CASE REPORT

# A serum sickness-like reaction to a commonly used acne drug

Patients with acne often take oral antibiotics to control the condition. This 39-year-old patient experienced a rare, serious adverse effect that resolved only after hospitalization.

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## CASE

A dermatologist prescribed minocycline for a 39-year-old female with acne to help her better control her persistent problems with the condition. The patient began taking the medication on the day it was prescribed, and approximately 13 days later, she awoke with swelling and hives on her thighs. She called her pharmacist, who instructed her to take diphenhydramine. She took a diphenhydramine tablet but also continued to take minocycline. She did not notice any improvement of her symptoms, and by the next morning, the hives had spread to cover the rest of her legs, as well as to her chest, buttocks, and back (see Figure 1).

The patient then went to the emergency department (ED), where she was found to have a temperature of 99.7ºF. All other vital signs were within normal range. Aside from the skin findings, the results of a physical examination were essentially unremarkable. She was given epinephrine, 0.3 cc SC, hydroxyzine, 50 mg IM, and prednisone, 60 mg orally. Her symptoms began to improve, and she was discharged with hydroxyzine, 25 mg (one tablet by mouth every 8 hours) and a Medrol DOSEPAK (methylprednisolone).

The following morning, 15 days after starting minocycline, she awoke with shortness of breath; swelling of her face, lips, ears, and tongue; and hives. She returned to the ED, where she was found to have a temperature of 100ºF and tachycardia (heart rate of 145 beats per minute). Other vital signs were within normal limits. She received two injections of epinephrine, 0.4 cc SC, diphenhydramine, 50 mg IV, famotidine, 20 mg IV, and Solu-Medrol (methylprednisolone), 250 mg IV. After some improvement was noted, she was discharged with instructions to follow up with her primary care provider the next day. At this point, the patient decided to discontinue the minocycline.

She saw her primary care physician the following day (16 days after starting the minocycline) with symptoms that continued to worsen and was given triamcinolone, 60 mg IM, and a prescription for a prednisone taper (40 mg for 2 days, then 30 mg for 2 days, then 20 mg for 2 days, then 10 mg for 2 days). She was instructed to continue taking either hydroxyzine or diphenhydramine and to discontinue taking methylprednisolone.

She returned to her primary care physician the following day with still worsening symptoms. She had a temperature of 100.6ºF with increased swelling of the lips and tongue. She also had severe heartburn and abdominal pain, which had developed over the progression of this drug reaction. At this time, she was admitted to the hospital. At the time of admission, she had a temperature of 100.6ºF (all other vital signs were within normal range). Her WBC count was slightly elevated at 12,400/µL, and a urinalysis revealed hematuria (no growth on culture).

IV corticosteroids were started, and the patient did not begin to improve until 3 days after admission (1 week after initial symptoms developed). She was discharged from the hospital after 4 days of inpatient care on the following regimen: a prednisone taper (60 mg for 2 days, then 40 mg for 5 days, then 20 mg for 7 days), hydroxyzine, 25 to 50 mg every 4 to 6 hours for itching, temazepam, 30 mg at bedtime, and alprazolam, 0.5 mg 3 times daily as needed. She was seen in our clinic that same day, and her discharge medications were continued. An OTC $H_2$-receptor antagonist was added for her severe "esophageal burning." An attempt was made to order a CH50 assay because complement levels (C3 and C4) can provide an objective measure-

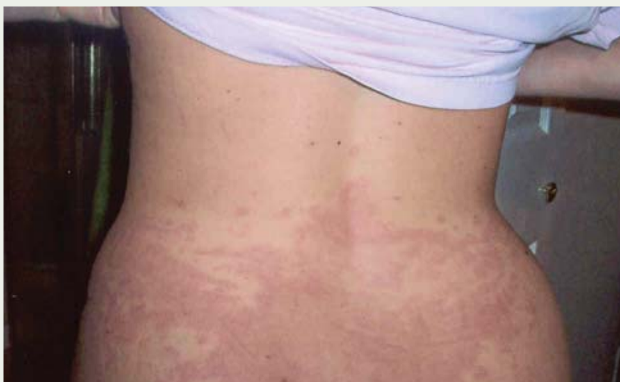

**FIGURE 1.** Hives in a patient taking minocycline

ment for serum sickness, but the patient's blood had already been discarded by the hospital.

The patient was contacted 1 week after being seen in our office. She had improved significantly since discharge. She still noted severe heartburn, but this had improved somewhat with ranitidine and antacids. She was seen again in the office the following week, and with the exception of mild heartburn, her symptoms had almost completely resolved.

## DISCUSSION

**Serum sickness** is a hypersensitivity reaction that occurs in response to the presence of certain antigens, most commonly medications.[1,2] Symptoms usually manifest within 6 to 21 days of exposure and include fever (10%-20% of patients), arthralgias (10%-50%), lymphadenopathy (10%-20%), and skin eruptions (95%). Patients may also experience joint and muscle aches, chest pain, and difficulty breathing. Laboratory studies may show leukocytosis, a slightly elevated ESR, and proteinuria or hematuria.[2] Treatment includes withdrawal of the inciting agent (if it can be identified) and symptomatic treatment with antihistamines, corticosteroids, and/or antipyretics.[2] Hospitalization may be necessary for severe cases or in cases where there is no identifiable cause. If the triggering agent is identified, future avoidance of it is mandatory because recurrence of serum sickness can be more rapid and severe with subsequent exposure.[2]

The earliest report of a serum sickness-like reaction associated with minocycline was by Puyana and colleagues in 1990.[3] That case occurred in a 19-year-old male who presented with fever, urticaria, lymphadenopathy, and joint symptoms, and other potential causes for his condition were excluded. In 1996, five additional cases were reported by Harel and colleagues.[4] These cases occurred in adolescents who had taken minocycline for 10 to 30 days, and symptoms included rash and arthralgias/arthritis, which resolved gradually after the medication was stopped. A retrospective study by Knowles and colleagues uncovered six patients with serum sickness-like reactions to minocycline.[5] The study also found that these reactions to minocycline often develop more quickly than hypersensitivity syndrome reactions (in 15.6 days vs 23.7 days).[5] Hypersensitivity syndrome reactions include internal organ involvement as well as fever and rash.[5]

**Conclusion** Based on this review of the literature, serum sickness-like reactions to minocycline appear to be extremely rare. However, it is possible that the majority of these reactions are unrecognized and hence not reported. Dermatologists and other clinicians seeing patients with severe or persistent acne that has been unresponsive to other therapies frequently prescribe minocycline, a tetracycline derivative. All clinicians should be aware of the possibility of a reaction when prescribing minocycline, especially when using the medication for an extended period. Generally, the systemic antibiotics used for acne have an excellent safety profile, but adverse effects have been reported with their use. The most common adverse effects associated with minocycline are dizziness and nausea; however, hypopigmentation of various tissues, autoimmune disorders, and serum sickness-like reactions have been reported in a few patients. The signs and symptoms of life-threatening events such as serum sickness must be recognized quickly, so that the inciting agent can be discontinued and proper care and management can be initiated. JAAPA

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### DRUGS MENTIONED

Alprazolam (Niravam, Xanax)
Diphenhydramine
Epinephrine
Famotidine (Fluxid, Pepcid)
Hydroxyzine (Vistaril)
Methylprednisolone, oral (Medrol DOSEPAK)
Methylprednisolone, for injection (Solu-Medrol)
Minocycline
Prednisone
Ranitidine (Zantac)
Temazepam (Restoril)
Triamcinolone

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3. Puyana J, Urena V, Quirce S, et al. Serum sickness-like syndrome associated with minocycline therapy. *Allergy.* 1990;45:313-315.
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### TEACHING POINTS

- Serum sickness is a hypersensitivity reaction that occurs in response to the presence of certain antigens, most commonly medications.
- Symptoms usually manifest within 6 to 21 days of exposure and include fever, arthralgias, lymphadenopathy, and skin eruptions. Patients may also experience joint and muscle aches, chest pain, and difficulty breathing. Laboratory studies may show leukocytosis, a slightly elevated ESR, and proteinuria or hematuria.
- Treatment includes withdrawal of the inciting agent and symptomatic treatment with antihistamines, corticosteroids, and/or antipyretics. Hospitalization may be necessary for severe cases or in cases where there is no identifiable cause.
- Life-threatening events such as serum sickness must be recognized quickly, so that the inciting agent can be discontinued and proper care and management can be initiated.

### COMPETENCIES

●●●●● Medical knowledge
●● Interpersonal & communication skills
●● Patient care
● Professionalism
● Practice-based learning and improvement
● Systems-based practice