Cold urticaria develops in response to exposure to cold stimuli, such as cold air, water or objects. Symptoms may vary from localized wheals to systemic reactions, sometimes leading to life-threatening conditions. Physicians need to be cautious when they administer cold fluid intravenously to patients who develop urticaria as a result of exposure to cold.

We report here a patient in whom cold urticaria and systemic symptoms occurred repeatedly after infusion of cold intravenous fluid. She developed both immediate and delayed reactions.

CASE REPORT

A 23-year-old woman presented for evaluation of skin rash, nausea and vomiting that occurred reproducibly after infusion of intravenous fluid. The first event had occurred when she had visited hospital for fever and cough approximately one year previously. Thirty minutes after being intravenously dripped with normal saline, vomiting and generalized urticaria had developed. Fluid infusion was immediately stopped and these symptoms disappeared gradually.

The second event had occurred when she had visited hospital for abdominal pain 8 months previously. She was intravenously dripped with normal saline for a few hours during evaluation of the abdominal pain. No abnormalities were found and the abdominal pain disappeared, so she was discharged. Several hours later she developed generalized urticaria that persisted for several days and gradually disappeared.

The third event occurred when she went skiing for a month. Dyspnoea and wheezing developed suddenly, and she visited hospital again. After inhaling a fast-acting beta-2 agonist nebulizer in the emergency room the dyspnoea and wheezing disappeared. However, when she was intravenously dripped with normal saline, vomiting and generalized urticaria had developed. Fluid infusion was immediately stopped and these symptoms disappeared gradually.

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DISCUSSION

Cold urticaria is an unusual type of urticaria that develops in response to cold stimuli. It occurs in 1–3% of all patients with urticaria (1). Symptoms may be localized wheals that develop in areas that come into contact with cold stimuli. In systemic manifestations,
cold stimuli may lead to systemic reactions, such as wheezing, hypotension, laryngeal oedema and life-threatening cardiovascular collapse.

Wanderer et al. (2) classified cold urticaria based on the severity of reactions. Type 1 refers to reactions confined to the area of skin that came into contact with the cold. Type 2 refers to generalized urticaria not associated with cardiovascular or respiratory symptoms. Type 3 refers to patients having one or more episodes associated with symptoms and signs indicative of respiratory or cardiovascular compromise.

In the literature, there is a case report of cold-induced urticaria resulting from fluid infusion in the operating room (3). Another case developed after exposure to cold air in the operating room (4). In addition, there are several reports about delayed symptoms of cold urticaria (5–7).

The pathogenesis of cold urticaria is known to involve mast cell activation followed by degranulation. Mast cell-derived factors, including histamine, leukotrienes, platelet-activating factor, and prostaglandin D2, have been detected in the circulation after cold exposures (8, 9). Our case was unusual in that immediate and delayed-type reactions coexisted. Eady et al. (10) examined skin biopsies of 5 patients after cold challenge and demonstrated delayed inflammatory cell involvement in primary cold urticaria. Amplified inflammatory cell involvement due to sustained cold stimulation may contribute to delayed-type reactions (9).

Avoidance of cold stimuli is the most important element of the management of cold urticaria (11). Therefore, in patients who develop cold urticaria from cold intravenous fluids, heating of fluids can be a preventive measure, but it requires attention and alertness on the part of physicians. In recent guidelines, the recommended first-line treatments for urticaria are new-generation, non-sedating H1-antihistamines (12). However, the clinical efficacy of H1-antihistamines may be unsatisfactory in cold urticaria. Several groups have suggested that leukotriene receptor antagonists could be used to relieve symptoms in patients with inadequate responses to antihistamines (13–15). In patients refractory to these conventional treatments, an anti-immunoglobulin E monoclonal antibody (omalizumab), etanercept (anti-tumour necrosis factor) and anakinra (anti-interleukin 1) could be considered (16, 17).

REFERENCES

1. Buss YL, Sticherling M. Cold urticaria; disease course and outcome – an investigation of 85 patients before and after therapy. Br J Dermatol 2005; 153: 440–441.
2. Wanderer AA, Grandel KE, Wasserman SI, Farr RS. Clinical characteristics of cold-induced systemic reactions in acquired cold urticaria syndromes: recommendations for prevention of this complication and a proposal for a diagnostic classification of cold urticaria. J Allergy Clin Immunol 1986; 78: 417–423.
3. Lockhart CH, Brownrigg JC. Anesthetic hazards of cold urticaria. Anesthesiology 1973; 38: 96–97.
4. De la Borbolla JM, Tapies S, Mbongo C, Lafuente A, Gaztaminza G. Cold urticaria: its importance in the operating room. J Investig Allergol Clin Immunol 2010; 20: 446–447.
5. Matthews CN, Warin RP. Delayed cold urticaria. Br J Dermatol 1977; 97 Suppl 15: 32.
6. Back O, Larsen A. Delayed cold urticaria. Acta Derm Venereol 1978; 58: 369–371.
7. Juhlin L. Cold urticaria with persistent weals. Br J Dermatol 1981; 104: 705–707.
8. Wanderer AA. Cold urticaria syndromes: historical background, diagnostic classification, clinical and laboratory characteristics, pathogenesis, and management. J Allergy Clin Immunol 1990; 85: 965–981.
9. Wanderer AA, Hoffman HM. The spectrum of acquired and familial cold-induced urticaria/urticaria-like syndromes. Immunol Allergy Clin North Am 2004; 24: 259–286, vii.
10. Eady RA, Keachy TM, Sibbald RG, Kobza Black A. Cold urticaria with vasculitis: report of a case with light and electron microscopic, immunofluorescence and pharmacological studies. Clin Exp Dermatol 1981; 6: 355–366.
11. Siebenhaar F, Weller K, Mlynek A, Magler M, Altrichter S, Vieira Dos Santos R, et al. Acquired cold urticaria: clinical picture and update on diagnosis and treatment. Clin Exp Dermatol 2007; 32: 241–245.
12. Zuberbier T, Asero R, Bindslev-Jensen C, Walter Canonica G, Church MK, Gimenez-Arnau AM, et al. EAACI/GA(2) LEN/EDF/WAO guideline: management of urticaria. Allergy 2009; 64: 1427–1443.
13. Di Lorenzo G, D’Alcamo A, Rizzo M, Leto-Barone MS, Bianco CL, Ditta V, et al. Leukotriene receptor antagonists in monotherapy or in combination with antihistamines in the treatment of chronic urticaria: a systematic review. J Asthma Allergy 2008; 2: 9–16.
14. Hani N, Hartmann K, Casper C, Peters T, Schneider LA, Hunzelmann N, et al. Improvement of cold urticaria by treatment with the leukotriene receptor antagonist montelukast. Acta Derm Venereol 2000; 80: 229.
15. Maltby NH, Ind PW, Causon RC, Fuller RW, Taylor GW. Leukotriene E4 release in cold urticaria. Clin Exp Allergy 1989; 19: 33–36.
16. Boyce JA. Successful treatment of cold-induced urticaria/anaphylaxis with anti-IgE. J Allergy Clin Immunol 2006; 117: 1415–1418.
17. Abajian M, Mlynek A, Maurer M. Physical urticaria. Current allergy and asthma reports 2012; 12: 281–287.