

Angioedema–Urticaria Due to Acitretin

Berna Solak, MD,* Nurcan Metin, MD, and Mustafa Teoman Erdem, MD

Acitretin is a synthetic oral retinoid that has been used for a number of dermatological diseases. Several side effects of acitretin have been reported such as teratogenicity, cheilitis, xerosis, dyslipidemia, and photosensitivity. Many drugs, mainly antibiotics and nonsteroidal anti-inflammatory drugs, can cause angioedema–urticaria. We present the case of angioedema–urticaria due to acitretin, confirmed by oral provocation test, in a 61-year-old man with psoriasis. To the best of our knowledge, only 1 case of angioedema due to oral acitretin has been reported in the literature so far. We report this case to draw attention that acitretin may cause angioedema–urticaria and to inform patients about this risk besides other side effects due to acitretin.

Keywords: angioedema, urticaria, acitretin

INTRODUCTION

We present angioedema–urticaria due to acitretin, confirmed by oral provocation test, in a patient with psoriasis. To the best of our knowledge, only 1 case of angioedema due to oral acitretin has been reported in the literature so far. Acitretin is a synthetic oral retinoid that has been used for a number of dermatological diseases. It has been reported that acitretin has several side effects such as teratogenicity, cheilitis, xerosis, dyslipidemia, and photosensitivity.¹ Angioedema and urticaria are among dermatological emergencies and may occur because of many drugs mostly antibiotics and nonsteroidal anti-inflammatory drugs.^{2,3} To the best of our knowledge, only 1 case has been reported with regard to acitretin as the cause for angioedema, and Cunha Filho et al reported 2 angioedema cases as a result of using retinoids. Of these, 1 occurred from acitretin and the other from isotretinoin.⁴

In addition, Saray et al⁵ have reported a case of angioedema and urticaria due to isotretinoin.

CASE

Our patient is a 61-year-old man who had had psoriasis for 30 years. He was given topical corticosteroid for the last month before he presented to our clinic, but there was no response. Therefore, we have started to treat with Narrowband UVB (Waldman UV 7002; GmbH & Co. KG, Germany, 3 d/wk) and oral acitretin [$0.5 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ (35 mg/d) Neotigason; Actavis, Istanbul, Turkey]. Three days after initiation of oral acitretin, swelling on his lips and urticaria on his trunk, legs, and arms appeared. We stopped acitretin and started IV steroid (methylprednisolone, 40 mg/d) and oral antihistaminic (levocetirizine, 5 mg/d) treatment. With this latter regimen, the lesions started to ameliorate. He had no history of any systemic disease or use of other drugs in the last month. The patient mentioned that he had never used acitretin or any other retinoic acid derivative. Total serum IgE was 259 IU/mL. The systemic investigation of the patient and routine laboratory tests were normal. Oral provocation test was planned because it is considered as a golden standard for many drugs.² One month later, after receiving the patient's consent, we performed oral provocation test with acitretin under favorable

Department of Dermatology, Faculty of Medicine, Sakarya University, Sakarya, Turkey.

The authors have no conflicts of interest to declare.

**Address for correspondence: Sakarya Universitesi, Tıp Fakültesi, Dermatoloji Ana Bilim Dalı, Sakarya 54000, Turkey. E-mail: drbernakilic@yahoo.com*

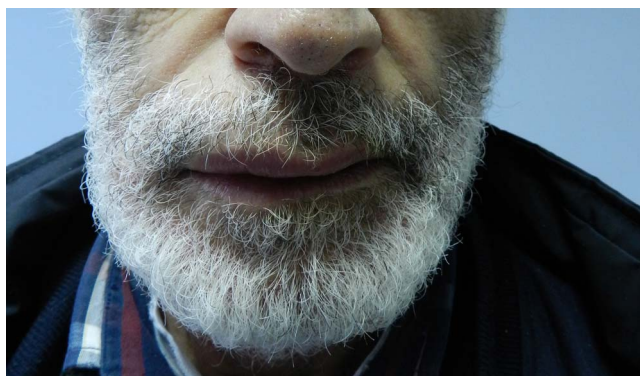


FIGURE 1. Swelling of the upper lip of the patient.

conditions. During the test, we gave the patient 10 mg acitretin capsule (almost one-third of therapeutic dosage). The day after we performed the test, swelling on his upper lips and urticaria on his trunk and arms reappeared (Figures 1, 2). Thus, we started IV steroid (methylprednisolone, 40 mg/d) for 2 days and oral antihistamin for a week. Meanwhile, the patient's psoriasis lesions were treated using only Narrowband UVB (cumulative UVB dosage: 50.67 J/cm²). Angioedema and urticaria were not present at the sixth month follow-up visit.

DISCUSSION

Drug-induced angioedema and urticaria can be developed based on either IgE-mediated immunological or non-immunological (pharmacologic) mechanisms.² In this case, angioedema and urticaria developed 3 days

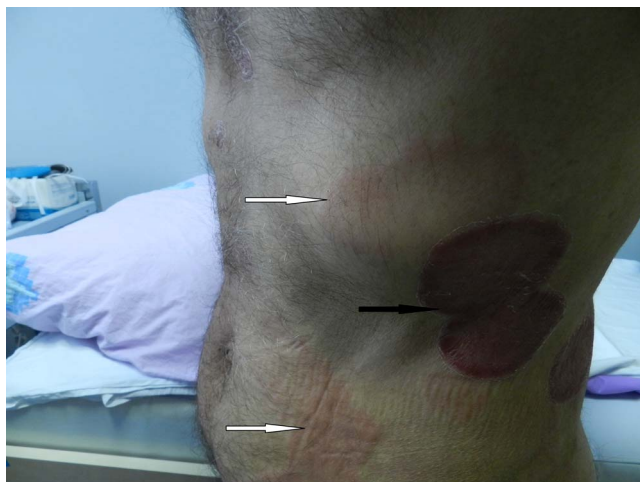


FIGURE 2. Urticaria plaques (white arrows) and psoriasis plaques (black arrow) on the trunk of the patient.

after the patient started to use the drug. The fact that angioedema and urticaria developed 3 days after our patient started to use the medicine shows a short time for IgE-mediated mechanism to form, and we thought this would be based on nonimmunological mechanism. Otherwise, if it was based on a nonimmunological mechanism, we would expect the reaction to occur after the first dosage. Research has shown that retinoic acid can activate cyclooxygenase enzyme through retinoic acid receptors and thus can increase prostaglandin E2 level. It is a fact that prostaglandin E2 inhibits degranulation of mast cells, which shows that retinoic acid would normally decrease the allergy. However, in our case, the angioedema and urticaria developed, which made us think that it is based on immunological mechanism rather than nonimmunological mechanism.^{2,6} Moreover, this claim can be supported with the high level of IgE in our patient. But, more research and case reports are needed to show the exact mechanism of angioedema and urticaria caused by acitretin.

Although it is a commonly used drug, there is only 1 case of angioedema due to acitretin reported in the literature. This might be due to 2 main reasons: physicians can disregard it, as they do not see the medicine as a suspicious agent or they might not report it although they detect acitretin as the cause of angioedema.

When searching the causes for angioedema and urticaria, we recommend considering acitretin among the suspicious agents. Moreover, it seems important to inform the patients using acitretin about the possibility of its side effects in terms of angioedema and urticaria.

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