

CONTACT POINTS

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Photoallergic contact dermatitis due to diclofenac

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Key words: diclofenac; medicaments; non-steroidal anti-inflammatory drugs; photoallergic contact dermatitis

Case Report

An 40-year-old man, with no previous history of allergy, was treated with Voltaren emulgel® (Novartis farmacéutica, Barcelona, Spain) 2 × a day (sodium diclofenac 1%), for elbow trauma. At D3, acute vesicular eczema appeared on the application area only. Cream application was stopped and topical corticosteroid treatment started, with complete resolution within 5 days. It was summer and the patient wore a short-sleeved shirt. 1 year before, he had complained of the same symptoms after Voltaren emulgel application on a finger. After these episodes, he had

tolerated topical application of pike-toprofen and methyl salicylate on sun-exposed areas and oral acetyl-salicylic acid without problems.

He was patch tested with the GE-IDC standard series, an NSAIDs series (salicylic acid 1%, bufexamac 5%, naproxen 5%, ibuprofen 5%, phenylbutazone 1%, diclofenac 1%, paracetamol 5%, indomethacin 5% and ketoprofen 2.5%, all in pet.; Laboratory Bial-Aristegui, Bilbao, Spain), Voltaren emulgel as is and diclofenac 1% pet. Photopatch testing was performed according to the Spanish Photobiology Group, with an NSAIDs series, Voltaren emulgel as is and diclofenac 1% pet. A PUVA 500 (Herbert, Waldmann, Germany) lamp was used, irradiating for 30 min ($5\text{ J}\cdot\text{cm}^{-2}$), with readings at D1 and D3 after irradiation. Results are shown in Table 1.

The same photopatch tests were performed in 5 controls with negative results.

Discussion

Diclofenac is a widely used NSAID derivative of phenylacetic acid. Most adverse reactions are gastrointestinal, though hepatitis, renal damage and immune-mediated haematologic disorders have also been described. From the allergic point of view, urticaria (1), angioedema (1, 2), anaphylaxis (2, 3), contact dermatitis (4) and delayed hypersensitivity (5) have

been reported. To our knowledge, this is the 1st case report of photoallergic contact dermatitis due to diclofenac.

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Table 1. Results of patch and photopatch testing

	% and vehicle	Patch test D2	Patch test D4	Photopatch D1	Photopatch D3
GEIDC standard series	–	–	NT	NT	NT
NSAIDs series	–	–	–	–	–
diclofenac	1% pet.	–	–	(except diclofenac) ++	(except diclofenac) ++
Voltaren emulgel®	As is	–	–	++	++

Drug eruption due to alendronate sodium hydrate

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Key words: alendronate; cutaneous adverse
drug reactions; positive lymphocyte
stimulation test; positive scratch-patch test.

Case Report

A 72-year-old woman had had osteoporosis for over 3 years, and had received drug therapy (alfacalcidol) in our hospital for 3 years. She was seen in December 2001 with numerous red papules and petechiae on the lower extremities that had started 10D before. She had been taking alendronate sodium hydrate (Fosamax®: Banyuu, Tokyo, Japan) 5 mg once a day orally for 3 weeks, in addition to alfacalcidol 0.5 µg once a day.

We performed patch tests and scratch-patch tests with 20%, 10%, 1%, and 0.1% pet. alendronate sodium hydrate and 3 excipients in Fosamax. Only scratch-patch tests with 20% and 10% pet. alendronate sodium hydrate produced erythema and papules with pruritus at D2 and D3. Patch tests and scratch-patch tests with 20% and 10% pet. alendronate sodium hydrate in 6 control subjects showed no reactions at D2 or D3. LST (lymphocyte stimulation test) with alendronate sodium hydrate was positive (stimulation index (SI) = 4.0, normal SI < 1.8).

Discussion

Several bisphosphonates, including alendronate, are effective antiresorptive agents for the prevention and treatment of osteoporosis as well as for the treatment of Paget's disease

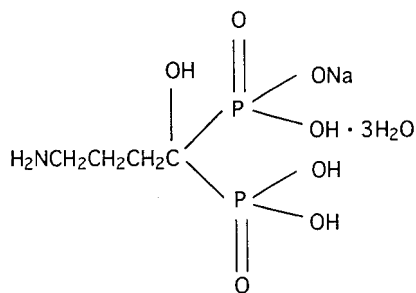


Fig. 1. Chemical structure of alendronate sodium hydrate.

of bone, myeloma, and bone metastasis (1, 2). They have strong antiresorptive activity and increase bone mineral density (2). Alendronate has been used in Europe and the USA (Fosamax) since 1995 and in Japan since 2001. It causes mainly gastrointestinal-tract adverse effects, e.g. abdominal pain, esophagitis, and esophageal ulcer (3), while drug eruption due to alendronate sodium hydrate is rare. Only 1 case with an urticarial drug eruption from alendronate has been reported (4). The structure of alendronate sodium hydrate is shown in Fig. 1.

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Septic arthritis as a complication of allergic contact dermatitis

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Key words: Basic Red 46; clothing
dermatitis; occupational; socks

Case Report

A 32-year-old concrete caster presented with a 16-month history of severe work-related foot and ankle dermatitis. He was exposed at work to concrete dust and a mould-releasing oil, the latter contaminating his lower legs and leather boots.

One month earlier, he had developed left ankle pain, and been found to show overlying erythema and reduced range of movement, with a raised WBC and ESR. Culture of aspirated joint fluid grew *Staphylococcus aureus*, and a septic arthritis of the left ankle joint was diagnosed and treated with prolonged intravenous antibiotics.

He was patch tested using Finn Chambers® on Scanpor® tape (Epitest, Tuusula, Finland), to an extended European standard series, a rubber series, Chemotechnique (Malmö, Sweden) textile dye series, and samples of the mould-release oil and his boots and socks (soaked in both oil and water). There were positive reactions to Basic Red 46 1% pet. (+++) and ethylenediamine 1% pet. (++), and equivocal reactions to his blue socks soaked in water and the inner leather from his own work boots soaked in water. There was no reaction to potassium dichromate 0.5% pet. and 0.25% pet.

Discussion

Basic Red 46 is used in the dyeing of acrylic products, including socks, and was not found to have been used in the patient's leather work boots. We suggest that he may have been exposed to Basic Red 46 in acrylic work socks and that this dye may also have leached into the leather of his work boots. The positive patch

test reaction to ethylenediamine was thought to relate to previous use of Kenacomb® (Bristol-Myers Squibb Australia Pty Ltd, Noble Park, Australia) cream.

We also propose that septic arthritis developed as a complication of this protracted allergic contact dermatitis. To the best of our knowledge, there have been no previous reports of such an association, though Kitamura et al. reported a septic arthritis of the hip associated with atopic dermatitis (1). Osteomyelitis has previously been reported in association with allergic contact dermatitis (2), atopic dermatitis (3, 4) and latex hypersensitivity (5). Septic arthritis of the ankle is an unusual disease, normally associated with trauma, underlying joint disease, or surgery (6).

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Hydroxymethyl pentylcyclohexene-carboxaldehyde (Lyrall®) as a fragrance allergen in the UK

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Key words: hydroxymethyl pentylcyclohexenecarboxaldehyde; Lyrall®; CAS 31906-04-4; fragrance mix; Myroxylon Pereirae resin; European standard series.

Hydroxymethyl pentylcyclohexene-carboxaldehyde (Lyrall®; HMPCHC) is an aldehyde lipophilic enough to penetrate skin (1). It is a synthetic fragrance ingredient most commonly found in personal care and household products. The frequency of HMPCHC as an ingredient in these products is quoted as being between 33 and 46%. A recent large multicentre study (1) reported an incidence of 11.3% positivity to fragrance mix (FM) and 2.7% positivity to HMPCHC.

Materials, Methods and Results

Over a 12-month period, 766 consecutive patients were patch tested to the British standard series, containing fragrance mix 8% pet. (FM) and Myroxylon Pereirae resin 25% pet. (MP), supplied by Hermal (Trolab), Reinbek, Germany. HMPCHC 5% pet was kindly supplied by Boots PLC, Nottingham, UK, and tested in parallel. The patch test allergens were applied using Finn Chambers on Scanpor (Epitest, Tuusula, Finland). Readings were made at day (D)2 and D4 and positive reactions recorded as recommended internationally.

The frequency of positive reactions to FM, MP and HMPCHC was 91/766 (11.8%), 49/766 (6.4%) and 16/766 (2%), respectively. 10/766 (1.3%) of patients were positive to both FM and HMPCHC and 3/766 (0.4%) reacted to all 3. Of the 16 patients with a positive reaction to HMPCHC, the

median age was 35 years (range 20–79 years), 44% were male and 31% gave an atopic history. 38% had eczema on the face and neck, 31% on the hands, 19% in the axillae, 6% on the trunk and 6% had generalized eczema. 4 patients gave a history suggestive of fragrance allergy and, of these, 3 were positive to HMPCHC and fragrance mix and 1 to HMPCHC alone. 62% of HMPCHC positive reactions were regarded as of current relevance to the patient, 19% of possible relevance, 13% of past relevance and 6% not relevant.

The association of a positive reaction to HMPCHC and FM was analysed with a χ^2 test in the whole patch test population and a *P*-value of < 0.0001 obtained. When fragrance-allergic patients alone were analysed the association was no longer significant.

Comment

Our 0.8% rate of reactions to HMPCHC (in the absence of a reaction to FM or MP) is lower than the 1.1% of Frosch *et al.* (1). However the 2% of our patch test population reacting to HMPCHC is similar to the 1.9% of Geier *et al.* (2).

The association between reactions to FM and HMPCHC could represent a cross-reaction between the 2 allergens or independent sensitization following increased exposure to fragrance allergens. The loss of the association when fragrance-allergic individuals alone were analysed suggests that the association is the result of increased exposure and that the allergens independently sensitize.

This data supports current reports that hydroxymethyl pentylcyclohexenecarboxaldehyde (Lyrall®) is a common fragrance allergen and lends further support to its inclusion in the standard series or any future fragrance mix.

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Occupational allergic contact dermatitis in hospital workers caused by methyldibromo glutaronitrile in a work soap

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Key words: allergic contact dermatitis; methyldibromo glutaronitrile; occupational.

Methyldibromo glutaronitrile is used as a preservative in soaps and many other products. Occupational allergic contact dermatitis from this agent is increasing in frequency (1–3).

Case Reports

Case no. 1

A 41-year-old atopic nursing auxiliary presented in December 1998 with a 3-month history of an itchy red eruption on the dorsum of her hands after using Leverline Soft® (DiverseyLever Ltd, Alfreton, UK), a hand washing soap on the hospital ward. She had suffered repeated episodes of this rash affecting her hands, suggestive of an allergic contact dermatitis, since a new formulation of this soap had been introduced in September 1998. There was a definite improvement when she was away from work. She avoided the new hospital soap with great improvement though had a similar reaction on her hands at home after

using Carex® (Cussons, Stockport, UK) an antibacterial hand wash.

Patch testing to the European standard series showed a ++ reaction to nickel and a + reaction to fragrance mix, and additional patch testing to the ingredients of Leverline Soft® gave + reactions to both methyldibromo glutaronitrile 0.1% pet. and 0.5% pet., with all other constituents negative.

Case no. 2

A 38-year-old accident-and-emergency staff nurse had had a 3-year history of intermittent outbreaks of a rash on the dorsum of both hands. It was also present on the palm of his right hand, with some spread to the forearms. He related it to the use of the acaricide Derbac-M® (SSL, Knutsford, UK) after an outbreak in his department. There was no previous history of eczema. On examination he had active dermatitis in the distribution described. A natural rubber latex prick test was negative and he was subsequently patch tested to an extended European standard series and a rubber additives series. He had a +++ reaction to methyldibromo glutaronitrile 0.3% pet. He was advised to avoid Cutan® (DEB Ltd, Belper, UK) hand wash and moisturizing cream and to provide his own emollient for the workplace. His skin showed considerable improvement with these measures.

Case no. 3

A 27-year-old staff nurse working on an elderly care assessment unit had noticed that her hands were dry, cracked and sore over a period of months. She had found some improvement by using E45 cream (Crookes, Nottingham, UK) as an emollient and avoiding latex gloves. A natural rubber latex prick test was negative. She was then patch tested to an extended European standard series. This gave a ++ reaction to methyldibromo glutaronitrile 0.3% pet. and she was advised to avoid the Cutan® hand wash used on the wards; again with substantial benefit.

Discussion

Methyldibromo glutaronitrile is also known as 1, 2-dibromo-2,4-dicyano-

butane. It is found mainly in the preservative Euxyl® K 400 (Schülke and Mayr GmbH, Norderstedt, Germany) combined with phenoxyethanol. This is used as a preservative in cosmetics and antibacterial hand washes but also found in glues, water-based paints, metalworking fluids and detergents. 4 cases of hand dermatitis in metal workers from methyldibromo glutaronitrile have been described, with no sensitization to phenoxyethanol (1). Recently, 3 men have been reported with allergic contact dermatitis from methyldibromo glutaronitrile secondary to abrasive soaps and barrier creams at their workplace (2). The prevalence of sensitization to methyldibromo glutaronitrile is increasing (4% in the Netherlands in 1994, compared to 0.5% in 1991) (4). In addition, reports due to the use of moistened toilet tissue are common, whereas occupational causes are rarer (5). The patient in case no. 1 had a definite rash on her hands within 24 h of using 2 different products containing the common ingredient methyldibromo glutaronitrile. The old formulation of the hospital soap did not contain this allergen and we understand that it is no longer the preservative used in Leverline Soft®.

Our other 2 patients routinely used a hand wash called Cutan® which is widely distributed throughout their hospital for staff use. It is known to contain methyldibromo glutaronitrile. The British Contact Dermatitis Society have recommended adding methyldibromo glutaronitrile to standard series in all UK patch testing centres, due to increasing numbers of cases of occupational allergic contact dermatitis due to this allergen.

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Contact urticaria from cinnamal leading to anaphylaxis

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Key words: contact urticaria; cinnamic aldehyde; anaphylaxis.

Case Report

A 42-year-old woman presented with an uncomfortable rash on her arms. She worked as a nurse on a renal unit and frequently prepared fluids for peritoneal dialysis. This commonly involved adding gentamicin and vancomycin to the dialysis fluid. She felt that her problems had coincided with a change in the type of gloves used at her hospital and had recently changed to a Biogel™ (Regent Medical, Broomsbourne, UK) glove. She continued to experience irritation developing on her arms at work. During one particular episode, she had developed a widespread rash, burning sensation within her head and abdominal symptoms that had necessitated treatment with hydrocortisone and chlorphenamine maleate intramuscularly. She was known to be asthmatic but had never suffered from eczema.

A natural rubber latex prick test was negative. She was patch tested to the European standard series, medicaments series (which includes genta-

micin), latex gloves and glutaraldehyde. These tests were removed the next day (D). Approximately 12 h after they had been applied, she had developed a widespread urticarial rash which required treatment with antihistamines. When the tests were removed at D1, no positive reactions were noted. At D4, however, a + reaction to fragrance mix was seen. She was therefore patch tested to the constituents of fragrance mix, which were applied for just 20 min. A strong urticarial reaction was seen to cinnamal (cinnamic aldehyde) and a weak reaction to cinnamic alcohol at this time. 40 min after the test, our patient developed widespread pruritus and erythema, and 5 min later, started to feel faint. A blood pressure reading was unrecordable. She was treated with 10 mg chlorphenamine maleate and 1 mg adrenaline intramuscularly and made a good recovery. Review of the 20-min test sites at D4 identified a + + reaction to cinnamal. All other tests were negative.

Our patient was later open tested to a range of fragranced products that she used in her workplace, including liquid soaps, moisturizing cream and an air freshener. The undiluted products were placed on her forearm for 30–40 min and she was observed for 2 h afterwards. No local or widespread reaction was seen.

It was concluded that she had immediate, as well as delayed, hypersensitivity to cinnamal and that this constituent of the fragrance mix was the most likely cause of the anaphylaxis.

Discussion

The contact urticaria syndrome (CUS) was first described in 1975 (1). It describes a response that can range from pruritus only (2) to a wheal-and-flare response or even anaphylaxis after cutaneous exposure to certain agents. This occurs in 30–60 min and usually settles within 24 h (3). However, delayed onset urticaria after 4–6 h has also been reported (3). There are more than 100 substances that can cause CUS (2). Cinnamal is well known to be one of these (4, 5). It can cause contact urticaria by releasing histamine and vasoactive substances without involving immunologic mechanisms. It has also been said that cinnamal may

induce an initial urticarial reaction and then a Type IV delayed hypersensitivity reaction, as happened in our patient (2). Anaphylactic reaction in the context of contact urticaria from cinnamal has not previously been reported, though it has for other substances, e.g. penicillin, epoxy resin, neomycin and chloramphenicol (1) and more recently benzophenone-3 (6) and natural rubber latex (7).

The occupational urticaria and anaphylaxis was eventually attributed to vancomycin sensitivity, which will be reported separately. The relevance of the reaction to cinnamal remains unknown, though following identification of this allergy the patient became aware of urticarial reactions and abdominal symptoms following the ingestion of spicy foods.

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