

Cold Urticaria Due To Amoxicillin–Clavulanic Acid

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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: 10.18176/jiaci.0999

Key words: Cold urticaria. Chronic urticaria. Amoxicillin-Clavulanic Acid.

Palabras clave: Urticaria *a frigore*. Urticaria crónica. Amoxicilina clavulánico.

To the Editor,

We read with great interest the Case Report in Practitioner's Corner entitled “**Cold Urticaria Triggered After Treatment With Amoxicillin–Clavulanic Acid**”, recently published in the *Journal of Investigational Allergology and Clinical Immunology* [1]. I think it would be very useful for the reader to clarify some issues about the case of cold urticaria in this exciting article.

Firstly; the main question in this case is whether the urticaria is chronic, as it lasts for several weeks, and whether it is a typical cold urticaria, as it is not only triggered by cold.

By definition, chronic urticaria is a type of urticaria lasting more than 6 weeks [2]. The urticaria described here lasts for a few weeks even if it recurs 2 times in 4 years. In total, it hardly exceeded 6 weeks for the 4 years.

The ice cube test is used to classify acquired cold urticaria as typical or atypical [3]. Since the ice cube test performed at the time of clinical findings in the patient is found to be negative in spite of being monitored for 30 minutes, it is difficult to say that the type of urticaria is a typical cold urticaria. Also, example given in the alprazolam case, it was positive at the beginning of urticaria [3]. From the case description, it makes me think that the urticaria is somehow spontaneous/idiopathic and also triggered by cold. The fact that it occurred a few times while being outdoors and manifested in different parts of the body (generalized urticaria) such as the neckline along with more intense (greater area and number of annoying, long-lasting lesions) episodes again confirmed that it is not typical cold urticaria. I wonder if the urticaria on his buttocks after sitting on cold stone benches when the ambient temperature was about 10°C was cold or pressure urticaria.

After all, it is well known that chronic spontaneous/idiopathic urticaria can recur with some drugs or be triggered by different physical inducers [4,5]. In the case described, the fact that the ice cube test performed 2 hours after the drug tolerance test became positive despite the negativity of the ice cube test while there were clinical findings in the beginning, raises suspicion about whether this is a typical cold- induced urticaria reaction in an atopic patient who we think may have chronic spontaneous urticaria. Could it be that the person had a flare-up of chronic spontaneous urticaria that day and the cold urticaria was induced by the ice cube test coincidentally, perhaps? Couldn't this have happened after the drug provocation test? In this case, it is important when (how many hours before or on the day) the ice cube test was performed before oral provocation and found to be negative. Also, how do the authors explain the pathophysiology of occurrence of a physical urticaria (cold urticaria) by a drug? How certain they can claim that this person's ice cube test would have been negative or would not have become positive if there had been no drug provocation that day? Again, the idea that this patient does not have a typical/simple cold urticaria is supported by the presence of urinary tract infection every time urticaria occurs in this patient. This infection by itself may have caused or triggered chronic urticaria in her past medical history [5,6].

Secondly; the acquired form of cold urticaria can be typical or atypical, depending on the positivity or negativity of the ice cube test. Typical cold urticaria is categorized into two groups: primary (idiopathic) (72%) and secondary cold urticaria (28%) [7]. The known causes of secondary type are cryoglobulinemia, hypothyroidism, celiac disease, infectious diseases, and drugs (penicillin, oral

contraceptives, etc.). Atypical forms of cold urticaria involve systemic forms, e.g. cold-dependent dermographism, cold reflex urticaria, and delayed cold urticaria [3,7]. If the case described in the article is typical cold urticaria, is it secondary or atypical cold urticaria? It would be good to mention and discuss these in the article.

Cold urticaria is known to be familial or acquired [3,7]. I wonder if the patient's family history has been thoroughly questioned.

Thirdly; after mentioning that the person described in the article is not atopic [1], the article later states positive skin tests for mites such as *Dermatophagoides pteronyssinus* and *Lepidoglyphus destructor*, meaning that the person is atopic, even without known allergic disease.

Fourthly; again, since she is a woman, I wonder if it was questioned whether she was using oral contraceptives, etc.? Cold urticaria with oral contraceptive use has been previously described in the literature [3,7]. Have autoimmune such as celiac disease or other rheumatologic diseases been investigated in this person?

Fifthly; it is also erroneous to claim that this is the first case of cold urticaria caused by penicillin-type drug in the literature. The development of chronic urticaria, including physical/inducible urticaria, due to penicillin-type antibiotics has been reported in the past [8,9]. The recently reported study should be taken into account when evaluating this case. This study found that chronic urticaria was at least 3 times more common in self-reported cases of penicillin allergy in the community [10].

In conclusion, I consider that awareness of cold urticaria should be increased for its accurate differentiation from other similar diseases.

Funding

None.

Conflict of interest

None.

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