**Author Contributions:** Drs Hillhouse and Stapleton had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Hillhouse, Florence, Pagoto.

**Acquisition, analysis, or interpretation of data:** Hillhouse, Stapleton, Pagoto.

**Drafting of the manuscript:** Hillhouse, Stapleton.

**Critical revision of the manuscript for important intellectual content:** All authors.

**Statistical analysis:** Hillhouse, Stapleton.

**Obtained funding:** Hillhouse, Stapleton, Pagoto.

**Administrative, technical, or material support:** Hillhouse, Stapleton, Florence.

**Study supervision:** Hillhouse, Stapleton, Pagoto.

**Conflict of Interest Disclosures:** None reported.

**Funding/Support:** Drs Stapleton and Hillhouse reported receiving grants R03CA165801 and R01CA134891, respectively, from the National Cancer Institute. Dr Pagoto reported receiving grant U48DP001933 from the Centers for Disease Control and Prevention.

**Role of the Funder/Sponsor:** The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.


---

**OBSERVATION**

**Erythema in Skin Adjacent to Area of Long-term Brimonidine Treatment for Rosacea: A Novel Adverse Reaction**

We describe a case of compensatory vasodilation in the vasculature surrounding the site of long-term brimonidine use for the treatment of rosacea.

**Report of a Case** | A 57-year-old woman with a medical history of rosacea, anxiety, hyperlipidemia, and hypertension presented with persistent, patchy erythema on the lateral face and neck of several weeks' duration. Seven months before presentation, she had been prescribed brimonidine, 0.33%, topical gel for persistent facial erythema secondary to rosacea. She reported appropriate use of the medication, applying the prescribed amount only to affected areas on her central face. Physical examination revealed marked bright erythema diffusely covering areas of the lateral cheeks, neck, and upper chest (Figure, A). Interestingly, there was clear sparing of the sites of brimonidine application on the central face.

Review of systems revealed only that the eruption was associated with mild burning. Prior to presenting to our clinic, she saw several other dermatologists. Over the course of these visits, several laboratory studies were ordered, including a complete blood cell count with differential, a complete metabolic panel, a lipid panel, and measures of C1, total complement, antinuclear antibody (ANA), and tryptase, all of which yielded normal results. A cutaneous punch biopsy of the left neck was performed and revealed nonspecific findings of photodamaged skin with telangiectasias and scant perivascular lymphocytic inflammation with
no specific evidence of an autoimmune etiology. The patient was advised to discontinue using the brimonidine gel and to follow up in clinic in 1 week. At 1-week follow-up, her symptoms improved dramatically (Figure, B), leading us to believe that her initial reaction was secondary to long-term brimonidine use.

Discussion | Since its approval by the US Food and Drug Administration in 2013, topical brimonidine gel has offered effective therapy for certain patients with persistent facial erythema secondary to rosacea.1 Previous studies reveal that most patients tolerate this therapy quite well without any adverse reactions.2 However, there have been reports of cutaneous adverse reactions at the site of brimonidine application. These include flushing, worsening erythema, burning sensation, and contact dermatitis, most of which present immediately or early in the course of therapy.3 Herein, we describe a patient who had been using brimonidine for nearly 7 months before developing what we believe to be a novel adverse drug reaction.

Interestingly, our patient’s symptoms were in areas surrounding the site of brimonidine use, sparing the tissue in direct contact with the gel. Brimonidine is a relatively selective α2 adrenergic agonist. Topical application causes vasoconstriction of superficial vessels at the site of application, allowing for the reduction of erythema. We hypothesize that the reaction seen in our patient represents a compensatory vasodilation of vessels in the surrounding skin due to chronic vasoconstriction at the site of long-term brimonidine use. Findings from history, physical examination, laboratory testing, and histopathologic examination ruled out several other etiologies, including photosensitivity and autoimmune conditions. We therefore conclude that this is a probable adverse drug reaction to brimonidine.4 A logical treatment for this adverse effect is discontinuation of brimonidine application. Because this is a relatively new therapy, these mechanisms are not well established, and further investigation is warranted.

Ryan Gillihan, BS
Tony Nguyen, MD
Ryan Fischer, MD
Anand Rajpara, MD
Daniel Aires, MD

Author Affiliations: School of Medicine, University of Kansas Medical Center, Kansas City, Kansas (Gillihan); Division of Dermatology, University of Kansas Medical Center, Kansas City, Kansas (Nguyen, Fischer, Rajpara, Aires).

Corresponding Author: Daniel Aires, MD, Division of Dermatology, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160 (daires@kumc.edu).

Published Online: June 17, 2015. doi:10.1001/jamadermatol.2015.1252.

Conflict of Interest Disclosures: None reported.


Buruli Ulcer Successfully Treated With Negative-Pressure Wound Therapy

Buruli ulcer (BU) is a slowly progressive lesion with local necrosis caused by Mycobacterium ulcerans.1 It is mostly seen in tropical areas,2,3 and the lack of awareness of BU in nonen-