin 200 mg TDS, were started as a prokinetic agent. After starting erythromycin, CK level started to rise and patient started complaining of persistent muscle ache. Slight increase of ALT and AST levels from baseline were also noted. However, the serum creatinine remained stable. Other causes of acute raise in CK such as trauma, cardiac event and hypothyroid were ruled out, leaving lovastatin induced myositis as a possible cause. However, since the patient was tolerating lovastatin for last 5 years, addition of erythromycin to the treatment regimen was alleged to have induced the incident. No other drugs that significantly could cause the interaction or directly raise CK were noted in the treatment regimen. Both erythromycin and lovastatin were stopped and CK level dropped to 1261u/l on the next day and subsequently reduced to 408u/l in 6 days. Both ALT and AST levels also returned to baseline levels (23u/l and 38u/l) in 6 days after discontinuation of lovastatin and erythromycin. By using the definitions, patient's condition was defined as lovastatin-erythromycin induced myositis. The rise and fall of CK level before and after the lovastatin-erythromycin induced myositis is presented in Figure 1.

DISCUSSION

Patient was prescribed T. Lovastatin 20 mg ON, 5 years ago and she did not experience any muscle ache or weakness before the current admission. According to ACC/AHA/NHLBI Clinical Advisory on the Use and Safety of Statins, several risk factors could predispose to the lovastatin induced myotoxicity, such as advance age, gender (female) and diabetes with CKD.[5] Despite the risk factors, the patient was tolerating lovastatin therapy. Therefore, it seems unlikely for lovastatin, after 5 years of use to produce acute myositis unless there is a precipitating cause. The current study suspected a drug interaction among lovastatin and erythromycin, as other causes for acute raise in CK level were ruled out. This is supported by Belloat and colleagues who reported that 58% of lovastatin-induced rhabdomyolysis were due to drug interactions.[6]

Lovastatin is metabolized by the cytochrome CYP450 system, mainly using the CYP3A4 pathway.[7] Drugs that inhibit or compete for the CYP450 pathway can cause elevations in lovastatin blood level with the resultant possibility of increased side effects like myositis. Erythromycin is a potent CYP450 pathway inhibitor, so we believe that this could have caused an acute increase of lovastatin concentration.[8] The exact fundamental mechanism of lovastatin–associated myopathy is still not very clear, however, it is attributed to the sarcolemmal cholesterol reduction, mitochondrial dysfunction due to decreases in coenzyme Q, and depletion of isoprenoids, cholesterol synthetic by-products that normally reduce rates of apoptosis (9). Furthermore, enhanced lipoprotein lipase-dependent triglyceride-rich lipoprotein particle uptake with cholesterol or phytosterol accumulation, and relative vitamin E deficiency is also reported as a potential lovastatin–associated myopathy.[9] In line to what is suggested by the current study, lovastatin-erythromycin induced rhabdomyolysis was reported by Spach *et.al.* where the concentration of lovastatin was increased 3 fold with biopsy of both quadriceps muscle specimens showing oedema and necrosis of individual muscle fibers in a patchy distribution.[10] In the same case report, rhabdomyolysis occurred after completion of 10 days course of erythromycin.[10] In the present scenario, a sharp increase of CK on the sixth day after adding erythromycin to the treatment regimen was observed. Since we detected this increase in CK level, and decided to discontinue both erythromycin and lovastatin, the patient did not developed rhabdomyolysis.

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CONFLICT OF INTEREST

The authors declare no competing interests. No funding was received for the study.

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