

Idiopathic Cold Urticaria and Anaphylaxis

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Abstract: Cold urticaria (CU) is a subtype of physical urticaria characterized by the development of urticaria and angioedema after cold exposure. Symptoms typically occur minutes after skin exposure to cold air, liquids, and objects. Most common method to confirm the diagnosis of CU is through ice cube challenge test, but 20% of patients with CU have negative ice cube challenge test results. The greatest risk with this kind of urticaria is the development of systemic reaction resulting in a hemodynamic collapse during generalized cold exposure. We report a case of a patient who developed CU and anaphylaxis during swimming and diving in the sea.

Key Words: cold urticaria, anaphylaxis, child, ice cube test, idiopathic (*Pediatr Emer Care* 2014;30: 38–39)

CASE

A 13-year-old girl was admitted to our hospital with history of multiple episodes of generalized urticaria while swimming in the sea. On the last episode, she experienced the feeling of fainting and dizziness after 10 minutes of diving into the Aegean Sea in June. She was immediately removed from the water, and she regained consciousness. She did not have any symptoms in warm water, and probably, because the patient is living in a warm climate region, she had no similar reactions during the winter months. There was no family history of cold urticaria. Her physical examination result was normal. An ice cube challenge test was performed, and it resulted to a wheal within 10 minutes (Fig. 1). Her laboratory test results, such as complete blood cell count, erythrocyte sedimentation rate, renal and liver function tests, thyroid hormones, C3, C4, and rheumatoid factor, were normal; laboratory test results for cryoglobulins, serology for viral hepatitis, infectious mononucleosis, toxoplasmosis, *Helicobacter pylori* infection, and stool analyses for parasites were negative except for antinuclear antibody (ANA) titer. Her ANA titer was found 1/320 positive. She had no clinical symptoms and physical examination finding for rheumatologic disease. Because ANA positivities are not important without clinical findings, this result was considered as irrelevant. Management of her condition involved avoidance of swimming in cold water and carriage of an adrenaline auto-injector.

Cold urticaria is an uncommon form of physical urticaria that is mostly idiopathic.¹ It can be classified into familial and acquired cases further divided into primary and secondary causes.² Chronic urticaria may be secondary to the following conditions: infections (such as hepatitis), drug use, cold agglutinins, vasculitis, and malignancy.¹ Although such association is rare, and laboratory workup is not generally recommended, we

did a basic workup to rule out the previously mentioned conditions because the patient had multiple episodes of urticaria and finally anaphylaxis.

The prevalence of CU is not well defined, and incidence of CU has been estimated to be 0.05%.³ Besides, within the physical urticaria entities, the frequency of CU varies between 5.2% and 33.8% depending on different studies and the geographical regions.⁴ Most studies indicate that CU affects individuals of both sexes with equal incidence.^{2,5}

The most common method to confirm the diagnosis of CU is through ice cube test, which we used in our patient. An ice cube in a plastic bag is applied to the subject's forearm for 5 minutes, and then, the skin is allowed to rewarm back to normal skin temperature for 10 minutes. The test is interpreted as positive when a wheal appears over the application site during rewarming. If the test is negative at 5 minutes, the cold stimulus is applied to the other forearm for 10 minutes.⁵ Our patient's ice cube test result was negative when the cold stimulus was applied for 5 minutes and became positive after the application period was prolonged for 10 minutes on the other forearm.

The main duration of illness is 4.8 to 9.3 years,² but a study with a long-term follow-up states that the disease resolved in 11% of patients within 5 years and 26% within 10 years, indicating that CU is a chronic, persistent condition.⁶ In a series of 30 children with CU, it is reported that the mean age of onset was 7 years, pointing out that the disease is important for pediatricians because they should diagnose CU mostly.

The severity of cold urticaria was defined by Wanderer et al.^{2,7} According to this classification, the clinical patterns of CU reflecting the symptom severity were defined as follows: (a) localized urticaria and/or angioedema, (b) systemic reactions characterized by 1 or more episodes of generalized urticaria or angioedema without hypotensive symptoms, and (c) severe systemic reactions with 1 or more episodes of generalized urticaria or angioedema associated with hypotension (dizziness, fainting, disorientation, shock). Although CU is rare, it is a potentially life-threatening condition.⁸ Extensive cold contact may result in systemic reactions, ranging from generalized urticaria to anaphylaxis with symptoms involving the respiratory, gastrointestinal, and cardiovascular systems particularly during aquatic activities.⁷ In a series of 30 children with cold urticaria, one third of the patients had a history of cold-induced anaphylaxis.¹ In this study, cardiovascular symptoms were the most frequently seen followed by respiratory symptoms. The primary determining factors for systemic reactions seem to be the surface area of the skin exposed, temperature, and duration of exposure, which might explain why aquatic activity is the most common trigger. Deaths may occur directly from anaphylactic reaction or by drowning when swimming in cold water. So it is important to identify patients with cold urticaria, counsel them or their parents, and provide them an adrenaline auto-injector, especially in countries where swimming period covers almost half of the year because of unique climate conditions.¹

The management of CU is generally frustrating. Treatment focuses on prevention of episodes (water temperature preferably >25°C), use of prophylactic antihistamines, and carriage of

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Disclosure: The authors declare no conflict of interest.

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ISSN: 0749-5161



FIGURE 1. Positive ice cube test result of the patient.

adrenaline auto-injector.⁵ So it is important to inform the patients about avoidance of cold stimuli. This is the simplest and most effective way to avoid serious episodes. Antihistamines that are known to be more potent or have broader action (eg, cyproheptadine, doxepin, or ketotifen) are the most effective in preventing episodes; however, all of them have significant adverse effects, such as sedation and weight gain due to increased appetite. A modest response also occurs from second generation nonsedating antihistamines, but its effect in preventing systemic reactions is unclear. Leukotriene receptor antagonists or steroids generally have not been shown to be effective.¹

In conclusion, cold urticaria is an uncommon form of physical urticaria that can cause life-threatening reactions. We

presented this case to draw attention to these systemic reactions and prevention strategies of cold urticaria.

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