

CONTACT POINTS

Primum non nocere: The importance of evaluating the effect of treatment and considering side effects

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To diagnose a patient with facial erythema is challenging. The diagnoses are commonly made clinically and could be indistinguishable by their overlapping features.¹ Polysensitization to topical medications treating facial erythema has been rarely reported and might be overlooked.

CASE REPORT

A 62-year-old man without a history of atopy had been experiencing episodic facial erythema for 30 years. He had been diagnosed with seborrheic dermatitis and treated with topical corticosteroids, and he had been patch tested and told he had reacted to hydrocortisone in the 1980s. After discontinuation of the steroid cream, facial erythema remained uncontrolled. Rosacea was later diagnosed, and the patient was twice treated with tetracyclines. Topical 1% ivermectin cream and 0.33% brimonidine gel (Mirvaso) were prescribed.

In 2018, his facial erythema was worsening. Patch testing, photo patch, and photo testing were performed. The patient did not react to allergens in the baseline, cosmetics, or corticosteroids series, or to personal products. The photo tests revealed normal responses. Blood tests for anti-nuclear antibodies was negative. The patient resumed using both brimonidine gel and ivermectin cream and was also prescribed both Fucidin cream (fusidic acid) and Locoid cream (hydrocortisone-17-alfa-butyrate) when his symptoms increased. He gradually developed a severe

facial rash with a burning sensation, with fluctuating severity, which never completely healed. He had been told that his skin was sensitive and so only used the medications when he felt that he started to have symptoms.

Skin examination showed ill-defined scaly erythematous patches with serum oozing and yellowish crusts on the face (Figure 1). He denied using other medications or cosmetics. Skin biopsy demonstrated nonspecific findings. Once again, patch testing was done with baseline, corticosteroids series, Mirvaso gel, and brimonidine 0.5% pet. The patient reacted +++ to Mirvaso gel, and weakly (+) to budesonide 0.01% pet. Because there was no reaction to brimonidine 0.5% pet., further patch testing with two higher concentrations of brimonidine was performed, namely, 5% and 10% pet., which showed positive reactions to both on day 3. Repeated open application test was performed with 0.33% brimonidine gel (Mirvaso), which gave a positive reaction within 1 week after starting application. The diagnosis of allergic contact dermatitis (ACD) caused by hydrocortisone, budesonide, and brimonidine with underlying rosacea was made. At 6-month follow-up, the patient has been clear of quickly reappearing severe episodes of facial dermatitis. What remains is dermatitis clinically appearing like a less severe seborrheic dermatitis.

DISCUSSION

This case demonstrated the importance of patch testing with topical medications in patients with facial erythema. The patient was said to

Informed consent has been signed by the patient for publication.

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FIGURE 1 Rosacea with allergic contact dermatitis to brimonidine

have reacted to hydrocortisone already in the 1980s. This reaction was not found when he was first patch tested again more than 20 years later. After that, it was recommended that the patient also could use hydrocortisone, since it was found negative at patch testing. In 2019 the patient was found to be allergic to budesonide. There is a possibility of cross-reaction between the groups.² An anti-inflammatory effect of corticosteroids can also cause false-negative results, which makes a patch test diagnosis more challenging.² Therefore, the patient had been tested three times before an accurate diagnosis could be confirmed, and the episodes of facial erythema for certain be connected to the use of corticosteroid that the patient was known to react to. Retesting should be considered, and a late reading is essential for diagnosing ACD in response to corticosteroids. In this patient, an alternative corticosteroid cream from a different group was prescribed to avoid cross-reaction.

Treatment options for rosacea are based on phenotypic features, and brimonidine gel has been commonly prescribed due to the strong evidence for treating erythema.¹ Although there was a reported prevalence of contact dermatitis as an adverse reaction to brimonidine by clinical observation,³ there were only a few reports confirmed diagnosis by patch testing.⁴⁻⁷ The method for patch testing with brimonidine has not been validated. Brimonidine 0.33% might be too low a concentration to identify ACD.^{6,7} Consequently, establishing clinical relevance could be problematic because the patient needed to be tested with relatively high concentrations. Of interest, this patient reacted to Mirvaso cream "as is" stronger than to pure brimonidine in the serial dilutions. This might be explained by other ingredients in the product that could enhance the penetration. Moreover, other topical medications for rosacea, including ivermectin, could also induce skin irritation.¹ Correlation between clinical dermatitis and exposure is often difficult from the history of the patient. In patients with episodic aggravation, there is often a large amount of medicaments tried before referral, and the patient cannot remember what has been tried

and when. In such circumstances, a repeated open application test (ROAT) could explain the relevant reaction.

This report highlights the significance of multiple causes of facial erythema in individuals, which may change over time. Patients with sudden flares, and where treatments only seem to give worse symptoms, should be referred for patch testing, since a damaged skin barrier may bring about polysensitization to the treatment. Once contact allergies have been found, the patient's original dermatitis can be investigated correctly. Patch testing with higher concentrations of brimonidine and a ROAT could be helpful in suspected cases of ACD.

CONFLICT OF INTEREST

All authors have neither conflicts of interest nor financial support to declare.

AUTHOR CONTRIBUTIONS

Thanisorn Sukakul: Data curation; validation; visualization; writing-original draft; writing-review and editing. **Jakob Dahlin:** Data curation; formal analysis; investigation; resources; software; validation; writing-review and editing. **Cecilia Svedman:** Conceptualization; data curation; investigation; methodology; project administration; supervision; validation; writing-review and editing.

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