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Article type : Letter to the Editor

Localized cold urticaria: an unusual form of cold urticaria

Keywords: cold urticaria; inducible urticaria; cold stimulation testing; localized cold urticaria

Manuscript word count: 592

Table count: 0

Figure count: 2

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/JDV.17697](#)

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Funding sources: none

Conflicts of interest: none

Cold urticaria (ColdU) is a common type of inducible urticaria, characterized by the appearance of wheals, angioedema or both upon cold exposure, either by direct contact or exposure to a cold ambient. Patients may have generalized cutaneous lesions and up to 30% may develop systemic symptoms, including dizziness, nausea, diarrhoea, abdominal pain, muscle weakness, respiratory distress or even anaphylaxis.^{1,2}

ColdU can be familial or acquired, the latter being further classified into primary or secondary to an underlying cause, such as cryoglobulins, infections or drugs.³ Diagnosis is based

on history and a positive cold stimulation test. However, rare and atypical forms of acquired ColdU, with negative results to the usual stimulation tests, have been reported.²

A 22-year-old male, engineering student, with no relevant personal or family medical history, reported a 2-year history of pruritic wheals and angioedema, solely on the hands and feet, after a few minutes of exposure to cold air or contact with cold surfaces. Wheals usually disappeared in 15-30 minutes, but angioedema lasted more than one day on several occasions. He denied urticarial eruptions in other locations, even when the whole skin was exposed to cold, and never developed systemic symptoms, namely dyspnoea, headache, fatigue or syncope. No other triggers such as drugs, food or infections could be identified.

Complete blood cell count, serum chemistry, protein electrophoresis, cryoglobulins, complement (C3, C4) and total serum immunoglobulin E (82 UI/mL) were normal. Anti-nuclear antibodies as well as infectious serologies (hepatitis B and C, human immunodeficiency virus, syphilis and Epstein-Barr virus) were negative.

Five-minute cold stimulation tests – TempTest® and ice cube test - performed on the forearm, were negative twice, with a 2-year interval. Considering patient's history, both tests were then performed on the palms and soles, and a 5-minute stimulation induced multiple, pruritic, erythematous papules with pseudopods in both locations (Fig. 1). The reactivity threshold was around 20° C for the TempTest® performed on the palms (Fig. 2). The patient was therefore diagnosed with localized cold urticaria (LCU).

Cold eviction and bilastine 20 to 80 mg/day allowed partial control of his symptoms, but there was no significant change in the reactivity threshold evaluated by the TempTest® after 6 months. As the patient denied any negative impact on his quality of life, no further treatments were attempted.

LCU is an atypical form of acquired ColdU, characterized by the occurrence of lesions in limited areas, even when the whole body is exposed to cold. Few cases have been reported, either primary (idiopathic) or secondary, the latter occurring in areas of previous insect bites,⁴ vaccination⁵ or allergen immunotherapy.⁶ We only found 6 published cases of idiopathic LCU, 5 of them involving the face,⁷ and none localized on the palms or soles. Higher cutaneous mast cell density on the head, hands and feet may explain these particular locations,⁸ although palms and soles have a thicker stratum corneum compared to the face, and therefore reduce access of the cold stimulus to the dermal mast cells.

The underlying pathophysiology of LCU is poorly understood. It may be related to an altered regional nerve sensitivity to cold or to a cutaneous chemical modified by cold, eventually enhancing mast cell degranulation.⁷ In our case report, however, the involvement of both hands and feet suggests a more central effect.

Treatment, as in other ColdU, includes trigger avoidance and second-generation antihistamines. In refractory cases, off-label use of omalizumab could be considered.⁹

With the report of this rare subtype of ColdU, we intend to raise awareness on the need to perform cold stimulation tests specifically on the reactive areas described by the patient.

Acknowledgments: The patient in this manuscript has given written informed consent to the publication of his case details.

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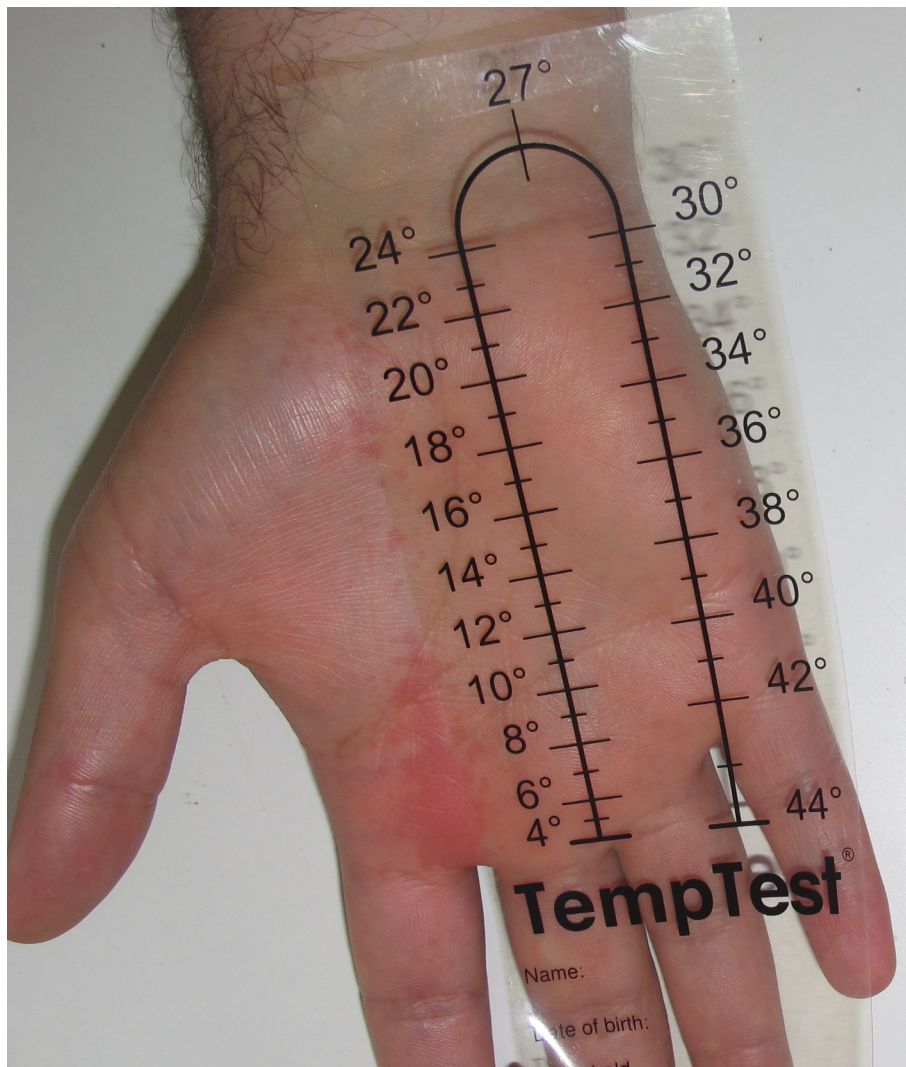
Figure Legends

Figure 1 – (a) Multiple confluent, erythematous papules after 5-minute cold stimulation with TempTest® and ice cube, respectively, on the right and left palms. (b) Positive reaction with linear, confluent, erythematous papules on the left sole, after 5-minute cold stimulation with TempTest®.

Figure 2 – Five-minute cold stimulation with TempTest® showing a reactivity threshold around 20°C.



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