

Acute Severe Urticaria From Minocycline

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PRACTICE POINTS

- Minocycline is a commonly prescribed long-term treatment for acne vulgaris.
- Minocycline-induced acute urticaria and anaphylaxis are rare adverse events.

To the Editor:

Minocycline is a commonly prescribed semisynthetic tetracycline derivative used for long-term treatment of acne vulgaris.¹ Given the continued popularity of minocycline and other tetracyclines in treating acne, more adverse side effects are being reported. We report a patient who experienced acute severe urticaria with angioedema from minocycline.

A 35-year-old woman with a history of acne vulgaris presented to the emergency department with urticaria and associated angioedema. Fifteen days after starting minocycline, she awoke with diffuse hives sparing only the abdomen that resolved with diphenhydramine. Later that day, she developed generalized pruritus, hives, and lip swelling. She received intravenous methylprednisolone, diphenhydramine, and famotidine in the emergency department. She returned to the emergency department the next day due to facial and lip swelling, diffuse urticaria that was most pronounced on the arms, and throat irritation. Intramuscular epinephrine was administered first followed by methylprednisolone, famotidine, and cetirizine. She was discharged and advised to start daily prednisone 50 mg and cetirizine 20 mg every evening.

She returned to the emergency department the following morning due to worsening generalized urticaria and angioedema of the lips. She denied any associated

respiratory, joint, or gastrointestinal tract symptoms. She had several urticarial plaques on the scalp, face, and body (Figure), only sparing the abdomen. Her hives were erythematous, raised, pruritic, and blanching. There was no residual purpura, ecchymosis, or hyperpigmentation associated with the urticaria, and each lesion was present for less than 24 hours. There was no swelling on examination. Additionally, she was afebrile. The C4 level was 18 mg/dL (reference range, 15–45 mg/dL). She did not develop eosinophilia (absolute eosinophil count, 0/ μ L [reference range, 50–500/ μ L]), lymphocytosis (absolute lymphocyte count, 1300/ μ L [reference range, 1000–4800/ μ L]), or abnormal liver or renal function. She was hospitalized for 3 days with severe urticaria and required 7 days of



Urticarial plaques on the back 3 days after the onset of symptoms and 15 days after initiating minocycline.

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prednisone 40 to 50 mg, fexofenadine 360 mg, and cetirizine 20 mg. A viral infection was considered as a possible etiology; however, she had no supporting signs or symptoms of an upper respiratory illness or other viral illness.

The patient's minocycline use was considered the most likely etiology, as an oral contraceptive was the only other medication. She was labelled allergic to minocycline and discharged with intramuscular epinephrine. She was evaluated in the outpatient allergy immunology clinic 9 days later, and all her symptoms had resolved. Due to the severity of our patient's reaction and the possibility of further severe reactions, an oral challenge was not carried out. Our patient was not interested in pursuing any further minocycline or other tetracycline-based therapy for her acne. She also was not interested in pursuing any minocycline skin-prick testing or oral challenge. One limitation to this case is our patient declining a confirmatory drug challenge; however, given the severity of the symptoms, the physicians involved agreed the patient's safety outweighed the benefits of confirmatory testing.

A PubMed search of articles indexed for MEDLINE and a Google Scholar search using the terms *minocycline*, *drug hypersensitivity*, *urticaria*, *anaphylaxis*, *minocycline allergy*, and *angioedema* yielded only 16 articles and correspondences. Reported adverse effects of minocycline included drug-induced lupus erythematosus, vasculitis, nausea, photosensitivity, and DRESS-like (drug reaction with eosinophilia and systemic symptoms syndrome) conditions. Three case reports of anaphylaxis/anaphylactoid reactions have been published,²⁻⁴ but cases of urticaria attributable to minocycline appear to be

exceedingly rare.^{2,3} Reports of serum sickness in patients aged 15 to 62 years were rare. Women were noted to experience a higher frequency of adverse effects compared to men.⁵ Symptoms typically presented 3 to 28 days after initiation of minocycline. Data currently suggest that the pathogenesis of hypersensitivity reactions to minocycline remains unknown⁶; however, one hypothesis is that minocycline or its metabolites act as a superantigen, resulting in lymphocyte overactivation and massive cytokine release.⁷

Minocycline generally is well tolerated by patients. Physicians should be aware that minocycline is a possible causative agent of allergic drug reactions. Our patient's presentation of severe acute urticaria with angioedema of the face and lips is a rarity.

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