Scholar: Pilot and Validation Studies ISSN: 2689-7644
Volume 4 Issue 1 Pages: 6 – 7 DOI:10.32778/SPVS.71366.2023.34

Lisinopril dose associated bullous lesion formation

Authors: Meghan Callahan OMS-III[1], Kirandeep Sehmi MD[2], Lauren Fill DO[3], Robert W. Hostoffer DO[3]

Affiliations:
1) Lake Erie College of Osteopathic Medicine, Elmira, NY, 2) Michigan State University College of Osteopathic Medicine, East Lansing, Michigan, 3) University Hospitals Cleveland Medical Center, Cleveland, Ohio

Keywords: Lisinopril, ACE-inhibitor, bullous lesions

Article History: Date received: 05/08/2023 Date revised: 08/10/2023 Date accepted: 08/12/2023
Corresponding Author: Meghan Callahan **E-mail:** Mcallahan68657@med.lecom.edu

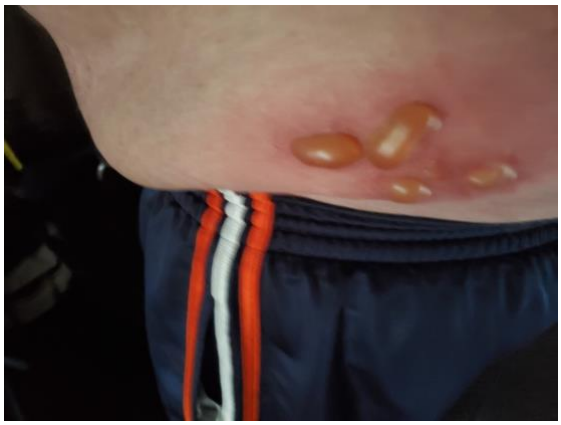
Introduction:

Lisinopril is a commonly used angiotensin-converting enzyme (ACE) inhibitor for patients with hypertension or congestive heart failure.[1] Common adverse reactions of this drug include bronchospasm, cough, and angioedema.[2,3] Clinical studies on lisinopril have shown that these adverse effects do not seem to be dose-related.[1,2] Bullae are circumscribed primary lesions containing serous fluids that are larger than 1 centimeter.[4] Drug-induced bullous eruptions have been previously documented with causal agents including methotrexate, penicillin, rifampicin, and clonidine.[5] Lisinopril-induced bullous pemphigoid (BP) has been reported in a female patient[6] and lisinopril-induced pemphigus foliaceus (PF) has been reported in two male patients.[7,8] The lesions from a histological sense resemble the typical pemphigus findings of suprabasal epidermal acantholysis, clefting and blister formation. The blister cavity may contain inflammatory cells including eosinophils and rounded acantholytic cells with intensely eosinophilic cytoplasm and a perinuclear halo. These correlations have been made through temporal relations of lisinopril use and skin biopsies of the eruptions that appeared within weeks of the start or dosage change of lisinopril. We report a unique case of a 65-year-old male with a dose-dependent lisinopril-induced bullae.

Case description:

A 65-year-old male presents to an outpatient allergy and immunology clinic with a blistering rash on his flank, belly button, and a cluster on the ankle that has been present since the end of May 2022 (Figure 1).

Figure 1: Photograph of tense blistering lesions



Photograph of reported case taken with consent.

The patient has no previous history of immunological deficiencies or recurrent infections. A complete radioallergosorbent test was performed which showed a complete lack of allergy to both stinging and venomous insects. No food testing was performed. A punch biopsy was performed on a new blister of the right upper leg. The pathology report revealed irregular acanthosis and spongiosis and areas of necrosis. The underlying dermis showed brisk perivascular and interstitial inflammatory infiltrates composed of lymphocytes and histiocytes, neutrophils and numerous eosinophils extending into the deep reticular dermis. At a deeper level, there were findings of a re-epithelializing blister, which contained sparse neutrophils and eosinophils. A PAS stain was negative for fungal organisms. The immunofluorescence was negative for C3, IgA, IgG, IgM and fibrinogen. Oral prednisone at a dosage of 40 mg per day with a wean of 10 days was prescribed which relieved the bullae, but it returned within five days of medication completion. His history is

significant for hypertension which was controlled by lisinopril for five years until a recent immediate dosage adjustment from 20mg to 40mg at the beginning of May 2022 to provide better control of his blood pressure, with no change to the other medications. There was no history of arthropod exposure, showing the only significant change in his social and medical history was the dosage change. The blood work including a complete blood count and erythrocyte sedimentation rate were normal except for a slight rise in the eosinophil count. The bullae began after 2 weeks of escalation of the lisinopril dosage. The patient was taken off lisinopril and placed on amlodipine and within days the bullae disappeared. This was the first time in over a month that the patient presented without new bullae and the healing of older ones. Topical creams and oral medication were not used or needed during the healing process.

Pemphigus is an autoimmune condition that causes blistering on the skin and in mucous membranes, with varying degrees of severity. Pemphigus can be triggered by a variety of factors including environmental, genetic, or a vaccination.[9] Pemphigus foliaceus is the least severe subtype, with patients presenting with painless sores on the scalp that spread throughout the body. Bullous Pemphigus is clinically characterized by diffuse, erythematous, pruritic lesions and biochemically with IgG disruption of hemidesmosomes.[6] Both conditions have been reported with an association to initiation of lisinopril or a dosage increase of the drug. The condition of these patients resolved when lisinopril was discontinued and topical steroid creams were used.[6]

Conclusion:

Our patient's presentation is unique, since it is not a known autoimmune condition, such as pemphigus, and did not respond to steroids, signifying it is solely a reaction to the increased lisinopril dosing. The biopsy was unrevealing for autoimmune disorders or arthropod involvement.
Lisinopril is a widely used drug to treat the common disorder of hypertension. We present the first case of an association with an increase in lisinopril dosage and a bullous reaction.

Author Contributions:
Meghan Callahan OMS-III, Kirandeep Sehmi MD, and Lauren Fill DO: Data analysis, literature search, preparation and clinical revision of the manuscript. Robert W. Hostoffer, DO: conception and design, acquisition of data, or analysis, interpretation of data, manuscript preparation and review.

Funding Sources: None.

Potential Conflicts of Interest Disclosures:
The authors disclose that there were no conflicts of interest or financial support in the development of this project. All data is authentic and accurate.

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