CASE REPORT

Occupational Anaphylaxis and Urticaria due to Cold Exposure: A Case Report

Chawapon Luengtongkam, MD[1], Naesinee Chaiear, MD, MMedSc, PhD[1], Phanumas Krisorn, MD, MSc[1]

[1] Department of Community, Family and Occupational Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

A 46-year-old male worked as a production line controller inspecting a cooling water system in a PVC pipe production line. While opening the cooling tank lid without wearing personal protective equipment, he was sprayed by a cool mist from the cooling tank. Approximately five minutes afterward, this exposure caused pruritic urticaria on the patient's arms, back, and face. The patient rinsed his face and arms with warm water, but the pruritic urticaria persisted, eventually leading to collapse. Hypotension was observed by the authors, subsequently diagnosed as anaphylaxis. The patient was transported to a hospital for treatment, which alleviated the symptoms. Later, the authors followed up the patient and reviewed his job history. The patient's initial symptoms, characterized by urticaria on his arms and back, began in 1996 at the age of 20 and were triggered by cold temperatures, such as bathing with cool water. These symptoms recurred twice a year. Based on this history, it was suspected that exposure to cold temperatures in the workplace might have been a contributing factor to anaphylaxis. According to information provided by the safety officer and supervisor, the patient might have been exposed to chlorodifluoromethane, a refrigerant, at a temperature of –40°C. He was later diagnosed with occupational anaphylaxis associated with cold urticaria, supported by the ACOEM Practice Guideline 2018 and the nine steps for occupational disease diagnosis outlined in the Association of Occupational and Environmental Diseases of Thailand Guideline. The present case highlighted the importance of following safety protocols in the workplace, such as avoiding exposure to cold temperature by adhering to standard operating procedures. When it is necessary to open the cooling tank lid, a face shield, goggles, or respirator must be worn as personal protective equipment.

Keywords: Anaphylaxis; Cold urticaria; Refrigerant 22

Received 17 September 2024 | Revised 30 November 2024 | Accepted 9 December 2024

J Med Assoc Thai 2025;108(1):88-93

Website: http://www.jmatonline.com

Anaphylaxis globally affected 50 to 112 cases per 100,000 person-years, with U.S. hospitalizations increasing by 37.6% between 2005 and 2014[1]. In Australia, fatal anaphylaxis rates rose by 6.2% annually between 1997 and 2013[2]. Major causes of fatal anaphylaxis in adults include medications, insect venom, and food[1]. Since 2017, 5,851 cases with data on the occupational link to anaphylactic episodes have been recorded, with 225 cases, or 3.8%, attributed to occupational allergens[3]. Work-related anaphylaxis, such as hypersensitivity to natural rubber latex (NRL) in medical gloves and bee venom in beekeepers, had also been reported[3-5]. Some chemicals, such as chlorodifluoromethane, do not inherently cause anaphylaxis on their own. However, the cold produced by these chemicals might trigger an anaphylactic reaction[6]. Although rare, cold urticaria has occasionally been observed[1,4,5,7]. Cold urticaria is a form of chronic inducible urticaria (CIndU). It presents a significant risk of anaphylaxis[1,7]. Chronic urticaria (CU) involves persistent pruritic wheals or angioedema lasting at least six weeks. Chronic spontaneous urticaria (CSU) occurs without a specific trigger, while CIndU is triggered by specific factors and can be categorized into physical and non-physical types[7]. Cold urticaria had a reported prevalence of 0.05% in one European study, with higher rates observed in northern climates. It was triggered by exposure of the skin to cold air, liquids, or objects[8]. Diagnosis often involves an ice cube test, but caution is considered due to the risk of anaphylaxis. One study reported a patient diagnosed with cold urticaria without performing the ice cube test. Instead, exposure to 20°C water confirmed the diagnosis[9]. Cold urticaria was the only subtype of CIndU known to cause life-threatening anaphylaxis, documented in over 20% of cases in eligible studies[7]. Occupational anaphylaxis (OcAn) can be triggered by specific workplace allergens, with symptoms

Correspondence to:

Chaiear N.

Department of Community, Family and Occupational Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.

Phone: +66-81-7081866, **Fax:** +66-43-202488

Email: naesinee@kku.ac.th

How to cite this article:

Luengtongkam C, Chaiear N, Krisorn P. Occupational anaphylaxis and urticaria due to cold exposure: a case report. J Med Assoc Thai 2025; 108:88-93.

DOI: 10.35755/jmedassocthai.2025.1.88-93-01699

appearing minutes to hours after exposure. Clinical presentation varies by exposure route and frequency, with repeated exposure often worsening reactions, though tolerance can develop. Diagnostic procedures identify the trigger, which must be avoided at work and elsewhere. Standard operating procedures were essential to prevent future exposure[10].

Case Report

The present case report described a 46-year-old male patient who experienced pruritic urticaria on his arms and back, as shown in Figure 1 and 2, which led to his collapse. While working as a production line controller, inspecting the cooling water system in a PVC pipe extrusion line under room temperature workplace conditions, which cooled PVC compound powder after it was boiled at 180°C to form cylindrical shapes, the patient opened a cooling tank lid without wearing personal protective equipment, which should have been worn. He was immediately sprayed to the face by a suspected refrigerant solution, based on information from the patient. The pruritic urticaria on his arms, back, and face occurred approximately five minutes after exposure with no signs of burns or frostbite. The patient rinsed his face and arms with warm water immediately after exposure and used oral chlorpheniramine and topical calamine lotion but failed to relieve the pruritic urticaria. This led to his collapse five minutes after exposure while walking to participate in the authors' occupational health service program. The authors measured the patient's vital signs, noting an initial blood pressure of 79/48 mmHg and a heart rate of 44 bpm, indicative of impending cardiac arrest. Consequently, the authors diagnosed the patient as anaphylaxis, called an ambulance, and the patient was transported to a hospital. At the hospital, his heart, lungs, and abdomen were normal upon physical examination. His complete blood count was normal. In the emergency department, the patient received 0.5 mL (0.5 mg) of 1:1,000 adrenaline intramuscularly, 4 mg of dexamethasone, and 10 mg of chlorpheniramine intravenously. These treatments restored his blood pressure to normal levels and alleviated his urticaria. During admission, he received 4 mg of dexamethasone and 10 mg of chlorpheniramine intravenously every six hours, along with a continuous drip of normal saline solution at 100 mL per hour. He experienced no further low blood pressure or urticaria and was discharged after one day of observation. After the patient was discharged from the hospital, the authors followed up to investigate the suspected cause of anaphylaxis, which the authors believed could be due to either cold temperature or chemical substances.

Figure 1. Urticaria on the patient's arms.

Figure 2. Urticaria on the patient's back.

The patient's job history was inquired about and was presented in Table 1. While working as a printmaker in a 16°C to 20°C room at a printing house, the patient experienced urticaria on his

Table 1. Chronology of the patient's job histories associated with main hazards in the workplace

Year	Age	Workplace	Main hazards in the workplace	Cold temperature in the workplace	Urticaria
1991-2013	15-37 years	A printmaker at a flexographic printing house	Ink mist (hydrocarbon solvents) and 16-20°C room temperature	Yes (16-20°C room temperature)	Yes
2013-2016	37-40 years	A cabinet maker at a wooden furniture manufacturing company	Wood dust and polycyclic aromatic hydrocarbons (PAHs)	No	No
2016-2020	40-44 years	A machine controller at rolling department of a PVC pipe manufacturing company	Heat from a boiler	No	No
2020-2023	43-46 years	A production line controller at extrusion department of a PVC pipe manufacturing company	Refrigerant	Yes (–40°C from chlorodifluoromethane)	Yes

arms and back. However, he did not have urticaria while working at a wooden furniture manufacturing company or in the rolling department of a PVC pipe manufacturing company. Additionally, his urticaria, which started in 1996 at age 20, was triggered by cold temperatures, such as bathing with cool water. These symptoms recurred twice a year and were managed with over-the-counter drugs, including oral chlorpheniramine and topical calamine lotion. The patient denied engaging in any hobbies, holding additional jobs, or being exposed to chemicals outside the workplace. On the day of the incident, the patient did not drink cold water, come into contact with ice, or bathe with cold water. Additionally, the patient did not consume any food or come into contact with animals while at work. The authors inquired the patient's supervisor and the workplace's safety officer about the chemical substances used in the cooling tank where the patient worked. The refrigerant was identified as chlorodifluoromethane, maintained at a temperature of –40°C. Other chemicals present included sodium hydroxide, methyl-1H-benzotriazole, 2-phosphonobutane-1,2,4-tricarboxylic acid, and maleic acid copolymer, all used to prevent scale formation. The supervisor and safety officer also noted that no other colleagues had previously experienced similar health effects, as personal protective equipment was consistently worn by other workers.

The patient's serum specific immunoglobulin E (IgE) levels were obtained to screen for general allergies such as food ingestion and animal exposure, with results documented in Table 2. Following the event, the patient continued performing the same job tasks. However, the workplace supervisor updated the standard operating procedures to require a face shield, goggles, or respirator be worn as personal protective equipment if the tank lid needed to be opened. Consequently, the patient did not experience any further urticaria or collapse when following these guidelines.

Table 2. The patient's food and animals allergen specific IgE levels

Allergen specific IgE	Quantitative results (kUA/L)	Class	IgE antibody levels
Aspergillus fumigatus	0.03	0	Undetectable
Bermuda grass	0.14	I	Very low
Cat dander	0.04	0	Undetectable
American cockroach	0.81	II	Low
German cockroach	3.90	III	Moderate
Dermatophagoides farinae	3.99	III	Moderate
Dermatophagoides pteronyssinus	2.42	III	Moderate
Dog dander	0.08	0	Undetectable
Latex	0.04	0	Undetectable
Shrimp	0.98	II	Low

Discussion

Since anaphylaxis in the workplace has been rarely reported both in Thailand and internationally, and given that it is a life-threatening condition, the present case report holds significant importance.

Based on the diagnostic criteria for anaphylaxis proposed by the World Allergy Organization Anaphylaxis Committee (2019), the present case report fulfills the requirements for a probable diagnosis of anaphylaxis. The patient presented with an acute onset of symptoms within five minutes of exposure to cold temperatures, specifically pruritic urticaria, indicating skin involvement. Additionally, the patient had a systolic blood pressure of less than 90 mmHg, which met the criterion for hypotension. According to the amended criteria, anaphylaxis is highly likely when there is an acute onset involving the skin, mucosal tissue, or both, along with at least one of the following: respiratory compromised, reduced blood pressure, or severe gastrointestinal symptoms. Given the patient's acute skin reaction and hypotension, these findings met the criteria for a

probable diagnosis of anaphylaxis[2]. This represented the first of nine steps in the diagnosis of occupational diseases and aligned with the American College of Occupational and Environmental Medicine (ACOEM) Practice Guideline (2018), which emphasizes the importance of establishing evidence of disease[11,12].

Initially, this case was thought to be idiopathic, then later the patient's anaphylaxis was believed to be work-related, triggered by cold temperatures in his work process. There was a cause of anaphylaxis in the patient's work process, which was cold temperature. The cold temperature was produced from chlorodifluoromethane. While no other agents were identified as causing anaphylaxis. This corresponded to the second of the nine steps in the diagnosis of occupational diseases, confirming the presence of cold temperatures at the patient's work process[11].

The patient was exposed to chlorodifluoromethane at –40°C while opening the cooling tank lid without personal protective equipment. Since chlorodifluoromethane has a boiling point of –41°C and a freezing point of –146.1°C, it remained in a liquid state at –40°C when the patient was exposed to its dispersion through direct skin contact on the uncovered face, both forearms, and back while opening the lid[13-16]. Because the patient rinsed his face with warm water and was only briefly exposed to the substance, frostbite did not occur[17]. This aligned with the third of the nine steps in the diagnosis of occupational diseases, which involved identifying the patient's exposure to chlorodifluoromethane[11]. Furthermore, the authors were able to diagnose the patient with cold urticaria, as there were no signs of fever, malaise, or joint pain, and the urticaria lasted less than 24 hours. The symptoms were consistently triggered by exposure to cold temperatures of –40°C from chlorodifluoromethane, confirming the diagnosis of cold urticaria. However, the ice cube test, a provocation test, was not performed due to the risk of potential anaphylaxis[7,18].

The fourth step of the nine steps in the diagnosis of occupational diseases was establishing a temporal relationship, which was demonstrated by the fact that the patient did not experience hypotension and pruritic urticaria prior to exposure to chlorodifluoromethane[11].

The patient's clinical presentation suggested an immediate hypersensitivity reaction, possibly Type I, due to exposure to the cold temperature of –40°C from chlorodifluoromethane, which could trigger anaphylaxis. Exposure to cold temperatures can induce the production of IgE antibodies that bind to mast cells. Subsequent exposure to cold activates these antibodies, leading to the activation of mast cells in two phases, an initial release of histamine followed by the production of arachidonic acid metabolites, such as leukotrienes and prostaglandins. These cytokines activate the kinin and complement systems, resulting in the onset of pruritic urticaria, with histamine release peaking within minutes[9,19-21]. In the present case, the health effects of exposure did not depend on a specific concentration or duration of cold exposure, as the pathophysiological mechanism explained the reaction. Therefore, the fifth step of the nine steps process for diagnosing occupational diseases, demonstrating sufficient exposure to cold temperatures, might not be applied in this scenario[11]. The third to fifth steps of the nine steps process for diagnosing occupational diseases, as previously mentioned, aligned with the ACOEM Practice Guideline (2018) in providing evidence of the patient's exposure[11,12].

The patient's generalized urticaria aligned with McManus et al.'s study, where most patients developed localized wheals or angioedema shortly after exposure to cold air, surfaces, or water[9]. Urticaria and low blood pressure occurred within five minutes of –40°C refrigerant exposure, contrasting with the absence of such symptoms before, highlighting the rapid onset of the reaction to cold temperature[10]. This demonstrated a clear temporal association. There was a study that described a 16-year-old who was diagnosed with cold-dependent exercise-induced anaphylaxis after biking to school in temperatures ranging from 2°C to 6°C[19]. This study supported the link between cold temperature and anaphylaxis, specifically in cases of cold urticaria similar to the present study. In Bumbăcea et al.'s study, a 38-year-old woman developed severe cold urticaria, including anaphylaxis, after swimming in cold seawater. Her symptoms worsened in winter and with exposure to cold wind, similar to the present study's patient who experienced urticaria while working in 16°C to 20°C room temperatures in the past[22]. A 45-year-old female pottery worker experienced intermittent swelling and itching of her hands for six months while working as a lithographer, which involved immersing transfers in a cold solution and applying them to pottery pieces. This case supported the link between cold temperatures in the work process and cold urticaria, similar to the present study[23]. These findings confirmed the consistency of the association across

various epidemiological studies. This supported epidemiological evidence linking cold temperatures to anaphylaxis, aligning with the sixth step of the nine steps process for diagnosing occupational diseases. It also corresponded with the ACOEM Practice Guideline (2018) in providing epidemiological data on anaphylaxis induced by cold exposure[11,12]. Although no other colleagues experienced the same health effects as the present patient, likely because the patient did not wear any personal protective equipment on the day of exposure, the inclusion criteria consisting of a confirmed diagnosis, exposure to cold temperatures, and supporting pathophysiology provide strong evidence to establish the work relatedness of the patient's condition.

Since there was no need for a differential diagnosis, as anaphylaxis and cold urticaria had already been confirmed, and the patient denied the use of latex gloves or consuming drugs known to cause anaphylaxis, such as penicillin derivatives, the seventh step of the nine-step process for diagnosing occupational diseases was not applicable in this scenario[11].

The other chemicals identified by the patient's supervisor and safety officer, including sodium hydroxide, methyl-1H-benzotriazole, 2-phosphonobutane-1,2,4-tricarboxylic acid, and maleic acid copolymer, were reviewed and found to be maintained at a temperature of 25°C, ruling out their involvement in the low temperature reaction. Additionally, based on their safety data sheets, none of these chemicals, including chlorodifluoromethane, exhibited allergenic properties sufficient to induce anaphylaxis[13-16,24]. Although some of the patient's serum specific IgE levels indicated potential sensitization, there was no evidence of exposure to other workplace allergens, such as food or animals. Furthermore, on the day of the event, the patient did not drink cold water, come into contact with ice, or bathe with cold water. The patient also denied having hobbies or additional jobs that could involve exposure to chemicals outside the workplace. These findings eliminated other potential causal factors unrelated to the refrigerant's temperature, which was measured at –40°C. This corresponded to the eighth step of the nine steps process for diagnosing occupational diseases, as well as the ACOEM Practice Guideline from 2018, which emphasized considering all relevant factors to confirm that cold temperature was the sole causative factor in this case[11,12].

As details mentioned above, this work-relatedness assessment was conducted by reaching a definitive diagnosis, gathering substantial information about individual exposures, compiling a detailed medical history, reviewing relevant scientific literature, analyzing epidemiological evidence of a causal relationship, and considering other pertinent factors. Based on these thorough evaluation, the authors concluded that this case represented anaphylaxis resulting from occupational exposure to cold[11,12]. However, the present case report presented a diagnosis based solely on history and clinical information, without confirmation through testing. Consequently, the diagnosis was considered probable. The present case highlighted the importance of following standard operating procedures in the workplace, such as using a monitor screen to inspect the cooling system instead of opening the cooling tank lid. If it is necessary to open the tank lid, a face shield, goggles, or respirator must be worn as personal protective equipment.

Conclusion

A 46-year-old Thai factory worker experienced an immediate allergic reaction to a –40°C refrigerant, presenting with urticaria and low blood pressure. He was diagnosed with occupational anaphylaxis due to cold, supported by evidence and individual exposure to the refrigerant. This case underscores the importance of adhering to standard operating procedures in the workplace to prevent refrigerant exposure, particularly for workers with underlying cold urticaria.

What is already known on this topic?

Cold urticaria, a type of physical urticaria triggered by exposure to cold, is known to cause life-threatening anaphylaxis. Occupational anaphylaxis can be triggered by various substances in workplaces with cold temperatures.

What does this study add?

Chlorodifluoromethane, which is used at –40°C, can trigger anaphylaxis in patients with underlying cold urticaria.

Acknowledgment

The authors thank (a) the experts for giving their opinions on the present study, and (b) Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, for the permission to access the patient's medical record.

Ethical approval

The Khon Kaen University Ethics Committee

reviewed and approved the current study for Human Research based on the Declaration of Helsinki and the ICH Good Clinical Practice Guidelines. Ethical reference number: HE661515.

Funding disclosure

The present study did not receive any funding in any form.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Motosue MS, Li JT, Campbell RL. Anaphylaxis: epidemiology and differential diagnosis. Immunol Allergy Clin North Am 2022;42:13-25.
2. Turner PJ, Campbell DE, Motosue MS, Campbell RL. Global trends in anaphylaxis epidemiology and clinical implications. J Allergy Clin Immunol Pract 2020;8:1169-76.
3. Worm M, Höfer V, Dölle-Bierke S, Bilo MB, Hartmann K, Sabouraud-Leclerc D, et al. Occupational anaphylaxis-data from the anaphylaxis registry. Allergy 2024;79:702-10.
4. Lee MJ, Do SH, Na HS, Kim MH, Jeon YT, Hwang JW. Anaphylaxis caused by latex surgical gloves immediately after starting surgery -a case report. Korean J Anesthesiol 2010;59 Suppl:S99-102.
5. Arcangeli G, Traversini V, Tomasini E, Baldassarre A, Lecca LI, Galea RP, et al. Allergic anaphylactic risk in farming activities: a systematic review. Int J Environ Res Public Health 2020;17:4921. doi: 10.3390/ijerph17144921.
6. National Center for Biotechnology Information. PubChem compound summary for CID 6372, Chlorodifluoromethane [Internet]. 2005 [cited 2024 May 27]. Available from: https://kku.world/hi7bf.
7. Prosty C, Gabrielli S, Le M, Ensina LF, Zhang X, Netchiporouk E, et al. Prevalence, management, and anaphylaxis risk of cold urticaria: a systematic review and meta-analysis. J Allergy Clin Immunol Pract 2022;10:586-96.e4.
8. Stepaniuk P, Vostretsova K, Kanani A. Review of cold-induced urticaria characteristics, diagnosis and management in a Western Canadian allergy practice. Allergy Asthma Clin Immunol 2018;14:85. doi: 10.1186/s13223-018-0310-5.
9. McManus NM, Zehrung RJ, Armstrong TC, Offman RP. Anaphylaxis caused by swimming: a case report of cold-induced urticaria in the emergency department. Clin Pract Cases Emerg Med 2021;5:307-11.
10. Moscato G, Pala G, Crivellaro M, Siracusa A. Anaphylaxis as occupational risk. Curr Opin Allergy Clin Immunol 2014;14:328-33.
11. Greaves WW, Das R, McKenzie JG, Sinclair DC, 2nd, Hegmann KT. Work-relatedness. J Occup Environ Med 2018;60:e640-e6.
12. Bandhukul A. Occupational diseases diagnosis by employing nine steps in occupational diseases diagnosis. J Dep Med Serv 2016;41:5-12. [In Thai]
13. Wernke MJ. Freons. In: Wexler P, editor. Encyclopedia of toxicology. 4th ed. Oxford: Elsevier; 2005:847-52.
14. Centers for Disease Control and Prevention. Chlorodifluoromethane. NIOSH pocket guide to chemical hazards. Atlanta, GA: CDC; 2018.
15. International Labour Organization. International chemical safety card: chlorodifluoromethane. Geneva: ILO; 2021.
16. National Refrigerants. Safety data sheet: R-22. chlorodifluoromethane [unpublished]. Bridgeton, NJ: National Refrigerants; 2021.
17. Persitz J, Essa A, Ner EB, Assaraf E, Avisar E. Frostbite of the extremities - recognition, evaluation and treatment. Injury 2022;53:3088-93.
18. Kulthanan K, Tuchinda P, Chularojanamontri L, Chanyachailert P, Korkij W, Chunharas A, et al. Clinical practice guideline for diagnosis and management of urticaria. Asian Pac J Allergy Immunol 2016;34:190-200.
19. Ii M, Sayama K, Tohyama M, Hashimoto K. A case of cold-dependent exercise-induced anaphylaxis. Br J Dermatol 2002;147:368-70.
20. Maltseva N, Borzova E, Fomina D, Bizjak M, Terhorst-Molawi D, Košnik M, et al. Cold urticaria - what we know and what we do not know. Allergy 2021;76:1077-94.
21. Pacheco KA. Clinical immunology. In: LaDou J, Harrison RJ, editors. Current diagnosis & treatment: occupational & environmental medicine. [Internet]. New York: McGraw Hill; 2021 [cited 2024 May 27]. Available from: https://kku.world/5hf6m.
22. Bumbăcea RS, Deaconu CG, Berghea EC. Management problems in severe chronic inducible urticaria: two case reports. Exp Ther Med 2019;18:960-3.
23. Fitzgerald DA, Heagerty AH, English JS. Cold urticaria as an occupational dermatosis. Contact Dermatitis 1995;32:238.
24. LSP Siam Intertrade Company. Material safety data sheet: AQUATREAT 9000. Products to prevent scale and corrosion in cooling water systems [unpublished]. Bangkok: The Company; n.d. [in Thai]