Complete diagnosis of heat urticaria in a regular clinical practice. Report of two cases

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Heat urticaria (HU) is a subtype of chronic inducible urticaria (CIndU) that is characterized by the appearance of pruritic wheals after exposure to or direct contact with a hot stimulus [1-7]. These wheals can be localized (limited to those areas closest to the heat source) or generalized and can have an immediate or a delayed onset [2-4]. However, in the study of HU, other causes of chronic urticaria (CU) should be ruled out [2,5].

Here we present two clinical cases of women with localized HU where other subtypes of chronic urticaria (CU) were ruled out, and the triggering threshold temperature was determined. Written informed consent was obtained from the patients for publication.

The first case was a 57-year-old woman (a clinical assistant) with hypothyroidism and a two-year history of recurrent episodes of evanescent and itchy hives appearing within minutes of exposure to or direct contact with different heat sources. The hives appeared in the area of direct contact or the body part closest to the heat source and sometimes remitted spontaneously. The second case was a 50-year-old woman (a professional cook) with a nine-month history of recurrent episodes of transitory itchy hives after direct contact with a frying pan. Her hives disappeared after the patient took antihistamines and oral corticosteroids. None of the patients had mucosal lesions, systemic symptoms, or a history of urticaria in other situations. Both tolerated walking in the sun, physical exercise and sweating, and reported impaired quality of life due to their symptoms.

To confirm the diagnosis of HU, we performed a challenge test with a beaker filled with hot water at 40ºC (the water was heated in a microwave oven, and its temperature was measured with a cooking thermometer) placed on the patients' forearms. This test was positive in both cases (Figure1a). Once the diagnosis was confirmed, we performed several tests (supplementary online summary table) to rule out other causes of CU.

A complete blood count, biochemical and thyroid profiles, complement and immunoglobulin levels, antinuclear antibodies, and tryptase levels were either negative or normal. A blunt-force dermographism test was also negative. Cholinergic urticaria (ChoU), and solar urticaria (SU) were ruled out after we

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performed an outdoor free running test and an intradermal methacholine test for ChoU and a direct sunlight (outdoor) exposure test, and a visible light (slide projector) exposure test for SU. To exclude auto reactivity (AR), we performed an autologous serum intradermal test (ASIT) at room temperature according to the protocol proposed by the EAACI task force consensus [8].

To confirm the etiopathogenesis proposed by Fukunaga et al. [6], we performed an ASIT after heating the serum to 40ºC and 60ºC and then waiting 20 minutes at room temperature as established in the protocol of Carballada et al. [7] before applying it to the patient's forearm. Both patients developed a wheal at the application site when the serum was heated to 60ºC. The ASIT was also performed on healthy controls at room temperature and after heating the serum to 40ºC and 60ºC but none developed a wheal.

Finally, to determine the threshold temperature, we performed successive heat provocation tests with a beaker filled with water at different temperatures (starting at 30ºC and increasing the temperature by 5ºC each time the test was negative). The threshold temperature was 40°C for the first patient and 35°C for the second patient (Figure 1c).

Both patients were successfully treated with second-generation oral antihistamines (cetirizine) and were advised to avoid exposure to heat sources if possible. After eleven years in the case of patient 1 and nine years in the case of patient 2 both have maintained excellent control with occasional doses of antihistamines.

CIndU (a subtype of CU) is classified into physical urticaria (triggered by pressure, sunlight, heat…) and non-physical urticaria (triggered by active or passive body warming and water) [1,3-5]. HU is a rare skin disorder [2-7] with an unknown prevalence in patients with CIndU [3,5]. It can be diagnosed using a TempTest supplemented with a heated ASIT to confirm its etiopathogenesis [5,6]. Other subtypes or CU should be excluded even though they are clinically very different.

Symptomatic dermographism (SD) can be diagnosed with a calibrated dermographometer or a FricTest [1], ChoU after exercise, passive warming [1,3], or a methacholine intradermal test [3], SU after a negative sunlight exposure test (visible light) or PhotoTest (UVB and UVA wavelengths) [3], and AR to serum components after a positive autologous serum ID test at room temperature [9].

The etiopathogenesis of HU is unknown. Fukunaga et al. suggested that the serum of these patients may contain a large molecule (different from IgE) that is activated by heat and may promote mast cell degranulation and histamine release as was demonstrated by a positive heated ASIT and a negative room temperature ASIT [5-7]. In our patients, the heated ASIT was positive at a temperature higher than the threshold temperature. The mean threshold temperature for HU is 44ºC [2-5].

Therapeutic options for heat urticaria are limited [3] and treatment should always be individualized based on patient characteristics. As a prophylactic measure, we recommend avoiding exposure to heat sources as much as possible, but this is not always possible for all patients (cooks or hairdressers, for example). The first-line treatment is non-sedating H1-antihistamines (increasing the dose up to fourfold), but sedating H1-

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antihistamines, H2-antihistamines or short courses of oral corticosteroids can be added [1-5]. In case of poor response, heat desensitization [2,3,5] (after which histamine release no longer increases with heat exposure [6]) or omalizumab (off-label use) could be used for better symptomatic control [1,2,4,7].

Although a detailed clinical history and a positive TempTest or positive heat challenge test would be sufficient to diagnose HU, it is advisable to make a differential diagnosis with more common subtypes of CIndU. Here we show how it is possible to perform a complete diagnosis of this rare skin disorder [2-7], which has many differential diagnoses, using standard equipment available in our routine practice instead of the recommended medical equipment [1] to improve the management of our patients.

Conflict of interests

The authors declare no conflicts of interests associated with this publication, and there has been no financial support for this work that could have influenced its outcome.

Previous presentation

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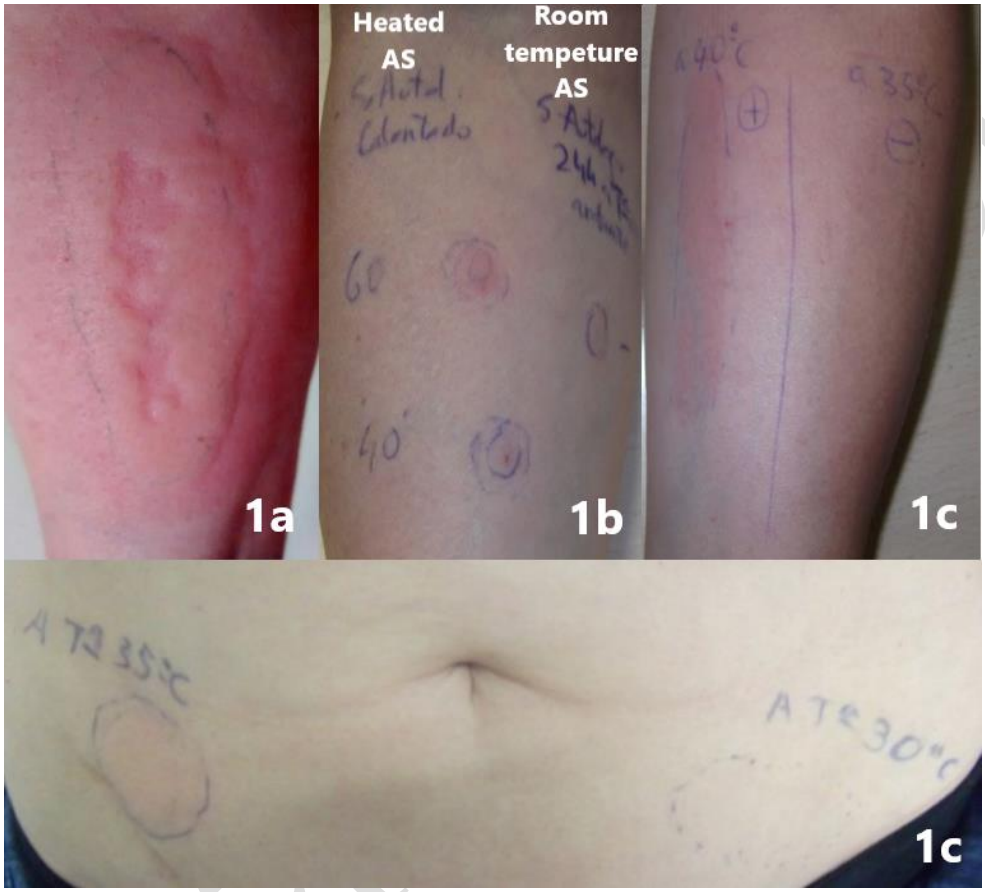
Figure. Diagnostic test results. 1a: A well-demarcated wheal after a heat challenge test using a beaker filled with water at a temperature of 40 ºC. 1b: A negative autologous serum intradermal test at room temperature and 40 ºC and positive after heating to 60 ºC. 1c: Threshold temperature at 40 ºC and 35 ºC of the first and second patient, respectively.



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