A Case of Immunologic Contact Urticaria to Chlorhexidine

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A 25-year-old woman developed generalized urticaria and an anaphylactic syndrome of sudden onset while she was being treated for her decubitus ulcer with chlorhexidine antiseptic solution.

Prick test with 0.5% chlorhexidine produced a wheal in a few minutes.

A passive intradermal transfer test (P-K test) to her mother was positive. These enabled us diagnose her as having an immunologic contact urticaria to chlorhexidine.

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Key Words: Immunologic contact urticaria, Chlorhexidine

Chlorhexidine gluconate, which has been used world-wide as a medical disinfectant, has been considered to be safe. However, adverse reactions to chlorhexidine have been reported. Contact Urticaria (CU) has been a rare adverse reactions to chlorhexidine and to our knowledge, has never been described in Korea.

We present a case of chlorhexidine-induced contact urticaria with anaphylaxis.

REPORT OF A CASE

A 25-year-old woman was referred to our clinic because of the sudden onset of generalized urticaria with anaphylaxis. She felt an itching sensation during topical treatment of her ulcers with 10% povidone iodine, 0.5% chlorhexidine and nitrofurazone (Furacine®) gauze application, she was being treated by the Department of Plastic Surgery for a decubitus ulcer. Immediately after the dressing application, dizziness, respiratory difficulty, lower abdominal crampy pain and generalized urticaria developed sequentially (Fig. 1). Systemic symptomes spontaneously disappeared in less than 30 minutes, but the urticaria persisted for another 1 hour. She had suffered from complete paraplegia for 2 years, caused by a L1 compression fracture from a fall, and decubitus ulcers on her buttocks for 18 months. The ulcers had been treated after debridement with two or three antiseptics including chlorhexidine without any problem.

She had no family history of skin or allergic disease. The chest X-ray and laboratory findings including CBC, U/A, LFT and VDRL were all within normal limit.

Open epidermal application tests, patch tests, and prick tests were performed on her forearm with 0.5% chlorhexidine, 1% and 10% povidone iodine, 3% hydrogen peroxide, 70% isopropyl alcohol, normal saline and Furacine® gauze. A

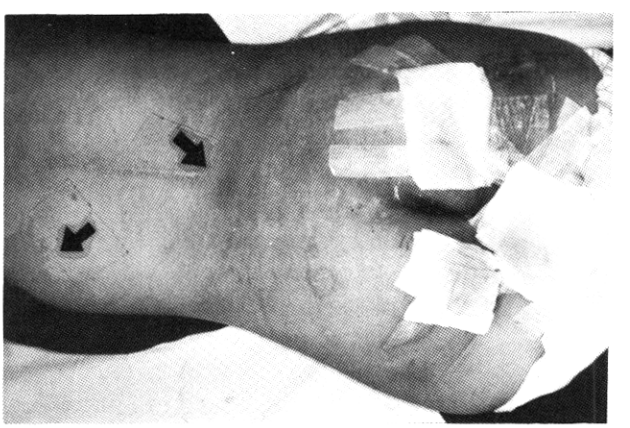

Fig. 1. Generalized urticaria after the decubitus wounds were treated with antiseptics.

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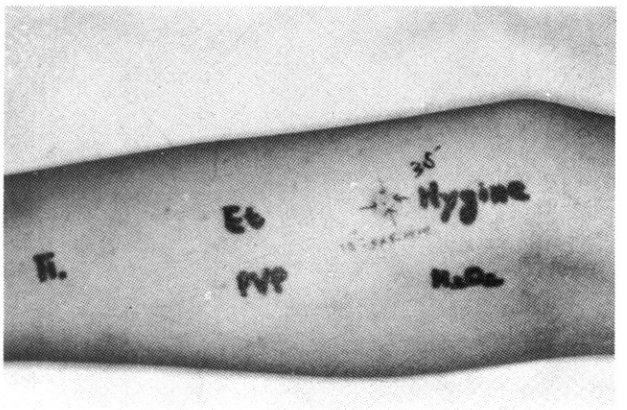

Fig. 2. Pruritic wheals at the site of prick test with 0.5% chlorhexidine (Hygine®).

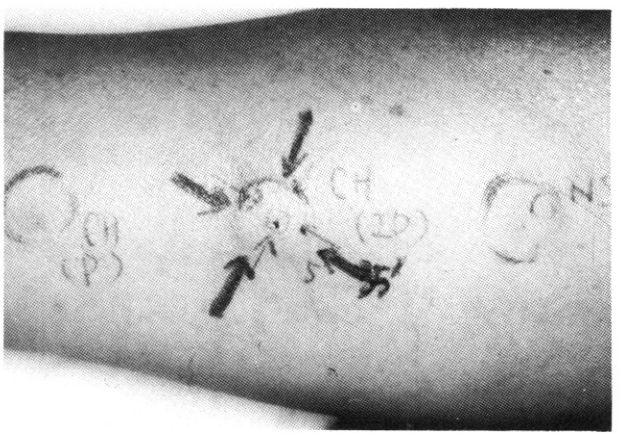

Fig. 3. Symptomless wheals at the site of P-K test with 0.5% chlorhexidine on patient's mother.

pruritic wheal developed at the site of prick test with 0.5% chlorhexidine 4 minutes later, and expanded gradually for the next hour (Fig. 2). At 72 hours after testing, there were no delayed reactions.

A passive transfer test (P-K test) was performed on her mother. A symptomless wheal developed at the site where the patient's serum had been injected when intradermally tested a with 0.5% chlorhexidine 5 minutes later.

DISCUSSION

CU is characterized by transient localized erythema, wheal or angioedema elicited by simple contact of skin or mucous membrane to a causative agent.[1] CU usually occurs 30 to 60 minutes after the contact and disappears within 24 hours. In our case, wheals were provoked immediately after the patient's skin was exposed to chlorhexidine and lasted for 1 or 2 hours.

The extent of wheal formation and occurence of an anaphylatic syndrome were related to the amount of chlorhexidine exposure. In a sensitized patient, the risk of CU and other adverse reactions has been known to be greater when higher concentration of chlorhexidine are used and when applied to wounds, where the epidermal barrier was impaired. Cheung & O'Leary[2] suggested that slight damage to the epidermal barrier is necessary to provoke immediate reaction to chlorhexidine, although it is not necessary as shown by a Okano's case[3] which showed positive by open epidermal application test.

According to Maibach and Johnson,[4] CU can be categorized into three major groups such as nonimmunologic CU, immunologic CU, and CU of uncertain mechanism. The principle mediator in immunologic CU is antigen-specific IgE, which causes degranulation of mast cells and basophils, although IgG antibodies have been postulated in some cases.[5] Using the cytotropic property of IgE, P-K testing has performed to demonstrate specific skin sensitizing antibodies in patient serum.[6]

Only 8 cases of CU to chlorhexidine have been described in the medical literature (Table 1). In 8 cases[4,7] of CU to chlorhexidine in Japan and Scandinavia, the immediate-type response was evaluated using the schematic test protocol which consisted of open epidermal application test, patch test, prick test or scratch test and intradermal injection in order. Ohtoshi et al[8] demonstrated specific skin sensitizing antibodies to chlorhexidine by P-K test and IgE RAST in a patient's serum. Our case showed a positive P-K test; thus, it is reasonable to assume that it is dueto an immunologic mechanism, although specific IgE antibody to chlorhexidine could not be measured in her serum.

Besides pure immediate type hypersensitivity to chlorhexidine, Karlsson[7] reported a case showing both delayed and immediate type hypersensitivity to chlorhexidine simultaneously, and the term of "contact dermatitis of immediate and delayed type" was suggested for this combined reaction. In our case, a delayed reaction was not noted up

Table 1. Summary of reported cases of immediate reaction to topical Chlorhexidine.

Patient No. (Age/Sex)	Concentration of Chlorhexidine	Area application	Timeof onset of symptomes (min.)	Symptomes	Skin tests (Concentration of Chlorhexidine)
1 (4) (9/M)	0.5%	palpebra urethra	within 40	Generalized urticaria Bronchospasm shock	scratch test (+) (0.05%) open application
2 (4) (15/M)	0.5%	wound on forehead	within 10	Facial urticaria Dyspnea	test (+), (1%) scratch test (+) (0.02%)
3 (4) (9/M)	0.05%	trauma on lip	10	Generalized urticaria Cough, Fatigue	Intradermal test (+), (0.002%)
4 (4) (26/M)	1%	penis	5	Generalized flushing Numbness, Dyspnea	Intradermal test (+), (0.0002%)
5 (4) (31/F)	0.5%	vagina	30	Generalized urticaria Dyspnea, Abdominal pain	scratch test (+) (0.5%)
7 (4) (66/M)	0.05%	urethra	45	Urticaria on trunk and extremity	scratch test (+) (0.5%)
8* (25/F)	0.5%	ulcer site	within 10	Generalizd urticaria Dyspnea, Abdominal pain	prick test (+) (0.5%)

* : present.
( ) : reference number.

to 72 hours after contact.

We described a case of immunologic CU confirmed by prick testing and P-K testing.

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