



Delayed-onset cold anaphylaxis after hymenoptera sting

Cold contact urticaria (CCU) is characterized by urticarial wheals and/or angioedema typically appearing in the exposed areas within minutes of contact with cold air, liquids, or objects. Serious anaphylactic reactions may occur during aquatic activities.^{1–4} Most cases of CCU are primary, but secondary CCU has been reported.^{5–8} We describe a patient who acquired CCU 12 days after a wasp sting.

A previously well, 68-year-old woman who was an avid swimmer experienced a local reaction to a wasp sting. She was stung on her right wrist and developed a local swelling that extended to the midupper arm. Twelve days later, she developed pruritus of her palms and soles and urticaria on her extremities after swimming for a few minutes in an outdoor swimming pool. Before this sting, the patient had no CCU symptoms and became symptomatic on the first swim she took. On the second swim, she developed generalized pruritus within seconds of entering the water. She exited the pool having developed generalized urticaria and immediately experienced lightheadedness, palpitations, vomiting, and diarrhea, with no oropharyngeal involvement. After taking 50 mg of diphenhydramine, she fell asleep, and 2 hours later her symptoms resolved. She avoided swimming thereafter but continued to develop urticaria after contact with cold objects. Her history was remarkable for previous large local reactions to stings. The patient was taking no medications and had no family history of CCU. Her phys-

ical examination findings were unremarkable. A 5-minute cold stimulation test (CST) on the volar forearm measured at 10 minutes after removal of a frozen vial demonstrated a wheal-and-flare response, with the largest diameters of 22 mm for the wheal and 40 mm for the flare. The results of sequential intradermal tests to venom extracts (Hollister Stier, Montreal, Quebec, Canada) were positive for honey bee (wheal of 8 mm and flare of 12 mm) and wasp (wheal of 10 mm and flare of 25 mm) at a concentration of 0.1 $\mu\text{g/mL}$, white faced hornet (wheal of 12 mm and flare of 35 mm), yellow hornet (wheal of 14 mm and flare of 40 mm), and yellow jacket (wheal of 12 mm and flare of 30 mm) at a concentration of 1.0 $\mu\text{g/mL}$. The results of laboratory investigations, including complete blood cell count with differential, erythrocyte sedimentation rate, C-reactive protein, hepatitis B and C serologic tests, anti-streptolysin O titer, antinuclear antibody, rheumatoid factor, complement levels, cryoglobulin, cold agglutinin, serum protein electrophoresis, quantitative immunoglobulins, peripheral blood flow cytometry, thyroid-stimulating hormone, and thyroid autoantibodies, were either within normal limits or negative. The patient was advised to avoid cold exposure and aquatic activities. She was prescribed cetirizine, 10 mg daily, for prophylaxis of CCU symptoms and supplied with epinephrine autoinjectors. She was offered venom desensitization therapy, which she declined. During the subsequent 12 months, she remained asymptomatic and gradually resumed

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Fig. 1. Yearly ice cube test results of wheal-and-flare reaction after application of a frozen water-filled vial for 5 minutes and traced at 10 minutes after removal (inner circle indicates the wheal; outer circle indicates the flare). The picture demonstrates the ice cube test procedure on October 5, 2010.

swimming at water temperatures of 20°C to 22°C. No interim stings occurred. A subsequent 5-minute CST while the patient was not taking antihistamines revealed a decreased response (wheal of 22 mm and flare of 27 mm), but she still experienced pruritus when handling cold objects. At 24 months, she was able to swim at water temperatures of 17°C to 18°C. Two months later she acquired another sting and within 2 weeks developed systemic urticaria when swimming at water temperatures of 17°C to 18°C. A subsequent 5-minute CST, 6 weeks after the sting, revealed a worsened response (wheal of 33 mm and flare of 52 mm) (Fig 1).

Our case report demonstrates a 68-year-old woman who acquired CCU 12 days after a wasp sting, which contrasts with the previously reported onset of CCU at 24 to 48 hours after sting.^{5,6} Like other reports, the patient had a history of large local reactions to stings. Contrasting published cases that measured venom specific IgE, we elected intradermal testing to venom extracts since it is a more sensitive test and is used to guide venom desensitization, although our patient did not ultimately pursue it.⁷ However, the role of venom desensitization on the natural course of sting-induced CCU remains unknown. Anfonso-Capra et al⁸ published the case of a 49-year-old woman with sting allergy who developed CCU after 2 months of rush desensitization with yellow jacket. Her CCU symptoms resolved after the treatment was ceased.

Our case is unique since the patient's presentation of CCU quickly evolved into anaphylaxis compared to solitary cutaneous symptoms reported earlier. Moreover, her CST result remained positive at 12 months, although the result was of a smaller size, and she was able to tolerate colder water temperatures. These results contrast the findings of a negative CST result and lack of CCU symptoms at 12 months after sting noted in literature.^{5,6} Hogendijk and Hauser⁵ published a case of recurrent CCU symptoms occurring 3 months after each wasp sting. Similarly, our patient experienced worsened CCU symptoms after the second sting, although much earlier, at 2 weeks. This finding was confirmed by

worsened CST wheal-and-flare response, which was not previously reported.

In conclusion, this case confirms the reported causal association between Hymenoptera stings and development of CCU. In addition, it demonstrates that the onset of CCU can be delayed by almost 2 weeks after the culprit sting and may worsen with further stings.

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