



# Atypical Ice Cube Test: A New Subtype of Cold-Induced Urticaria?

**Evangeline Clark<sup>1,2\*</sup>; Quentin Samaran<sup>1,2</sup>; Aurélie Du-Thanh<sup>1,2</sup>; Olivier Dereure<sup>1,2</sup>; Nadia Raison-Peyron<sup>1,2</sup>**

<sup>1</sup>Department of Dermatology, Montpellier University Hospital and Montpellier University, Montpellier, France.

<sup>2</sup>UCARE center, Montpellier, France.

**\*Corresponding Author(s): [Evangeline Clark](#)**

Department of Dermatology, Hospital Saint Eloi, 80 avenue Augustin Fliche, 34295 Montpellier cedex 5, France.

Tel: + 33-4-67-33-69-56, Fax: +33-4-67-33-69-58;

Email: [e-clark@chu-montpellier.fr](mailto:e-clark@chu-montpellier.fr)

Received: Apr 02, 2021

Accepted: May 27, 2021

Published Online: May 31, 2021

Journal: Journal of Clinical Images

Publisher: MedDocs Publishers LLC

Online edition: <http://meddocsonline.org/>

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**Keywords:** Cold dermographism; Inducible urticarial; Cold urticarial; Case report; Chronic urticaria.

## Clinical Image description

A 45-year-old non atopic woman with persistent asymptomatic i.e non itchy dermographism since childhood was referred for evaluation of urticaria of 9-month duration specifically occurring on cold-exposed areas, associated with pharyngeal dysesthesia triggered by contact with cold beverages or food. She reported cold weather-related occurrence of pruritus with linear lesions, but failed to remember whether the lesions appeared or not on scratched areas. Symptoms had initially appeared a few weeks after an insect bite on her left cheek, and she denied the occurrence of any severe systemic symptoms such as anaphylaxis since the beginning of the eruption. Familial

medical history did not include cold urticaria, livedo or Raynaud's phenomenon. H1-antihistamine drugs (four times the recommended dose everyday) were quite efficient with instant disappearance of symptoms.

An Ice Cube Test (ICT) was performed on the volar side of her right forearm and read at 1, 3 and 5 minutes. This test is considered positive if there is a formation of a wheal within 10 minutes after the ice cube stimulus removal. Surprisingly, the ICT initially showed barely visible wheals, but itchy linear wheals resembling typical symptomatic dermographism later appeared on the whole forearm, the ipsilateral arm and the face, about



**Cite this article:** Clark E, Samaran Q, Du-Thanh A, Dereure O, Raison-Payron N. Atypical Ice Cube Test: A New Subtype of Cold-Induced Urticaria?. J Clin Images. 2021; 4(1): 1093.

thirty minutes after the initial contact with the ice cube (Figure 1). The patient was then monitored for the subsequent hour in the hospital, but did not manifest any further symptoms. A TempTest® measurement was also carried out to determine the critical temperature threshold triggering a flare, but was uninterpretable with no linear pattern. Furthermore, various blood tests (hemoglobin level, white cell count, ESR, liver function tests, TSH level, cryoglobulins, cold agglutinins, anti-thyroid peroxidase or anti-thyroglobulin antibodies) were performed with negative or normal results.



**Figure 1:** Positive ice cube test performed on the right forearm.



**Figure 2:** Extension of the urticarial eruption on the left forearm, right forearm and right hand.

## Discussion

Cold induced urticaria is a well-known subtype of inducible urticaria, first described in 1872. Its incidence is estimated between 2 to 3% of the whole population [1] and the disease-related burden can be important [2]. Diagnosis is mainly based on clinical history and ICT [3]. In atypical cold induced urticaria (ACU), symptoms can be unusual and/or ICT can be negative or display an atypical pattern. These atypical forms include systemic ACU, localized ACU, follicular ACU, cold-induced cholinergic urticaria, cold-dependent dermatographism, delayed cold urticaria and localized reflex cold-induced urticaria<sup>4</sup>. Interestingly in our observation, ICT result and clinical pattern did not really match any of the previously described ACU forms and the possibility of a currently not reported, particular subset of cold-induced atypical reaction somehow related to the patient's background of asymptomatic dermatographism can be hypothesized. However, this cannot fully explain wheals extension to her whole arm and face.

Cold-induced contact urticaria pathophysiology remains elusive: Various hypotheses have been raised, including the role of cold receptors on mast cells, or a cold-induced unmasking of an endogenous skin antigen. On another hand, the association of cold-induced contact urticaria and dermatographism is rarely reported, and the presence of both mechanical stimuli- and cold-responding receptors on mast cells remains possible.

We report the first case of cold-induced urticaria with an atypical ICT which does not fully match any of the known subtypes of cold-urticaria descriptions, thus raising the possibility of a new entity, corresponding to an atypical cold-dependent dermatographism with secondary reflex diffuse extension. This case highlights the highly variable profile of chronic inducible urticaria and especially of cold induced urticaria.

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