

## CASE REPORT

## ANGIOEDEMA; AN UNREPORTED ADVERSE EFFECT OF PITAVASTATIN

Saba Naz, Muhammad Wali Saleem\*, Agha Waqar Haider\*\*

CJW Medical centre-USA, \*Student Khyber Medical College, Peshawar-Pakistan, \*\*Cardiology Department, Chippenham Hospital, Richmond VA-USA

Angioedema is a life-threatening reaction characterized by swelling of the face, lips, tongue or larynx. Known adverse effects of Pitavastatin do not include angioedema. We report first case of a 55-year-old Asian male developing post exposure angioedema to 2 mg Pitavastatin. Note that the patient showed no history of hypersensitivity. Relationship between Pitavastatin and angioedema was assessed by Naranjo scale.

**Keywords:** Angioedema; Pitavastatin; Allergic reaction; Statin, Adverse effects

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## INTRODUCTION

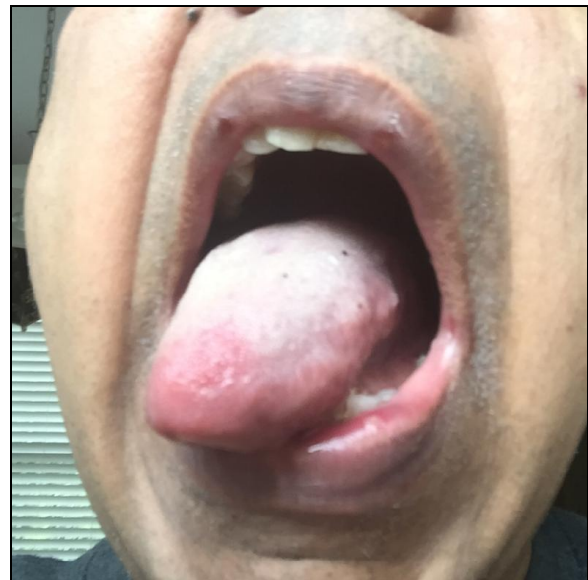
Angioedema is a life-threatening reaction that can cause the swelling of mucosal membranes in the face, lips, tongue, or larynx. It can be caused by an allergic reaction from exposure to foods or drugs. Pitavastatin is an HMG-CoA reductase inhibitor therapy for patients that have primary hyperlipidaemia. It helps to decrease the elevated total cholesterol, low density lipoprotein cholesterol, apolipoprotein B, triglycerides, and increase the high-density lipoprotein cholesterol. When taking the drug, there are some interactions that can alter the effectiveness of the drug. These adverse reactions include back pain, constipation, diarrhoea, myalgia, and pain in the extremities but no angioedema cases have been reported.<sup>1</sup> Approximately, 17.5% of patients with cutaneous drug eruptions have angioedema. In addition, it is estimated that 32% of angioedema cases are caused by drugs.<sup>2</sup> In the past there have been reports of urticaria with or without angioedema seen after exposure to a few statins but no such cases have been reported for Pitavastatin.<sup>3</sup>

## CASE REPORT

A 55-year-old Asian male patient was seen for intolerance to statins and evaluation of hyperlipidaemia. The patient was recently prescribed 2 mg Pitavastatin by his primary care physician (PCP) to treat hyperlipidaemia. He had also started a heart healthy diet and regular exercise program. The patient gave a family history of coronary heart disease and high cholesterol. He has no past history of allergies to medications or food substances as well as no adverse hypersensitivity reactions. Soon after starting the treatment, patient noticed numbness, tingling and swelling of tongue and lips. He was referred to our clinic for further evaluation and

treatment. After a careful review patient was advised to stop Pitavastatin and Ezetimibe was prescribed. Patient was encouraged to continue with diet and exercise program.

Patient tolerated this therapy well but 2 months later he restarted Pitavastatin when Ezetimibe and diet did not bring the lipid to target levels. 24 hours later, patient reported swelling of tongue, lips, and mouth (Figure-1). It confirmed our suspicion that patient was having angioedema due to Pitavastatin. Patient was advised to stop Pitavastatin and he was referred to the emergency room where ant-allergic medications and steroids were used. On a follow up visit 2 weeks later, the allergic symptoms had resolved and patient was continuing with Ezetimibe and life style modifications.



**Figure-1:** Patient with angioedema showing marked swelling of the tongue and lips with ulceration.

## DISCUSSION

Angioedema can be classified on etiological or pathophysiological basis. Broadly, these include allergic angioedema, angioedema due to angiotensin converting enzyme inhibitor (ACE-I), angioedema due to non-steroidal anti-inflammatory drug (NSAID), hereditary angioedema (HAE), inherited angioedema with normal C1 esterase inhibitor, and acquired C1 esterase inhibitor deficiency. Angioedema can result from histamine release following mast cell degranulation or from increased accumulation of bradykinin either via increased production or decreased inactivation.<sup>4</sup> The mechanism of statin-induced angioedema is unknown, the effect may be mediated by bradykinin which then cause vasodilation and, potentially, angioedema.

This case report of angioedema due to exposure to Pitavastatin is unique since the patient had no past history of drug allergies. At the time of symptom onset, our patient was not receiving medications that have been linked to angioedema. Angioedema has been reported in association with many drugs usually after exposure to ACE inhibitors and other drugs including Statins. To our knowledge angioedema has not been reported in association with

Pitavastatin. Our conclusion is derived from the fact that initial exposure to Pitavastatin was associated with mild symptoms of angioedema. These symptoms resolved with cessation of therapy. Moreover, these symptoms recurred with re-exposure to the offending drug and resolved once again on discontinuation of Pitavastatin. Assessment of the drug reaction on the Naranjo scale showed a score of +10 indicating a strong association between the drug and the adverse reaction.<sup>5</sup>

Clinicians need to be aware of potentially life-threatening adverse effect of Pitavastatin and exercise caution when prescribing these drugs.

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### Address for Correspondence:

Saba Naz, CJW Medical centre-USA

Email: nazsaba@yahoo.com