

Uncommon urticaria

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INTRODUCTION

A 16-year-old girl was evaluated for an episode, which occurred while swimming in the sea, of widespread urticaria, weakness and pharyngeal constriction, tachycardia, paleness and collapse, which resolved with the administration of an oral antihistamine (epinephrine



Figure 1 Our patient's cold stimulation test, in which wheals appeared after applying ice to her forearm for 3 and 5 minutes.

autoinjector was not available). Over the past year, she had also experienced recurring episodes of itchy wheals on her fingertips and hands after taking food from the refrigerator or washing salad with cold water, and a single episode of diffuse urticaria after another dive into the sea, and she reported an episodic sensation of pharyngeal constriction while eating ice cream. Physical examination was unremarkable. A skin test with ice application was performed ([figure 1](#)).

TEST YOUR KNOWLEDGE

1. What is the most likely diagnosis based on this clinical presentation and skin test?
 - A. Cryoglobulinemic vasculitis
 - B. Cold typical urticaria
 - C. Aquagenic urticaria
 - D. Cold atypical urticaria
2. What is the mainstay of management?
 - A. Oral antihistamine
 - B. Epinephrine autoinjector
 - C. Omalizumab
 - D. All answers are correct

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ANSWERS TO THE QUESTIONS

Answer for question 1

The diagnosis is cold typical urticaria, a form of chronic inducible urticaria characterised by the development of wheals, angioedema or systemic symptoms in response to cold exposure.¹ The aetiopathogenesis is not clear; however, the most prevalent hypothesis is that immunoglobulins (IgM or IgG) anti-IgE, stimulated by cold, cross-react with the IgE attached to the mast cells inducing their degranulation.² Usually, wheals resolve within 1 hour and even if oropharyngeal angioedema and generalised reactions (up to anaphylactic shock) are not common, they can occur.^{3,4}

Cold urticaria is a chronic condition that resolves over time and has an average duration of 6 years, but cases of over 20 years have also been reported.⁵

The cold stimulation test is diagnostic and prognostic because if wheals appear within 3 min, a significant risk of severe reactions is reported.² This test should be performed with ice in a thin plastic bag to avoid cold damage to skin and prevent water contact with skin to avoid confusion with aquagenic urticaria.⁶ The temperature at which wheals appear is also a prognostic factor: the higher the temperature at which lesions appear, the higher the risk of severe disease.^{5,7}

Typical cold urticaria should be distinguished from the atypical form by the weal formation area. In the atypical form, wheals appear in different areas from the one stimulated by cold, and the cold stimulation test is negative. Atypical cold urticaria seems to be related to the decrease of general body temperature and not direct cold stimulus.

In aquagenic urticaria, lesions appear after contact with water, regardless of its temperature, and if correctly done (with ice in a plastic bag) the cold stimulation test is negative.

Cryoglobulinemic vasculitis presents in most cases with purpuric lesions and ulcers and only very rarely with only wheals. A blood test for circulating cryoglobulins and a skin histology will confirm the diagnosis.

Answer for question 2

The prescription of an epinephrine autoinjector and an anaphylaxis management plan is highly recommended, as well as avoidance of sudden exposure to cold, as both environmental cold and cold food should be considered possible triggers.

The most effective treatment is oral antihistamines, which seems to be successful if used for both

prevention and treatment of symptoms.⁸ High-dose antihistamine seems more effective than standard dose.⁶ Second-generation H1 antihistamines (eg, cetirizine, loratadine) are preferred and can be administered for long periods. In patients unresponsive to antihistamine treatment, omalizumab (anti-IgE monoclonal antibody) has shown to be an effective treatment option in reducing attack severity and induces changes in critical temperature thresholds required to induce symptoms.^{5,6,9} Cold desensitisation therapy, by continuous daily exposure to cold (after a short hospitalisation) has also been reported.¹⁰

Epinephrine autoinjector administration remains the first-choice treatment option for severe acute reactions with systemic involvement.

Patient's outcome

One year after the evaluation, the patient still had a poor quality of life, despite daily high-dose oral antihistamine assumption. She avoided eating ice cream and diving in the sea or pool (symptoms occurred also in a heated swimming pool), and she had to give up synchronised swimming, the sport that she had always done and that fascinated her. For these reasons, omalizumab treatment has been proposed, and the patient is considering this option.

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