

Cold-Induced Urticarial: An Introduction

Eric Clarke[†] and Tabitha Davidson[†]

Introduction

Cold-Induced Urticarial (ColdU) is a type of chronic inducible urticaria that is quite frequent. When the skin is exposed to cold air, liquids, or objects, it develops wheals and, in some cases, angioedema. Despite significant advances in our understanding of the syndrome and its management in recent years, ColdU remains a difficult therapeutic challenge. Patients with ColdU can suffer for years before being recognised, and therapy requires a tailored approach. ColdU has a major impact on quality of life, similar to other kinds of chronic urticaria. A case of severe and refractory ColdU accompanied with cryoglobulinemia is described here, and it was successfully treated using rituximab. Hypertension and monoclonal B-cell lymphocytosis were among her medical conditions [1,2]. Years before the presentation, the latter had been diagnosed. Because lymphocyte counts remained steady during follow-up, a wait-and-see approach was continued. Chronic urticaria and auto-inflammatory disorders were not found in the family history. Treatment with at least three different H1-antihistamines at up to four times the normal dose, omalizumab dosed up to 600 mg subcutaneously every four weeks, and cyclosporin up to 5 mg/kg were all ineffective. Further examinations were conducted due to her ColdU's severe and refractory character. This identified monoclonal IgG (type I cryoglobulins), which were linked to monoclonal B-cell lymphocytosis. Whole exome

sequencing revealed no alterations linked to auto-inflammatory diseases. Cold urticarial is a skin reaction to cold that appears within minutes after cold exposure. Affected skin develops itchy welts (hives) [2]. People with cold urticaria experience widely different symptoms. Some have minor reactions to the cold, while others have severe reactions. For some people with this condition, swimming in cold water could lead to very low blood pressure, fainting or shock. Cold urticaria occurs most frequently in young adults. If you think you have this condition, consult your doctor. Treatment usually includes preventive steps such as taking antihistamines and avoiding cold air and water [3].

In this report, we describe a case of full clinical remission of ColdU coupled with type I cryoglobulinemia in a patient with monoclonal B-cell lymphocytosis after therapy with rituximab.

Immunoglobulins that precipitate at temperatures below 37°C are known as cryoglobulins. Precipitation can cause vessel blockage, which can lead to immune-complex vasculitis and tissue damage. Cryoglobulins are divided into three categories based on their clonality and immunoglobulin type. Monoclonal immunoglobulins, primarily IgG or immunoglobulin M, are seen in Type 1 and are most commonly encountered in clonal B-cell disorders. Type 2 is a mix of monoclonal and polyclonal immunoglobulin M and polyclonal

Received: 29-May-2022,
Manuscript No. IJOCS-22-67099

Editor assigned: 01-June-2022,
PreQC No. IJOCS-22-67099(PQ);

Reviewed: 11-June-2022,
QC No. IJOCS-22-67099(Q);

Revised: 15-June-2022,
Manuscript No. IJOCS-22-67099(R);

Published: 20-June-2022, DOI:
10.37532/1753-0431.2022.16(6).248

Editorial Office, International Journal of Clinical Skills, London, United Kingdom

[†]Author for correspondence: Eric Clarke, Editorial Office, International Journal of Clinical Skills, London, United Kingdom, Email: ijclinicalskill@journalres.com

immunoglobulin G that is linked to autoimmune disorders and hepatitis C infection [1,4]. Type 3 cryoglobulins are a combination of polyclonal immunoglobulin M and IgG. Findings on the skin. Skin purpura, necrotic ulcers, cold-induced acrocyanosis, and the Raynaud phenomenon can all occur in patients with cryoglobulinemia. The pathophysiology of ColdU, a relatively rare form of cryoglobulinemia, has yet to be explained. Rather of vasculitis, which would be expected in normal cryoglobulinemic skin lesions, our patient showed characteristic, superficial wheals that matched urticaria. In this situation, the cryoglobulins may be matching an epitope on mast cells and basophils, resulting in IgG-mediated degranulation. Unfortunately, due to the technical limitations of dealing with cryoglobulins in vitro, we were unable to execute a basophil or mast cell activation test. However, the dramatic effect of rituximab on B-cell depletion supports the presence of autoreactive immunoglobulins in this patient, and the evident link to ColdU suggests a pathophysiologic function. Cryoglobulins are a type of cryoglobulin. Cryoglobulinemia should be considered in refractory ColdU, notwithstanding its rarity. Five of 104 patients in a major French cohort study had cryoglobulinemia, while a recent comprehensive review and meta-analysis of 14 relevant studies with a total of 1151 ColdU patients found that 3.0% (19/628) of patients had detectable cryoglobulin levels. We also found two case reports that were relevant to our situation. One case documented a 13-year-old kid who acquired ColdU after developing hepatitis B-associated type cryoglobulinemia. His ColdU vanished along with his cryoglobulins once his hepatitis B illness was cleared [4,5]. The other example was of a patient with cryoglobulinemia and chronic lymphocytic leukaemia who solely had ColdU as a clinical symptom. The patient was given 10 mg of chlorambucil once a day for 6 days, weeks, followed by a maintenance dose of 2 mg per day and steroid treatment. The ColdU improved as a result of hematologic remission, while complete remission was not obtained. Finally, 46% of 35 ColdU patients had detectable cold agglutinins, while 27% had cryoglobulins. None of these trials looked

into the possibility of using rituximab to treat cryoglobulin-associated ColdU. Rituximab is a monoclonal antibody that targets B-cells and is used to treat both autoimmune and hematologic conditions, such as rheumatoid arthritis. The use of rituximab for ColdU is off-label, and it was done in the setting of an academic hospital after various on-label treatments had failed. Off-label use of rituximab should be carefully examined at all times, as rituximab can cause substantial side effects. Reactions to infusion are the most prevalent and might range from headache and fever to bronchospasm, hypotension, and anaphylaxis-like reactions in rare situations [5].

Finally, certain cases of ColdU may be caused by cryoglobulinemia. The significance of cryoglobulins in the pathophysiology of ColdU has yet to be fully explained, and more research is needed. Until then, we recommend testing for cryoglobulinemia in patients with refractory ColdU, and if cryoglobulins are found, B-cell depleting medication can be considered.

■ Symptoms

Itchy welts (hives) on the area of skin that was exposed to cold for a short time. As the skin warms, the response worsens. Hands swell while they are handling cold objects Lips swell after ingesting cold food or drink The following are examples of severe reactions: Anaphylaxis is a whole-body reaction that might result in fainting, racing heart, limb or torso swelling, and shock. Swelling of the tongue and throat, which makes breathing difficult Symptoms of cold urticaria appear shortly after the skin is exposed to a quick drop in air temperature or cold water. A flare-up of symptoms may be more prevalent in wet and windy weather. Each episode could last up to two hours.

The most heinous reactions Swimming in cold water, for example, causes full-body exposure. It's possible that such a reaction will cause you to pass out and drown. Consult your doctor if you get skin issues as a result of cold exposure. Even if the reactions are minor, your doctor will want to rule out any underlying issues. If you have a whole-body reaction or difficulty breathing following a sudden exposure to cold, get emergency help.

References

1. Maltseva N, Borzova E, Fomina D, et al. Cold urticarial-What we know and what we do not know *Allergy*. 76(4), 1077-1094 (2021).
2. Maurer M, Metz M, Bindslev Jensen C, et al. Definition, aims, and implementation of GA(2) LEN urticaria centers of reference and excellence *Allergy*. 71(8), 1210-1218 (2016).
3. Ramos-Casals M, Stone JH, Cid MC, et al. The cryoglobulinaemias *Lancet*. 379(9813), 348-360 (2012).
4. Bracken SJ, Abraham S, MacLeod AC. Autoimmune theories of chronic spontaneous urticarial *Front Immunol*. 10(627) (2019). [Google Scholar] [CrossRef]
5. Koeppel MC, Bertrand S, Abitan R, et al. Urticaria caused by cold. 104 cases *Ann Dermatol Venereol*. 123(10), 627-632 (1996).