

CASE REPORT

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Cold Urticaria and Anaphylaxis Due to Ice Cube Challenge Test

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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 anything cold like air, liquid or an object. Ice cube challenge test is commonly used method to confirm the diagnosis of CU. The major complication of CU is anaphylaxis. In all CU cases, even in testing, it is important that anaphylaxis should be kept in mind, and special precautions should be taken. We wanted to report as the first known case of anaphylaxis which is occurred in during the ice cube challenge test in the published literature.

Keywords: Anaphylaxis; angioedema; urticaria

Cold urticarial (CU) is a common type of physical urticaria that is characterized by rashes and swelling, which are triggered upon the release of histamine and other pro-inflammatory mediators from mast cells after skin exposure to cold (cold air, objects, liquids and swimming in the sea or pool).¹ Symptoms generally occur within a few minutes following the exposure and are limited to the affected skin area. Extensive or prolonged exposure may lead to systemic reactions.² The pathophysiology of CU has not been fully explained yet, but immunoglobulin E (IgE) cause of-mediated mast cell activation possibility is considered. In CU; histamine, leukotrienes and other proinflammatory factors, are thought to occur as a result of the release of mediators from mast cells.³ There are 2 main types of CU; familial and acquired, can be viewed in the title. Acquired CU is known as primary and secondary urticaria.¹ While primary acquired CU is idiopathic;

secondary reasons are insect bites, food allergies, drug use and underlying chronic diseases were accused for CU. There are also some subtypes such as localized CU, delayed CU and reflex CU.⁴

Ice cube challenge test is a commonly utilized confirmatory method for the diagnosis of CU. However, this approach is associated with negative result in 20% of CU patients.² Briefly, development of a local itchy rash with a palpable swelling with clear boundaries at the site of ice exposure (10 min) on the forearm is considered to signify a positive test result.⁴ A major complication of CU involves a systemic reaction resulting in hemodynamic collapse after generalized cold exposure.²

CASE REPORT

A 53-year-old housewife was admitted with the complaint of fainting after the exposure to cold water. She

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reported episodes of faintness when swimming in cold ambient air and water temperatures in their summer house during the past 5 year period. Furthermore, these episodes were also associated with the development of shortness of breath and itchy rashes afterwards. In her first episode, she sought for medical assistance in an emergency room where she received injections of pheniramine maleate and dexamethasone. Contact with poisonous fish or sea algae was proposed as a potential explanation of her symptoms.

Thereafter, the patient started to have injections of combined pheniramine maleate and dexamethasone preparations before having a sea bath which showed significant symptomatic benefit. Also, she avoided contact with water in cold weather as well as limiting the duration of swimming. However, in the past 4 month period, she started to have symptoms such as faintness, respiratory difficulty, low blood pressure, and feeling of compression in the neck after having shower with cool water, requiring an emergency visit on a total of 3 different occasions. She was again given antihistamine and corticosteroid injections. She reported having no such symptoms after warm or hot shower. Furthermore, she also reported having itchiness and rashes in cold-exposed areas of her skin when she was outside her house during the cold winter days.

She was a non-smoker and other than amlodipine for high blood pressure, she had no regular use of medications. Family history for atopy was negative. At her presentation to our outpatient unit, her physical exam and routine laboratory test results were normal. Hepatitis markers, cryoglobulin, antinuclear antibodies and anti-dsDNA were also negative. She had normal levels of IgE, complement 3-4 and eosinophil count. A prick test with inhaled allergens was carried out with no findings suggestive of generalized atopy. There were no signs of dermatographism.

Based on a history of symptoms developing after exposure to cold, an ice cube challenge test to evaluate a probable diagnosis of CU was deemed appropriate. At 15 minutes into the test, erythematous papular skin lesions developed in the test area shown in [Figure 1](#). Just a few minutes after the emergence of



FIGURE 1: Erythematous papular skin lesions.

initial lesions, itchiness in the throat with shortness of breath, coughing and rashes began to appear. Vital signs at that time included an arterial blood pressure of 85/55 mmHg, and heart rate of 103 bpm. A diagnosis of anaphylaxis was made and immediate treatment with 0.5 mg of subcutaneous adrenaline was administered followed by 45.5 mg of intravenous pheniramine maleate infusion in 100 mL of physiological saline. The patient improved within 2 to 3 minutes with complete disappearance of the signs of symptoms after 20 minutes. At that time, her blood pressure was 140/85 mmHg with a heart rate of 92 bpm. She was closely followed up for 6 hours uneventfully after which she was trained on the use of adrenaline auto-injector in case of the emergence of symptoms suggesting anaphylaxis. In addition to adrenaline auto-injector, she was also prescribed desloratadine 5 mg/day and subsequently discharged.

Informed consent form was obtained from the patient.

DISCUSSION

CU represents a sub-group of physical urticarias characterized by the development of urticaria and angioedema after cold exposure. A major complication of CU involves a systemic reaction resulting in hemodynamic collapse after generalized cold exposure.² Since we failed to detect any studies reporting the development of anaphylaxis during an ice cube challenge test, we decided to report on this

patient, who, we believe represents the first patient ever to experience a reaction during the ice cube challenge test.

CU has 2 main types as familial and acquired, can be viewed in the title. Acquired CU can be primary or secondary.¹ Primary CU is idiopathic and includes 90% of cases. In secondary CU, insect bite, food allergies, drug use, vasculitis, infections, malignancy pathologies such as (chronic lymphocytic leukemia, lymphosarcoma) held responsible. In addition, chickenpox, viral hepatitis, infectious mononucleosis, human immunodeficiency virus, syphilis, borreliosis, helicobacter pylori colonization, acute toxoplasmosis and some parasitic infections have been reported to cause secondary CU.^{5,6} Abnormal serum proteins (cold agglutinins, cryoglobulins and cryofibrinogen), paroxysmal cold hemoglobinuria, diseases secondary to CU associated with cold cholinergic urticaria, familial cold autoinflammatory syndrome should be considered.⁵⁻⁷ In our patient, these secondary etiological factors were ruled out, thus we regard this case as having primary CU. Non-sedating H1 receptor blockers in conventional doses represent the first choice treatment in CU. Depending on the severity of symptoms, doses can be incremented up to 4-fold. In patients with a history of systemic reactions or anaphylaxis, emergency kits containing adrenaline auto injector, oral corticosteroids and antihistamines should be prescribed.⁸ In our case, we observed a rapid positive response with the adrenaline and antihistamine injection. In refractory patients, anti-E monoclonal antibody (omalizumab), etanercept (antitumor necrosis factor), anakinra (anti interleukin-1) are preferable.⁹

In case of more extensive or prolonged exposure, skin manifestations may be aggravated as to induce a systemic reaction and even anaphylaxis. A major complication of CU involves a systemic reaction resulting in hemodynamic collapse after generalized cold exposure. However, in our case although the cold exposure involved only a very small duration of time and surface area, anaphylaxis has been observed. Thus, despite limited time and extent of exposure, systemic allergic reactions such as anaphylaxis can also develop during ice cube challenge test.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Musa Salmanoğlu; **Design:** Veysel Özalper; **Control/Supervision:** Ercan Karabacak; **Data Collection and/or Processing:** Deniz İncaman; **Analysis and/or Interpretation:** Musa Salmanoğlu; **Literature Review:** Musa Salmanoğlu; **Writing the Article:** Musa Salmanoğlu; **Critical Review:** Musa Salmanoğlu; **References and Fundings:** Musa Salmanoğlu; **Materials:** Musa Salmanoğlu.

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