

Case Report: Allergic Contact Dermatitis to Topical Brimonidine Demonstrated With Patch Testing: Insights on Evaluation of Brimonidine Sensitization

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Figure 1. Diffuse edematous erythema with vesicles and bullae limited to the application zone of brimonidine tartrate (A) and after 5 days of systemic corticosteroids initiation and cessation of brimonidine (B).

Rosacea is classically characterised by persistent or transient erythema, telangiectasia, inflammatory papules, and pustules. It affects mainly the central region of the face and can be induced by multiple factors like heat and exercise. Brimonidine tartrate 0.33%, an α_2 -receptor agonist used to treat glaucoma, has been recently approved by the US Food and Drug Administration as first-line treatment of persistent erythema in rosacea. Allergic contact blepharitis caused by brimonidine eye drops has been described on numerous occasions in the past 10 years without an epicutaneous testing correlation to demonstrate the causality. Only recently, some authors have described allergic contact dermatitis (ACD) to brimonidine gel with inconsistent patch testing results.¹ We report the case of 1 patient with rosacea who developed ACD following treatment with brimonidine 0.33% with a positive patch test reaction associated with a photoexacerbation.

Case Report

A 59-year-old woman with rosacea presented with bouts of very severe facial dermatitis while using brimonidine tartrate

gel 0.33% (Onreltea). She developed an eczematous dermatitis in the treated area 24 hours after use, which worsened with each application and possibly with sunlight exposure (Figure 1).

Patch testing was performed with the North American Standard series (NAS-80), cosmetics, fragrances, and sunscreens series as well as with her personal products. Those included Onreltea gel (as is). Custom preparations of brimonidine 0.33%, 0.5%, 1%, 5%, and 10% in petrolatum were also tested. Photo patch testing (5.0 J/cm² ultraviolet A [UVA] exposure at 48 hours) was performed with the

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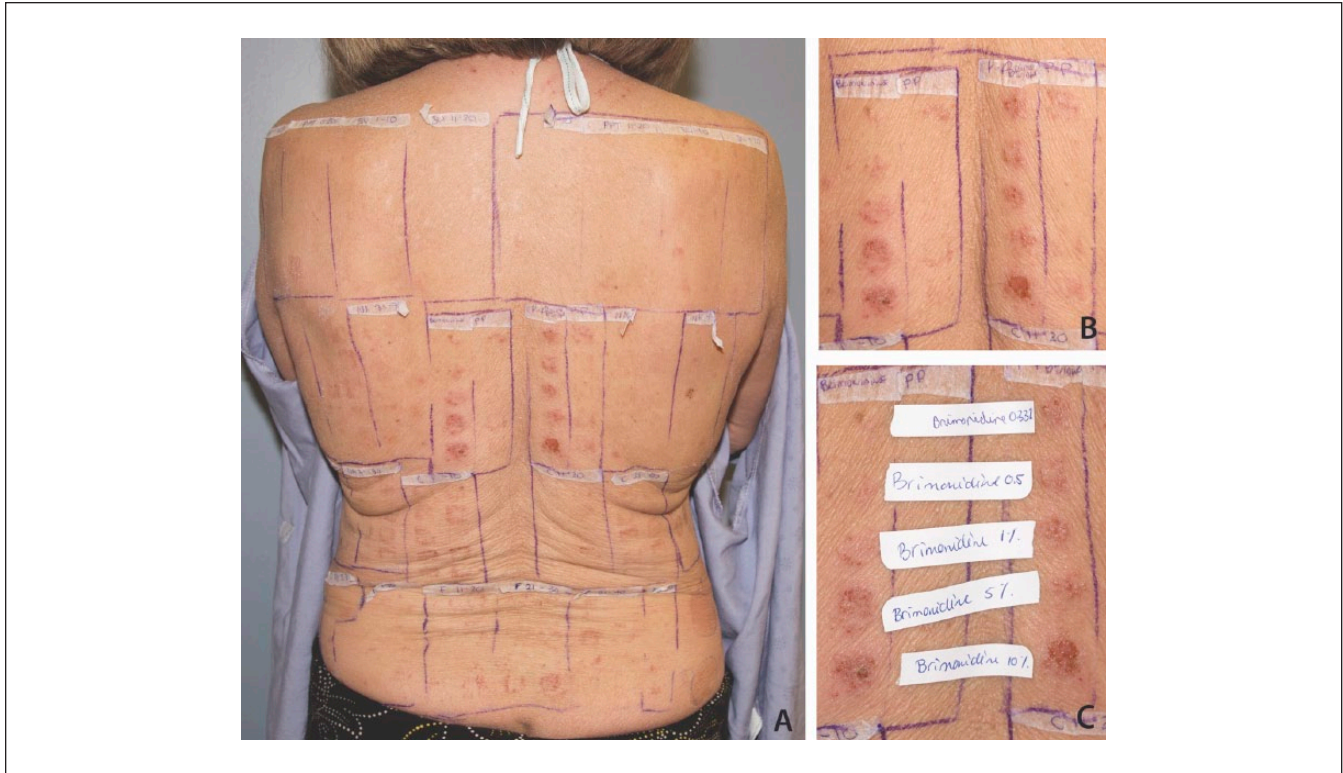


Figure 2. General view of patch tests results at 96 hours. (A) Comparative view of brimonidine dilutions and personal products with (right) and without (left) ultraviolet A exposition (B, C).

Table 1. Pertinent Patch Test Results at 48 and 96 Hours.

Product	48 Hours	48 Hours UV	96 Hours	96 Hours UV
Onreltea (as is)	–	±	2+	2+
Brimonidine 0.33%	–	–	±	2+
Brimonidine 0.5%	–	–	±	2+
Brimonidine 1%	–	–	1+	2+
Brimonidine 5%	±	–	2+	2+
Brimonidine 10%	1+	1+	2+	2+
Lauryl-glucoside	–		2+	
Methylisothiazolinone 0.02%	–		1+	
Decyl glucoside 5%	–	–	1+	±
Avene XeraCalmAD oil	1+		1+	

Abbreviation: UV, ultraviolet; –, No skin changes; ±, Faint erythema; 1+, Erythematous papules; 2+, Oedematous erythema and vesicles; 3+, Bullae and ulceration.

sunscreen series, the patient's own products, and the different dilutions of brimonidine.

The results demonstrated increasing reactions from brimonidine 0.33% to 10% and Onreltea gel (as is) (Figure 2). No reaction was elicited on the excipients of the product—namely, phenoxyethanol. Other positive reactions are summarized in Table 1. A surprising finding was that she had a clinically significant photoexacerbation of her reaction to brimonidine in a concentration-dependent manner. Controls were performed on 6 individuals with the brimonidine dilutions and Onreltea gel (as is), with and without ultraviolet (UV) exposure, and all results were negative.

Discussion

Even though many phase II and III trials sustained the efficacy and safety of topical brimonidine,¹ its use in rosacea was known to be a possible causal agent in ACD in approximately 1% of patients (product monograph). An open-label study for brimonidine tartrate (Mirvaso) in 345 patients for 12 months showed 2.2% of contact dermatitis (irritant or allergic not specified).²

Concurrently, ocular allergic reactions to brimonidine have been extensively described in the field of ophthalmology, albeit without patch testing, and was estimated to occur in 14% to 26%.³ Some authors recently described cases of ACD to topical brimonidine in the treatment of

rosacea, and only 2 found a positive patch test reaction and therefore could conclude to a proven ACD but with the product as is alone.^{4,5}

To our knowledge, this is the first case of positive patch test results to pure topical brimonidine. Our findings suggest that the optimal dilution for detecting brimonidine contact allergy is 1% petrolatum. Testing with commercial preparations of brimonidine (cutaneous and ophthalmic) could miss real allergy because of their lower concentration and different vehicle. It would also not differentiate between an allergy to brimonidine and an allergy to a non-medicinal ingredient. Given the high prevalence of sensitization to the ophthalmic brimonidine solution and as more patients use brimonidine gel to treat rosacea, brimonidine should be considered when investigating patients with eyelid and facial dermatitis.

Furthermore, phototoxicity had not been previously described in the literature with topical brimonidine.¹ Considering the fact that it is used mainly on the face, UV exposure may play an unrecognised part in the pathogenesis underlying brimonidine adverse reactions. Further photopatch testing with brimonidine would have to be performed to confirm this hypothesis.

In summary, this case highlights the possible role of photoexacerbation in the development of brimonidine allergy and demonstrates the optimal brimonidine concentration to be tested.

Declaration of Conflicting Interests

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Informed Consent

The patient provided signed consent for publication of the case report and images.

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