

Aphthous Ulcer—A Rare Effect of Losartan

Ayaana Jain, Anushree Deshpande*

Department of Pharmacy Practice, KLE College of Pharmacy, Belgaum, Karnataka, INDIA.

ABSTRACT

The most common type of oral mucosa ulcer is an aphthous ulcer, which manifests as a painful sore on the mucous membranes of the mouth or genitalia.¹ We describe a case of a male patient who was admitted to the hospital due to anorexia, generalized weakness, weight loss, trouble opening the mouth, glossitis, and aphthous ulcers. The patient's history and recent medication history indicated that the symptoms began to appear when losartan for hypertension was started. The use of losartan was stopped, and the patient's glossitis and mouth ulcers were treated symptomatically. After 15 days of drug withdrawal, the symptoms began to subside. According to the WHO and Naranjo ADR assessment, Losartan had a "possible" connection with the oral toxicity seen in this patient.

Keywords: Aphthous ulcers, Mucous membrane, Glossitis, Losartan, ARBs, FDA.

INTRODUCTION

Aphthous stomatitis, also called "canker sores," is an idiopathic illness that results in recurrent, excruciating aphthous ulcers on the non-keratinized oral mucous membranes. Aphthae, aphthosis, and aphthous stomatitis are other names for them.² With cardiovascular medications like beta-blockers, oral toxicities such as xerostomia, angioedema, oral lichen planus dysgeusia, gingival enlargement, scalded mouth syndrome, cheilitis or glossitis, and aphthous ulcers are frequently observed.³ Patients with hypertension and heart failure frequently utilize Angiotensin Receptor Blockers (ARBs).⁴ Back discomfort, diarrhea, myalgia, sinusitis, and upper respiratory tract infections are some of the frequent side effects linked to ARBs. Oral mucosa-related allergic responses caused by losartan have not been frequently documented. Symptoms of the above case were resolved within 10 days of medication discontinuation. We report a case of Losartan-Induced Aphthous Ulcers.

CASE REPORT

A 47-year-old male patient had an abrupt presentation of loss of appetite, generalized weakness, weight loss, glossitis, slurred speech, mouth ulcers covering the entire oral mucosa, and lips coupled with excruciating pain and trouble eating. Additionally, he complained of hypertension for 7 years and was prescribed Losartan 50 mg daily (Tab. Zilos) monotherapy since then. He visited our hospital for generalized weakness and loss of appetite. On admission, the patient was found to have normocytic hypochromic anaemia with masked anisocytosis, which was verified to be pancytopenia with dimorphic anaemia. The patient has been chewing tobacco for 10 years.

When the oral cavity was examined, tongue hypopigmentation and B/L fibrous bands were seen. The patient additionally reported having trouble opening his mouth for the past three years. He was consequently admitted to our hospital for additional care. The patient was vitally stable at the time of admission.

Received: 08-12-2022;

Revised: 28-01-2023;

Accepted: 04-02-2023.

DOI: 10.5530/ijopp.16.2.26

Address for

correspondence:

Dr. Anushree Deshpande,

Doctor of Pharmacy,

Assistant Professor,

Department of Pharmacy

Practice, KLE College of

Pharmacy Belgaum,

Karnataka, INDIA.

Email id: anushreedesh-

pande@klepharm.edu



www.ijopp.org

However, he complained of excruciating pain from ulcers, trouble opening his mouth, and difficulty chewing or swallowing. The dermatologist Multiple erosions over the buccal mucosa, B/L fibrous bands, and hypopigmented tongue indicative of aphthous ulcers, and glossitis suspected to be secondary to drug use. [Figure 1] The patient has been prescribed Rebamipide 100mg, Povidone-iodine (2% W/W), Candida mouth paint, and Lactobacillus. Laboratory investigations revealed reduced hemoglobin (5.8gm%), for which 2 pints of PCV were administered. RBC levels were also lower (2.11). The results of the other investigations were normal. After being hospitalized for nine days, the patient felt better after discontinuing the Losartan 50 mg. Each medicine underwent a review for potential side effects. Given the prior history and the temporal relationship with the history, there was a strong correlation between losartan and glossitis and aphthous ulcers. As a result, the de-challenge technique was used, and losartan was stopped on the fourth day of hospitalization. All other medications were kept up. When the patient returned for a follow-up appointment 15 days later, his blood pressure was under control and his oral mucosa symptoms were reducing [Figure 2]. The patient was able to open his mouth and tolerate the diet.



Figure 1: Aphthous ulcers on the lower lip while on the drug.



Figure 2: Lower lip after stopping the medicine.

Table 1: Naranjo Adverse drug reaction probability scale.

Sl. No.	Question	Score
1	Are there previous conclusive reports on this reaction?	+1
2	Did the adverse event appear after the suspected drug was administered?	+2
3	Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1
4	Did the adverse event reappear when the drug was re-administered?	0
5	Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1
6	Did the reaction reappear when a placebo was given?	0
7	Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	0
8	Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	0
9	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	0
10	Was the adverse event confirmed by any objective evidence?	+1
	Total Score	+4

According to the WHO Uppsala Monitoring Centre with a NARANJO score of “04”⁵ based on the calculation presented in Table 1, the adverse drug reaction can be classified as “possible”.

DISCUSSION

The findings in this case study can be regarded as rare side effects of ARB losartan. The patient’s subjective complaints were dysphagia, difficulty opening the mouth, heaviness in the tongue, slurred speech, and coughing followed by severe mouth ulcers (aphthous ulcers).⁶ No other suspects were thought to have contributed to the patient’s serious condition, except a recent adjustment to his anti-hypertensive drugs. Additionally, the effective rechallenge technique supports the negative impact. Pancytopenia with dimorphic anaemia may be related to complaints of generalized weakness. Angioedema, vasculitis, cutaneous lymphoid hyperplasia, and erythema multiforme are cutaneous responses associated with ARBs.⁷ There are reports of aphthous mouth ulcers brought on by ARBs such as telmisartan, candesartan, and irbesartan. The buildup of bradykinin, an inflammatory mediator and peptide that widens blood vessel, is directly linked to mouth ulcers.

According to FDA statistics, 0.25% of ARB users had trouble swallowing.⁸ The data suggests that losartan-induced aphthous ulcers are a rare occurrence.⁹

CONCLUSION

Oral toxicity is regarded as an unusual adverse effect of ARBs. Previous research, however, points to a link with oral ulcers. As a result, it is important to consider the possibility that ARBs and oral toxicity are related. Clinicians need to be cautious about the rare side effects of ARBs. To find the causative agent, an ADR assessment and its management should be completed right away. The ability to research and avoid major adverse drug reactions is expanded by the reporting of rare side effects.

All authors state that they had complete access to the study data that support the publication. All authors conceive the study and participated in its design and read and approved the final manuscript.

ACKNOWLEDGEMENT

We sincerely thank the Principal of Jawaharlal Nehru Medical College, Medical Superintendent of KLE Dr. Prabhakar Kore Charitable Hospital Belagavi, MD of KLEs Dr. Prabhakar Kore Hospital and Medical Research Centre Belagavi, Principal of KLE College of Pharmacy Belagavi, and Head General Medicine Department, KLEs Dr. Prabhakar Kore Hospital and Medical Research Centre Belagavi.

Funding

There was no particular funding allocated for the completion of the investigation.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

WHO: World Health Organization; **ADR:** Adverse Drug Reaction; **ARBs:** Angiotensin Receptor Blockers; **FDA:** Food and Drug Administration.

Ethical Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Written informed consent was obtained from a legally authorized representative of the patient for the publication of this case report and accompanying images.

REFERENCES

1. Aphthous Ulceration (Aphthae, Ulcers) | Derm Net. Available from: dermnetnz.org [cited 9/1/2023].
2. Plewa MC, Chatterjee K. Aphthous stomatitis. StatPearls Treasure Island. 2021.
3. Manunza F, Atzori. Letter to Editor Global dermatology irbesartan-induced aphthous stomatitis. 2015;2:62-3.
4. Balakumar P, Kavitha M, Nanditha S. Cardiovascular drugs-induced oral toxicities: A murky area to be revisited and illuminated. Pharmacol Res. 2015;102:81-9. doi: 10.1016/j.phrs.2015.09.007, PMID 26409645.
5. Zaki SA. Adverse drug reaction and causality assessment scales. Lung India. 2011;28(2):152-3. doi: 10.4103/0970-2113.80343, PMID 21712934.
6. Goffin E, Pochet JM, Lejuste P, De Plaen JF. Aphthous ulcers of the mouth associated with losartan. Clin Nephrol. 1998;50(3):197. PMID 9776426.
7. Madinier I, Berry N, Chichmanian RM. Les ulcérations orales d'origine médicamenteuse [Drug-induced oral ulcerations]. Ann Med Interne (Paris). 2000;151(4):248-54. PMID 10922951.
8. Losartan and mouth ulcers-a phase IV clinical study-From FDA report-ehealthme.com [cited Jan 11, 2022]. Available from: <https://www.ehealthme.com/ds/losartan/mouth-ulcers/>; 2022.
9. Will you have swallowing difficulty with losartan-From FDA reports-eHealthMe. 2018.