COLD URTICARIA

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Abstract: *Idiopathic cold urticaria is the most common type of cold urticaria characterized by rapid onset of pruritic hives, swelling, and possible severe systemic reactions including hypotension and shock after cold exposure. This essay presents the case of a 58-year old female, who had urticaria at the level of the areas exposed to cold, the diagnosis being confirmed by the ice cube test.*

Keywords: *urticaria, cold, ice cube test*

Rezumat: *Urticaria la frig idiopatică este cel mai comun tip de urticarie la frig, caracterizată prin debut rapid al papulelor pruriginoase, edemului şi posibile reacţii adverse sistemice, incluzând hipotensiune şi şoc după expunerea la frig. Prezentăm cazul unei paciente de 58 de ani, care a avut urticarie la nivelul zonelor expuse la frig, diagnosticul fiind confirmat prin testul cu cubul de gheaţă.*

Cuvinte cheie: *urticarie, frig, test la cub de gheaţă*

Urticaria is a cutaneous superficial erythematous inflammation, which becomes pale under pressure and is characterized by pruritus, erythema and edema. Angioedema is a severe form of urticaria that also affects the profound cutaneous tissue.

Cold urticaria is a form of physical urticaria characterised by the rapid onset of pruritus, erythema and edema after cold exposure. At the level of the body, edema is localized at the level of that part that came into contact with the cold, although the symptoms are often maximal, as a result of heating the exposed area. (1) This affection may occur in any age group, irrespective of gender.

In case of suspecting such a diagnosis, it may be easily recognized with the help of the ice-cub test. (2) Cold urticaria has been reported in relation with a series of diseases, characterized by abnormal immunoglobulins that have cold-dependent properties. Thus, it may be encountered in cryoglobulinemia, the cold agglutinin disease, cryfibrinogenemia, paroxysmal cold hemoglobinuria. The mechanism that produces urticaria in these affections remains unknown. The therapy in this case is that of the basic disease and is based on antihistaminics. Cryoglobulinemia may be associated to cutaneous vasculitis, as well as to the cold urticaria. Immune reactants (C3, IgM) in the lesions of these vessels were evidenced in one case. (4) In other patients, leukocytoclastic vasculitis was observed in relation with the cold urticaria and circulating immune complexes were obviously present. (5, 6)

In the majority of the patients, these abnormal circulating proteins are not evidenced and the affection is called idiopathic. 4-8 minutes after removing the ice cub, histamine release occurs, (7) which contributes to the decrease of the diastolic hypertension with 50 mmHg. Provoking test studies revealed bedsides histamine, the release of the mast cell constituents. These include eosinophilotactic peptides, (8, 9) neutrophilic chemotactic factor (NCF), (10) platelet activation factor (PAF), (11) and prostaglandin D2. (12)

This affection responds to antihistaminics, ciproheptadin being the most efficient. It is possible that the vasoactive factors, others than the histamine, should contribute to the urticaria reaction in the patients who do not respond well to ciproheptadin or other histamines.

Antihistaminics are recommended as a first line treatment, but their efficacy is sometimes unsatisfactory. Histamine is the main mediator, but leukotrienes are also involved in pathogenesis. Starting from this hypothesis, a group of Italian researchers accomplished a study that demonstrated that the combined therapy with antihistaminics (Cetirizine 10 mg once a day) and leukotriene receptor antagonists (Zafirlukast 20 mg twice a day) was superior, in comparison with these medications, administrated in an isolated manner. (13)

It was in the same Italy, where it was evidenced the fact that Cinnarizine in large doses may be considered an efficient and well tolerated treatment in this type of urticaria. (14)

The prognostic and the severity of the cold urticaria vary significantly. Sometimes, it may be solved spontaneously, but it may also last for years, the evolution not being predictable. Desensitization tests have been made in these patients, but precautions must be taken due to the risk of anafilactoide symptoms. This may be used in the patients not responding to the other therapies.

Regarding a series of 4 patients, when making the cold effort test, symptoms similar with those of cholinergic urticaria were registered, that did not occur when making the effort test in a warm environment.

Regarding this affection, the cold exposure is systemic and more local and should be suspected if the patients' symptoms suggest either the cold urticaria or the cholinergic urticaria and if the standard tests for this affection are negative. Making an effort in a cold room or running in winter days lead to generalized urticaria, thus confirming the diagnosis. This type of urticaria was named cold-induced cholinergic urticaria.

Another type of urticaria is the cold systemic urticaria. The symptoms are not related to effort or other activities and the results of the ice cube test are negative. Cold-evoked histamine releases (with or without effort) were observed in the cold-induced cholinergic urticaria, as well as in the cold systemic urticaria. The treatment with Hydroxyzine and Ciproheptadin in large doses was successfully used.

Cold-depended dermographisme consists in the formation of hives and occurs if the skin is scratched and grows cold. In this case, the ice cube test and the systemic provocation to cold do not produce any symptoms. The simple scratch of the skin may produce dermographisme with the dramatic accentuation if that particular area grows cold. The treatment consists in large doses of antihistaminics once a day.

Regarding the localized cold urticaria, only the area exposed to the cold is affected and was reported after predisposing conditions, such as: injuries due to the cold, or in the place of the allergen injection, immunotherapy or insects bite. In this case, we can talk about the presence of abnormal certain mast cells locally placed.

One of the affections, called localized cold reflex urticaria, was also reported, case in which the ice cube test was positive and the lesions occurred in the neighbouring contact area and not in the area where the ice cube was placed. The occurrence of urticaria resembles to the lesions of the cholinergic urticaria. The cutaneous test with acetylcholine or metacholine for the cholinergic urticaria is negative, although the symptoms of such a patient resemble to the cold-induced cholinergic urticaria, as a result of the effort-induced urticaria observed in a cold environment.

Therefore, the cold-dependent symptoms may be classified as follows:

1. Idiopathic cold urticaria;
2. Cold urticaria associated to abnormal serum proteins: cold agglutinin, cryoglobulin, cryofibrinogen, Donath-Landsteiner antibodies;
3. Cold systemic urticaria;
4. Cold-induced cholinergic urticaria;
5. Cold-depended dermographisme;
6. Cold late-phase urticaria;
7. Localized cold urticaria;
8. Cold reflex urticaria.

"Urticaria a frigore" – case presentation

We present the case of the patient B.R., a 58-year old female, living in Păltiniș, a pensioner (who formerly worked as a clerk), who came to the allergology unit in December 2007, for recurrent episodes of urticaria due to cold exposure. From anamnesis point of view, the patient had been recording for 2 years a cutaneous eruption with erythematous hives accompanied by edema at the level of the extremities exposed to cold in the cold season. The symptoms also occurred when the patient handled objects in the refrigerator, disappearing 10-15 minutes after the environment changed its temperature.

The objective examination revealed pruriginous and erythematous hives and maculae at the level of the face, hands and neck, that disappeared a few minutes after the patient had stayed in a warm environment.

The paraclinical examination did not reveal any changes (erythrocyte sedimentation rate, hemoleukograme, glycaemia, urine culture, urea, creatinine, glutamic-piruvic transaminase**,** glutamic-oxaloacetic transaminase, peripheral blood picture, plate culture of faeces). The HB antigen and the anti-HCV antibodies were negative. The cold urticaria is sometimes associated to the presence of serum cryoglobulins and their absence does not invalidate the diagnosis, these being negative in our case. T4 and TSH (thyroid-stimulating hormone) registered normal values.

The involvement of the physical factor (the cold) was confirmed through allergologic cutaneous testing with an ice cube that evidenced an erythematous hives very pruriginous, exceeding the edges of the ice cube after having been removed few minutes after, surrounded by erythema (positive intense test). (pictures 1, 2).

Picture no.1. Positive intense ice cube test

Picture no. 2. Positive intense ice cube test

The diagnosis set up based on anamnesis, objective examination and on the ice cube test was the idiopathic cold urticaria.

As a therapeutic strategy, the treatment with the oral, unsedative antihistaminics H1, was established for the cold season in combination with Desloratadin 5mg/day and Levocetirizin 5mg/day and prophylaxis

measures regarding the exposure to cold water or to objects of low temperature, food or cold drinks. Moreover, the cold exposure of the entire body (for example, swimming) may cause the massive release of mediators, resulting in hypotension. It would be useful to change the domicile in a subtropical area.

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