

Atorvastatin Induced Vasculitis

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ABSTRACT

Adverse drug reactions are regarded as an important public health problem as they may be potentially life-threatening. The World Health Organization defines Adverse drug reaction (Adverse Drug Reaction) as a response to a drug which is noxious, unintended, which occurs at doses normally used in human for prophylaxis or diagnosis of a disease or for modification of physiological function. We report two adverse drug reaction case reports. Case 1: A forty six years old Indian female adult developed Vasculitis over both legs and back after four months. Patient was prescribed Tablet Atorvastatin 20 mg, Tablet Atenolol 25 mg, Tablet Levothyroxine sodium 100 mg and Tablet Acetylsalicylic acid 100 mg. Patient had been treated with methylprednisolone and azathioprine. Case 2: A fifty six years old Indian female adult had been treated with Atorvastatin 10 mg, Telmisartan 40 mg and Zolpidem 10 mg for essential hypertension. Patient had been treated with methylprednisolone. Hence there is a need for awareness of the adverse events related to statins therapy to avoid life-threatening complications.

Keywords: Pharmacovigilance, Adverse Drug Reaction, Atorvastatin, Vasculitis, Suspected Unexpected Serious ADR (SUSAR)

INTRODUCTION

Medicines are used to treat illnesses as they have the ability to modify the altered physiological process in the body. But at the same time, due to various predisposing factors, drugs always pose certain amount of risk in the form of unwanted or unintended effects known as adverse drug reactions (ADRs).¹ Adverse drug reactions are regarded as an important public health problem as they may be potentially life-threatening. The World Health Organization defines Adverse drug reaction (ADR) as a response to a drug which is noxious, unintended, which occurs at doses normally used in human for prophylaxis or diagnosis of a disease or for modification of physiological function. The typical pharmacological classification of ADRs by Rawlins and Thompson² separates these into two major sub types: Type A reactions, which are dose dependent and predictable, and Type B reactions which are

not dose dependent and unpredictable. The majority of ADRs are Type A reactions. Type B reactions comprise approximately 10-15% of all ADRs and include hypersensitivity drug reactions. ADRs are regarded as the one of the leading causes of increased health care cost, morbidity and mortality.³

Vasculitis is a condition that involves inflammation of the blood vessels and can affect any of the body's blood vessels including arteries, veins, and capillaries. If a blood vessel is inflamed, it can narrow or close off; rarely the blood vessel will stretch and weaken, causing it to bulge. This bulge is known as an aneurysm. Inflammation can be short-term (acute) or long-term (chronic) and can be so severe that the tissues and organs supplied by the affected vessels do not get enough blood. The shortage of blood can result in organ and tissue damage, even death.⁴

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Drug induced Vasculitis is the inflammation of blood vessels caused by the use of various pharmaceutical agents including antibiotics, *Thiazide* diuretics, *Thiourea*, oral anticoagulants such as warfarin and coumarin, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs).⁵

Statins are the most effective and best tolerated agents for treating dyslipidemia. These drugs are competitive inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, which catalyse the early, rate-limiting step in cholesterol biosynthesis.⁶ Statins are well tolerated and have very few side-effects. Adverse reactions include photo sensitivity, hepatotoxicity, myopathy and muscle weakness. A rare hype sensitivity syndrome has been reported which is characterized by at least one of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, ploymyalgia rheumatic, Vasculitis, purpura, thrombocytopenia, leukopenia, haemolytic anaemia, toxic epidermal necrolysis and dermatomyositis.⁷ Atorvastatin is frequently prescribed among statins with initial dose of 10 mg daily, may be adjusted at intervals of 4 weeks up to a maximum of 80 mg daily.⁸ Recently, some cases of statin-induced Vasculitis have been reported. In this study, we report two cases of Vasculitis probably induced by atorvastatin.

MATERIAL AND METHODS

National Coordination Centre-Indian Pharmacopoeia Commission (IPC) collects the spontaneous adverse drug reaction reports/ Individual Case Safety Reports from its member regional centres or ADRs Monitoring Centres under the Pharmacovigilance Programme of India (PvPI). The reports submitted to IPC through VigiFlow (ICSRs Management system) have been stored in global ICSR database i.e. VigiBase™. The two cases were identified during the signal generation from the VigiBase™.

CASE NO: 1

A 46-year old man presented with fever and rashes over both legs and back. The patient was a known case of hyperlipidemia and was prescribed with tablet atorvastatin 20 mg for last 4 months. He was also taking atenolol 25 mg and acetylsalicylic acid 100 mg for hypertension and levothyroxine 100 mg for hypothyroidism. The patient was diagnosed as a case of Vasculitis and hospitalized. Patient was treated with methylprednisolone and azathioprine and the outcome was recovering.

CASE NO: 2

A 56-years old Indian female adult was treated with Atorvastatin 10 mg, Telmisartan 40 mg and Zolpidem

10 mg for essential hypertension. She complained of rashes over back and right hand and later on diagnosed as a case of Vasculitis. Patient was treated with methylprednisolone.

DISCUSSION

Statins are considered well-tolerated lipid-lowering agents with an excellent safety profile and therapeutic range. Their effects have been an area of intense research to show additional benefits of these lipid-lowering agents.⁹ Patel et al discuss how statins, even at high doses, provide an effective decrease in LDL and even promote anti-inflammatory effects within atherosclerotic plaques.¹⁰

We are now reporting two cases of vasculitis induced by atorvastatin. Complete resolution of symptoms occurred with administration of a tapering dose of steroids. Causality assessment of the adverse drug event (ADE) was carried out using WHO-UMC criteria and Naranjo's Scale. In both the cases, the patient improved on providing the treatment. However data on the challenge (withdrawal of the drug) is unclear. Hence, the ADE was possibly caused by atorvastatin (WHO-UMC criteria: Possible; Naranjo's Score: 4, possible). The severity of the reaction was moderate in nature (modified Hartwig and Siegel's Scale),¹¹ and it was definitely preventable (modified Schumock and Thornton criteria).¹²

Haroon et al reported a similar case of ANCA-associated systemic Vasculitis that was induced by atorvastatin.¹³ In a study it was reported that among 54 reports from FDA 0.04% have Leukocytoclastic Vasculitis associated with use of atorvastatin.¹⁴ In a study comparing the values of Common Carotid Artery (CCA), Intima-Media Thickness (IMT) to the incidence of stroke, Myocardial Infarction (MI) and death in patients with Takayasu's Arteritis (TA), it was reported that CCA-IMT is increased in TA and regression of IMT is possible with immunosuppressive treatment and atorvastatin.¹⁵ Alissa S et al reported a case of ANCA-associated systemic Vasculitis that was induced by simvastatin.¹⁶

CONCLUSION

Statins are frequently prescribed for a variety of indications such as diabetes mellitus, ischemic heart disease, hypertension, cerebrovascular diseases. Hence there is a need for awareness of the adverse events related to statins therapy to avoid life-threatening complications.

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CONFLICTS OF INTEREST

The authors declare that no conflict of interest and there this study was not funded.

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