

CONTACT POINTS

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Allergic and systemic contact dermatitis to methylparaben

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Key words: medicaments; mucolytic; parabens; systemic contact dermatitis.

Parabens are alkyl esters of parahydroxy benzoic acid that are mainly used in cosmetics, medication and food (1, 2). Contact sensitization to parabens is not very frequent, except in patients under topical treatment for leg ulcers and/or stasis dermatitis. Most studies show a low prevalence of sensitization, around 1% (3), but frequency oscillates between 0% and 4.2%, with some isolated reports which show a frequency of 10.9% (4–6).

Several cases of allergic contact dermatitis – and a few of contact urticaria (7), located angioedema and bronchospasm (6) – to parabens (5, 6) have been published. In patients with previous contact sensitization to parabens, systemic contact dermatitis has been reported after the administration of systemic medication with parabens (8–10). We present a patient with allergic contact dermatitis to methylparaben who developed a systemic contact dermatitis after the ingestion of an oral mucolytic.

Case Report

A 72 years-old male with a 1-month history of cutaneous eruptions in his interdigital web, thighs and arms related to the oral ingestion of a mucolytic. He referred itchy, erythematous-oedematous and squamous plaques in the external lateral region

of his thighs, in the same areas where he had been applying 0.05% capsicum oleoresine gel for 2 years due to a paresthesic meralgia. The cutaneous lesions spontaneously remitted in a few days. Patch tests with Spanish standard series, capsicum oleoresine gel and its components were positive to thiomersal, capsicum oleoresine gel and one of its components, methylparaben, at D2 and D4. A ROAT with capsicum oleoresine gel was positive on the third day. The diagnosis was allergic contact dermatitis.

Later on, the patient reported the progressive appearance of itchy cutaneous lesions 4 days after beginning an oral treatment with a mucolytic, at a dose of 10 ml/day for 3 consecutive days due to a pharyngoamigdalitis. The cutaneous lesions were erythematous-oedematous, bilateral, and almost symmetrical plaques, located in the II, III and IV interdigital web of his hands, arms, glutea region, thighs and eyelids. The previous positive patches of capsicum oleoresine gel and methylparaben were reactivated. The lesions disappeared 1 week after suspending the oral medication and with a topical corticoids treatment.

Epicutaneous tests with a mucolytic were positive to one of its components, methylparaben 3% pet. at D2 and D4. After informed consent, oral administration of placebo and 200 mg of methylparaben were administered. The systemic administration of methylparaben produced isolated erythematous-oedematous plaques in his trunk with reactivation of the patch test reactions, which disappeared spontaneously after several days. Oral placebo did not produce a flare-up of the dermatitis.

Discussion

Our patient was probably sensitized to methylparaben as a result of a prolonged topical treatment, the positive ROAT confirming its clinical relevance. Later on, he developed a systemic contact dermatitis caused

by the methylparaben in the mucolytic. The following facts support this diagnosis: personal antecedents of cutaneous eruptions related to oral medication; temporary relationship between the oral administration of the mucolytic and the appearance of the cutaneous lesions; positive patch test to methylparaben; reactivation of the dermatitis in the previous patch tests; and the appearance of cutaneous lesions after the oral administration of methylparaben.

Systemic contact dermatitis caused by parabens is not very frequent, although it has been reflected in the literature (8–10). The clinical history together with a careful evaluation of the patch tests is the most important pillars leading to the clinical diagnosis. With parabens, the reactivation of the dermatitis in the areas of the patch has not been previously reported, although it is a feature described in systemic contact dermatitis. Some authors have used the oral overload with parabens in patients with contact sensitization and cutaneous lesions. However, although worsening of the dermatitis was demonstrated in some patients, most of them didn't present any type of reaction (11). Patients with allergic contact dermatitis caused by parabens often tolerate the ingestion of meals that contain it, without having to restrict these types of food (12).

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Erythema multiforme-like generalized allergic contact dermatitis caused by *Alpinia galanga*

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Key words: allergic contact dermatitis; *Alpinia galanga*; erythema multiforme; herbal remedy; spice.

This study reports a case of localized contact dermatitis and subsequently generalized erythema multiforme-like eruptions after topical application of herbal remedies. Patch tests showed there was an allergen in fresh and dried *Alpinia galanga*, which is also a popular spice in Southeast Asian cuisines.

Case Report

A 54-year-old woman suffered from low back pain and neck pain due to lumbosacral and cervical spondylosis. She was a housewife. She only used the root of the *Alpinia galanga*. First, she fired thin slices of galanga and then mixed them with oil of *Cinnamomum camphora*. She prepared and applied herbal remedies by herself over neck and back to relieve the pain every 2 days. After 1 week, severe burning and itching erythematous plaques with vesicles and bulla appeared over the contacted area (Fig. 1). 10 days later, target-shaped, urticaria-like plaques developed over the unexposed area,

including the chest, abdomen, hands and lower extremities (Fig. 2). A skin biopsy of the back and left knee showed perivascular mononuclear cell infiltration in the papillary dermis, exocytosis and prominent dyskeratosis in epidermal keratinocytes with a subepidermal cleft formation (Fig. 3a,b). Thus, a diagnosis of erythema multiforme-like generalized allergic contact dermatitis due to herbal remedies was made. Subsequent investigations showed normal findings in blood routine and serum immunoglobulin IgG, IgA, IgM and IgE and negative finding in ANA. The skin lesions improved within 1 month with oral administration of prednisolone (0.5 mg/kg/day) and topical care with zinc oxide ointment. 2 months later, we performed patch tests using Finn chambers with powdered fresh or fried *A. galanga* (series dilution concentration: 100%, 10%, 2%) with petrolatum, *C. camphora* oil, their mixtures and European Series Standard Battery over the back. Application time was 48 hr. Readings taken at 48, 72 and 96 hr showed a strong reaction (++)

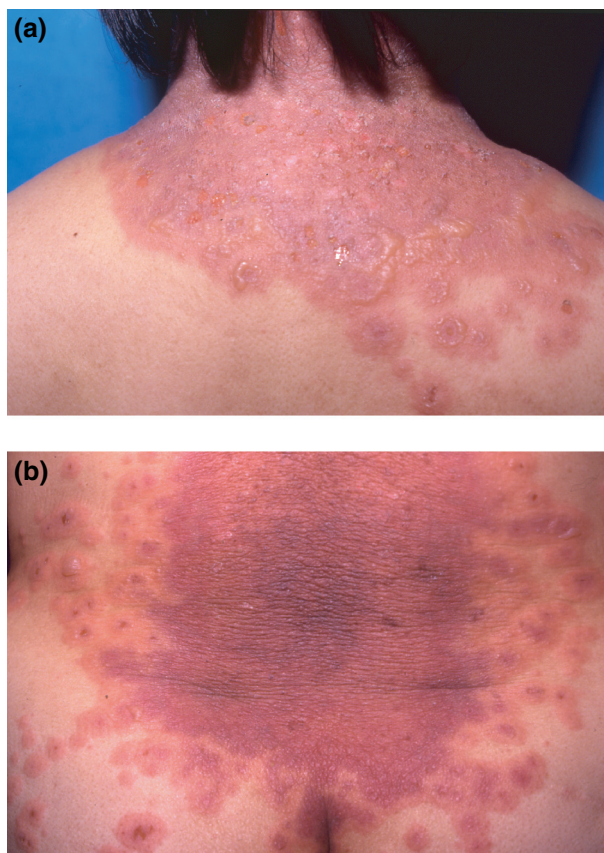


Fig. 1. Confluent erythema with bulla and satellite target lesions in the neck (a) and back (b) developed by directly applied topical herbal medication.

Fig. 2. Multiple erythematous patches and bulla with target lesions over the nonexposure site such as left knee (a) and abdomen (b).

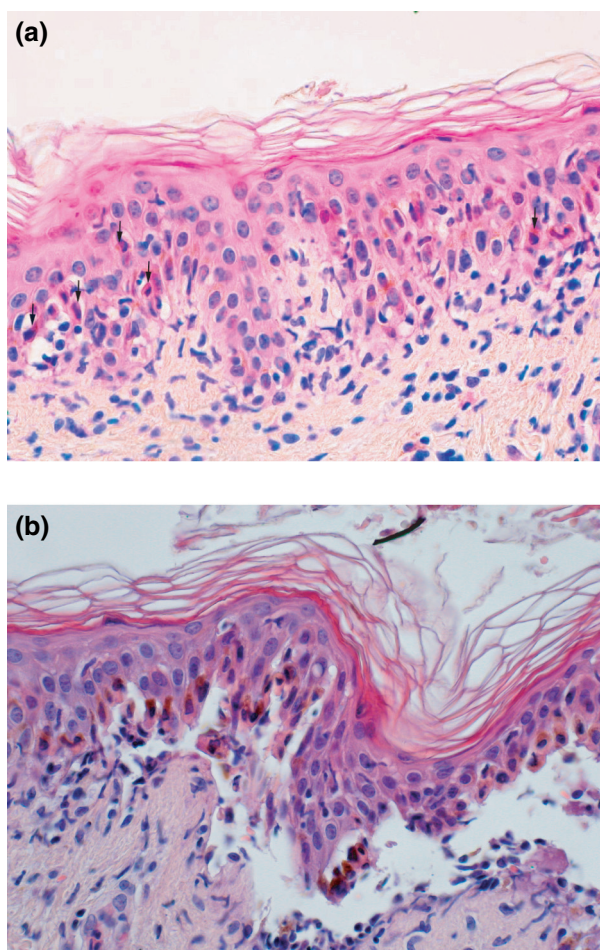
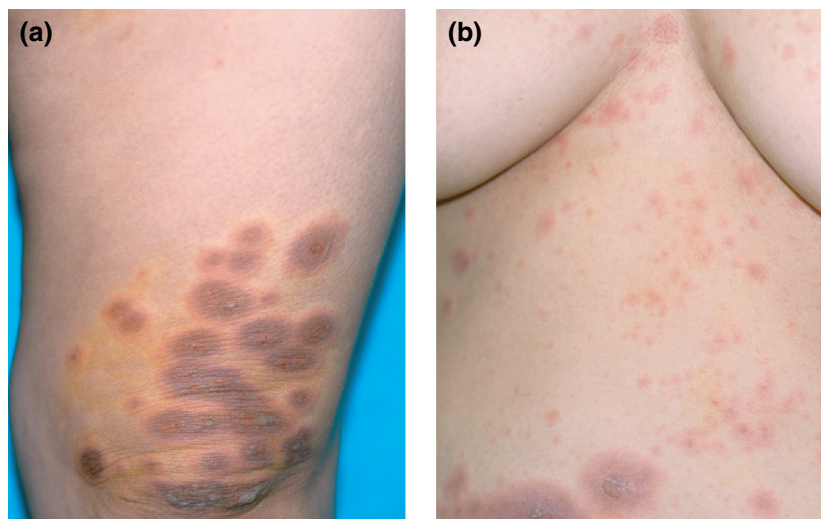


Fig. 3. Skin specimen from back lesion stained with haematoxylin and eosin showed perivascular mononuclear cells infiltration in papillary dermis, exocytosis with microspangiosis, scattered dyskeratosis of keratinocytes (a, original magnification $\times 200$) and a subepidermal cleft formation (b, original magnification $\times 200$).

to ++++) to *A. galanga*, in both fresh and fried forms, and to the fragrance mix (sorbitan sesquiolate) (Table 1).

Discussion

Erythema multiforme-like allergic contact dermatitis is rare and has been reported to be caused by

contact with plants (1–3), exotic wood (4), topical medication (5–7), cosmetics (8, 9) and specific environmental exposures (10–12). This study reports the first case caused by *A. galanga*.

Alpinia galanga belongs to Zingiberaceae (the ginger family). Its rhizome (rootstock) is commonly used in herbal medicine and as a spice in food. The pharmacologic actions are anti-inflammation (13), anti-oxidation, anti-allergy (14), gastroprotection (15), hypoglycaemic effect (16) and a marked immunostimulating activity (17). Our patient used it to relieve pain. The fresh rhizome contains up to 1.5% essential oil. The major constituents are 1,8-cineole, α -fenchyl acetate, camphor, methyl cinnamate, guaialol and sesquiterpenes (18). In dried galanga, the essential oil has a quantitatively different composition than fresh galanga with less variety in aroma components (cineole and farnesene, mostly) (19). The patch tests showed that the immunostimulating component was present in both the fresh and the dried galanga in the case reported here.

Allergic contact dermatitis is a T cell-mediated immune response. Mechanisms of tissue damage include direct cytotoxicity against keratinocytes, mostly mediated by $CD8^+$ T cells, and the T-cell release of cytokines that amplify the inflammatory response by targeting resident skin cells (21). Besides local reactions, secondary dissemination may occur with the manifestation of erythema multiforme-like, purpuric and vasculitis-like eruptions and so on. It is currently thought that

Table 1. Result of patch tests

Allergens	Day 2	Day 3	Day 4
Fresh <i>Alpinia galanga</i>	+++	+++	+++
Fried <i>A. galanga</i>	++	++	++
Fresh <i>A. galanga</i> 10% petrolatum (pet.)	++	++	++
Fried <i>A. galanga</i> 10% pet.	++	++	++
Fresh <i>A. galanga</i> 2% pet.	+	++	++
Fried <i>A. galanga</i> 2% pet.	+	++	++
Oil of <i>Cinnamomum camphora</i>	—	—	—
Mixtures of 1+7	++	++	++
Mixtures of 2+7	++	++	++
Petrolatum	—	—	—
Fragrance mix (sorbitan sesquioleate)	+	+	+
Sorbitan Sesquioleate	+	+	+

erythema multiforme is a cell-mediated delayed-type hypersensitivity leading to the damage of keratinocyte (22). The haptens in *A. galanga* would also be a strong allergen to T cells and increase mitogenic activities and systemic spreading. Consequently, we can see localized allergic contact dermatitis with disseminated erythema multiforme clinically.

Our report shows there is a strong allergen in *A. galanga* that can induce erythema multiforme-like generalized allergic contact dermatitis to specific populations. Herbal medicine and Southeast Asian cuisine are the most frequent sources of this allergen.

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Contact dermatitis around a tracheostoma due to salbutamol sulfate and Aldecin®

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Contact dermatitis around a tracheostoma is quite rare. So far, there have been only 2 reports about this in medical literature. We, in this study, report herewith contact dermatitis in a 61-year-old Japanese man around a tracheostoma due to salbutamol sulfate and Aldecin®. The patient used inhaled Sultanol® and Aldecin® for the treatment for allergic asthma. On examination, it was found that there was lichenified, exudative erythema with pigmentation around the tracheostoma. Patch testing with 1% aq. Sultanol® and Aldecin® revealed a positive reaction. Furthermore, patch testing for salbutamol sulfate 1% pet. also showed positive reaction. Although the contact allergen of our patient has not been fully determined (beclomethasone or other ingredients), this must be the first reported case of double contact dermatitis around a tracheostoma from salbutamol and Aldecin®.

Key words: contact dermatitis; asthma; patch test.

Case Report

A 61-year-old Japanese man was referred to our department because of pruritic eruption around the tracheostoma. 4 years before admission, he was diagnosed with laryngeal squamous cell carcinoma; a total laryngectomy and a tracheostoma were conducted. 1 year before admission, inhaled salbutamol sulfate aerosol (Sultanol®; 0.13% of salbutamol sulfate and other ingredients: 1,1,1,2-tetrafluoroethane) and beclomethasone dipropionate aerosol (Aldecin®; 7 mg of beclomethasone dipropionate in 12 g of Aldecin® and other ingredients: oleic acid, dichlorodifluoromethane and trichloromonofluoromethane) were started for

allergic asthma. After that, the patient noticed a worsening itch around the tracheostoma. On examination, it was found that there was lichenified, exudative erythema with pigmentation around the tracheostoma (Fig. 1). There were no symptoms inside the trachea. We suspected contact dermatitis from the Sultanol® and Aldecin®. The dermatitis cleared with oral prednisolone. He was patch-tested with 1% aq. Sultanol® and Aldecin®, using Finn chambers on Scanpor® (Norgesplaster A/S, Vennessla, Norway). Readings were made at 48, 72 hr and 7 days, according to International Contact Dermatitis Research Group (ICDRG) recommendations. He showed positive reaction to Sultanol® (++) and Aldecin® (++) . We performed patch testing of Aldecin® 2 weeks after that of Sultanol®. Pursuing this further, we also performed patch testing for salbutamol sulfate 1% pet., to which he showed a positive reaction (++) . Unfortunately, we could not obtain any ingredients of Aldecin® (major ingredient: beclomethasone dipropionate) from the pharmaceutical company. Therefore, we diagnosed this patient's condition as contact dermatitis induced by salbutamol sulfate and Aldecin®. Direct insertion of the inhalation device into the trachea has prevented his symptom.

Discussion

Contact dermatitis around a tracheostoma is quite rare, and to our knowledge, it has previously been reported only twice (1, 2).

Salbutamol, a selective β -adrenergic stimulant of the bronchi, is an

anti-asthma drug. Side-effects from salbutamol are quite rare, and there has been only one report of contact dermatitis (3). In that report, the concentration used in patch testing was 5% pet. In this report, we induced a positive reaction at a lower concentration (1% pet.)

Inhaled corticosteroids are also used in asthma. Allergic side-effects from inhaled corticosteroids are less common than those of topical corticosteroids. Among them, allergic reaction to beclomethasone dipropionate is rarely reported. There have been only 2 reports of allergic contact dermatitis from beclomethasone dipropionate (4, 5). Although the contact allergen of our patient has not fully been determined (beclomethasone or other ingredients?), to our knowledge, this is the first reported case of double contact dermatitis around a tracheostoma from salbutamol and Aldecin®.

The reason why these inhalants did not exacerbate the patient's asthma and did not provoke stomatitis but caused dermatitis is unknown. We speculate that the immune system of the mucous membrane might differ from that of the skin, as Tani et al. (5) suggested.

The reason why oral prednisolone, which also belongs to the corticosteroids, cleared the patient's symptoms is unknown. According to their chemical structures, corticosteroids are divided into 4 groups – A, B, C and D (6). While beclomethasone dipropionate belongs to group D (ester group corticosteroids), prednisolone belongs to group A (6). Therefore, we speculated that the antigenicity between the corticosteroid groups differs.



Fig. 1. Clinical appearance of lichenified, exudative erythema with pigmentation around the tracheostoma.

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Connubial allergic contact dermatitis to Euxyl K 400

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Key words: connubial; consort dermatitis; euxyl K 400.

Connubial or Consort allergic contact dermatitis is a dermatitis in which lesions are due to a substance used by the partner. Reported cases are produced after the use of perfumes (1), cosmetic products containing *Compositae* plants extracts (2), hair

care products (3) and feminine hygiene products such as vaginal lubricants containing propyleneglycol, spermicides containing mercurial salts (4), antiseptics such as clorhexidine or nifuratel and antifungal agents like clotrimazole (5). To our knowledge, this is the first case reported of connubial allergic contact dermatitis by the widespread conservative used Euxyl K 400.

Case Report

A 29-year-old woman complained of recurrent episodes of vesicular and papular lesions located on the limbs presented along the previous year. Lesions were grouped but in different areas of the extremities at each episode. The last time the patient had a clear hand form-like lesion on her right thigh after the recent use of a moisturizing hand cream by her husband (Tulipan Negro®). She had a long history of itching after the use of many cosmetics, and the only moisturizing agent used by the patient was liquid petrolatum. The application of the suspected cream on the antecubital area resulted with an eczematous lesion at 30 min after the first application. Patch tests with the Spanish standard series (GEIDC) and cosmetic series (Chemotechnique® Diagnostics Vellinge, Sweden) were observed after 2 days and 4 days and revealed positive to the following agents: Euxyl K 400 (+++), methyl dibromoglutaronitrile (+++), cobalt (++), cocamidopropylbetaime (+), benzothiazole (+), essential oils (+) and clorometil-isotiazolin-3-ona-Khaton (+). Balsam Peru and fragrance mix were negatives. It was revealed that the hand cream used by the husband contained methyl dibromoglutaronitrile. It did not contain any other components to which the patient was sensitized. The diagnosis was connubial allergic contact dermatitis by methyl dibromoglutaronitrile.

Discussion

Euxyl K 400 contains 2 active ingredients: 2-phenoxyethanol and methyl dibromoglutaronitrile. This last element is the main factor of allergic reactions (6). Since the introduction of methyl dibromoglutaronitrile as a preservative in 1985, it has emerged as an increasingly common cause of allergic contact dermatitis in Europe. Its expanding usage is

probably the main factor of the increase of reported cases during the last few years. The sensitized rate in Europe was 0.7% in 1991, while in 2000 it rose to 3.5% (7). This fact led the European Commission in 2002 to prohibit its usage in cosmetics and industrial products, being only permitted in rinsing products at a maximum concentration of 0.1% (8). After that disposition, other allergic contact dermatitis by methyl dibromoglutaronitrile cases have been subsequently reported concerning rinsing products (9). Moreover, there have been reported cases of allergic contact dermatitis due to the usage of personal care products. In March 2005, The European Commission recommends that the use in cosmetics of methyl dibromoglutaronitrile should be prohibited until information on safe consumer levels becomes available (10). Our case shows that methyl dibromoglutaronitrile is able to produce allergic dermatitis on sensitized patients even if patients do not apply it on themselves, and a limited usage of this preservative should be encouraged.

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Occupational trachyonychia due to psoriasis: report of a case successfully treated with oral acitretin

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Key words: nail psoriasis; occupational nail disorders; systemic acitretin; trachyonychia.

The nails are useful tools in many occupations but because of their exposed position are vulnerable to mechanical and chemical trauma (1). Repeated occupational trauma may induce several nail dystrophies and also precipitate nail changes in patients already affected by a dermatological disease as psoriasis.

In each case, nail fragility, roughness, onycholysis or other nail abnormalities may reduce the ability to manipulate small objects and limit manual performances. This may be a serious problem for subjects involved in occupations that require precise digital skilling such as jewellers and musicians (2, 3).

One of the possible manifestations of psoriasis related to occupational trauma is twenty nail dystrophy

(TND), a nail disorder characterized by longitudinal ridging with loss of the lustre.

TND, also called trachyonychia, is caused by inflammatory diseases that disturb nail matrix keratinization such as lichen planus, alopecia areata, psoriasis and eczema (4).

Case Report

Our patient was first visited in November 2004. He was a 38-year-old Caucasian man, in good health who consulted us because of fingernail and toenail painless abnormalities. This patient was a jeweller, and fingernail abnormalities gave him problems in performing his job.

Most of the nails, especially the 1st, the 2nd and the 3rd fingernails in the left hand and the 1st, the 3rd and the 5th in the right hand, were affected by subungueal hyperkeratosis, excessive longitudinal ridging, roughness and loss of lustre with dark staining of the nail plates. The other nails showed milder

abnormalities, such as pitting (Fig. 1). The patient also presented a plaque of psoriasis on the right palm. A diagnosis of TND due to psoriasis was made.

The patient was treated with oral acitretin at the daily dose of 0.3 mg/kg. After 3 months, the nail dystrophy was improved. Nails presented less roughness and ridging, and subungueal hyperkeratosis and pitting almost disappeared.

The patient did not show any side-effect because of retinoids during treatment.

Therapy was discontinued in June 2005, after 7 months of treatment. Nail dystrophy was completely recovered (Fig. 2), and the patient was able to continue his job.

Discussion

Manual workers, as goldsmith, are often subject to microtrauma from performing their work. In our patient, the repeated trauma to the nail matrix acted as a triggering



Fig. 1. Occupational trachyonychia because of psoriasis before treatment.



Fig. 2. Occupational trachyonychia completely recovered after systemic acitretin, despite some subungueal haematoma caused by working trauma.

cause to nail psoriasis (Koebner phenomenon).

The importance of nails in our patient's working ability suggested choosing a systemic therapy, as acitretin.

In the literature, an other case of nail psoriasis in a goldsmith is reported (5). In that case, nail abnormalities recovered with systemic acitretin 0.5 mg/kg/die. We preferred a lower dosage (0.3 mg/kg/die) to avoid nail side-effects. In fact, nail fragility as well as paronychia and multiple pyogenic granulomas arising from the proximal and lateral nail folds are typical side-effects of treatment with systemic retinoids (6).

This case shows that low-dose short-term acitretin therapy is effective in TND because of psoriasis worsened by occupational trauma. This treatment gave back to our patient his ability as jeweller without inducing any side-effect.

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Contact urticaria and allergic contact dermatitis to lidocaine in a patient sensitive to benzocaine and propolis

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Key words: allergic contact; anaesthetics; benzocaine; dermatitis; lidocaine; local; patch tests; propolis; quinones; urticaria.

Allergic contact dermatitis (ACD) to lidocaine is rare (1); simultaneous occurrence with type I hypersensitivity is extremely rare (2), while concomitant delayed contact sensitivity to lidocaine and benzocaine seems to be exceptional (3). In 1998, Weightman and Turner (3) reported 2 patients with ACD from lidocaine and positive patch test to benzocaine.

Patients and Methods

Among 128 patients who were evaluated for allergy to lidocaine between 1988 and 2004, there was only 1 patient with a history of sensitivity manifesting as dermatitis. A 47-year-old non-atopic woman had a 6-month history of a recurrent dermatitis of the perianal region. During the last episode of dermatitis, she was admitted to the hospital because of a widespread dermatitis and sudden occurrence of angioedema and generalized urticaria 1 hr after application of a lidocaine-containing antihemorrhoidal Novorectol-H[®] ointment. 6 weeks later, patch and scratch-chamber tests were performed. She had previously received local anaesthesia for dental care that was always well tolerated.

Patch and scratch-chamber testing

Patch tests (PTs) were applied to the back for 2 days using Finn Chambers

on Scanpor tape (Epitest Ltd Oy, Tuusula Finland). Readings were made after 20 min, on D2 and D3, and on D5 to D8, as recommended by the ICDRG (4). The patient was patch tested with Modolex[®] ointment (containing lidocaine hydrochloride 4% and calcium dobesilate 4%) as is, Novorectol-H[®] ointment (containing cortisone 0.5%, lidocaine 5%, bismuth subgallate 5% and zinc oxide 5%) as is, and with Hemoroidal ointment (containing propolis) as is, the European standard and specific series (Hermal-Trolab[®], Reinbeck, Germany) as well as with lidocaine 1% preservative-free aqueous solution, 2% pet. and 5% pet. In order to assess immediate contact urticarial reaction, PTs were removed 20 min after application, and if gave no response, reapplied immediately at the same site (3). Additionally, scratch-chamber testing was done subsequently. Scratch-chamber tests (SCTs) were performed on the arm according to the ICDRG recommendations, with allergens that produced $\geq +$ PT reaction on D2 and/or D3 (5). The local reaction was regarded as positive if the mean diameter was greater than that of the negative control (normal saline, pet.) by more than 5 mm (+), 5–10 mm (++), 10–15 mm (+++) or with pseudopodia (+++). The scoring was done according to the morphology and severity of symptoms (5, 6). Control tests were performed on 20 atopic patients. Patients with current atopic manifestations, positive skin tests and specific IgE to common inhalant allergens were considered atopics.

Results

Positive PTs were obtained to ointments, lidocaine, benzocaine, propolis, monobenzene, hydroquinone, nickel sulfate, fragrance mix, cinnamyl alcohol, lemon grass oil, lemon oil and peppermint oil (Table 1). There was no PT urticarial reactivity to any allergen, except a slight erythema to balsam of Peru. Type I reaction with erythema and swelling of eyelids and lips, generalized urticaria and dyspnea developed in association with immediate urticarial SCT to lidocaine and Novorectol-H[®] (Table 2). Control SCTs with lidocaine as well as with other allergens subsequently tested were negative.

Table 1. Positive patch tests

Allergen	Concentration (%)	Vehicle	D2	D3	D8
Modolex [®]	As is	As is	++	+++	+++
Novorectol-H [®]	As is	As is	++	+++	+++
Hemoroidal	As is	As is	++	+++	+++
Nickel sulfate	5	pet.	++	++	NR
Fragrance mix	8	pet.	++	++	NR
Hydroquinone	1	pet.	++	++	NR
Benzocaine	5	pet.	++	++	NR
Lidocaine hydrochloride	15	pet.	++	+++	NR
Propolis	10	pet.	++	++	NR
Monobenzene	1	pet.	++	++	NR
Cinnamyl alcohol	1	pet.	++	++	NR
Lemon grass oil	2	pet.	++	++	NR
Lemon oil	2	pet.	++	++	NR
Peppermint oil	2	pet.	++	++	NR
Lidocaine hydrochloride	5	pet.	++	+++	NR
Lidocaine hydrochloride	2	pet.	++	+++	NR
Lidocaine hydrochloride	1	Aqua	++	+++	NR

NR = not read.

Table 2. Scratch-chamber testing with lidocaine

Allergen	Concentration (%)	Vehicle	20 min
Novorectol-H [®] ointment	As is	As is	++
Lidocaine hydrochloride	1	aqua	+++
Lidocaine hydrochloride	2	pet.	++
Lidocaine hydrochloride	15	pet.	++
Benzocaine	5	pet.	—

Discussion

Most recently, Waton et al. (7) reported the first case of contact urticaria to Elma[®] cream, due to lidocaine. Sensitization to lidocaine in our patient may have occurred and manifested firstly as ACD, which is similar to the case reported by Downs et al. (2). SCTs were performed in order to exclude a false-negative PT reaction. SCTs with Novorectol-H[®] as is and lidocaine were positive after 20 min and associated with generalized cutaneous and extracutaneous reactions, thus classified as contact urticaria syndrome (CUS) stage between 2 and 3 (6).

ACD to lidocaine has rarely been reported since 1998 (8, 9), when Weightman and Turner (3) reported 29 cases of ACD to lidocaine in Australia, and reviewed 33 cases previously reported worldwide.

Simultaneous occurrence of type I and type IV hypersensitivity to lidocaine was previously reported by Downs et al. (2); only the latter was confirmed by patch testing.

Sensitivity to benzocaine was separately acquired, since there is a wide

variety of topical over-the-counter benzocaine-containing products on the market in Serbia and Montenegro. Moreover, it accounts for 2% of all clinically relevant allergies among patients with ACD (10). Patients sensitive to amide LAs are unlikely to demonstrate cross-sensitivity to ester LAs (11). In 1998, Weightman and Turner (3) described 2 patients with positive PTs to lidocaine and benzocaine, without comment whether it was cosensitization or cross-reactivity between amide and ester LAs (3).

The patient could become sensitized to propolis through the use of an over-the-counter propolis-containing Hemoroidal ointment. Propolis is among the allergens to which all patients with anogenital complaints should be tested (12). The patient was sensitive to hydroquinone. Reactivity to monobenzene was considered as cross-reaction with hydroquinone.

Conclusion

As far as the world literature is concerned, our patient sensitive to lidocaine, benzocaine and propolis

represents the 1st case where both immediate and delayed sensitivity to lidocaine were confirmed by positive skin tests and only the 3rd report on concomitant sensitivity to 2 unrelated local anaesthetics.

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Contact dermatitis to Furacin®

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Key words: contact dermatitis; Furacin®; nitrofurazone; polyethylene glycol.

Furacin® (Seid, Barcelona, Spain) is a topical antimicrobial containing nitrofurazone 0.2% and, as vehicle, polyethylene glycol (PEG).

Nitrofurazone or nitrofur (5-nitro-2-furaldehyde semicarbazone) is a strong sensitizer, causing severe allergic contact dermatitis (ACD) mainly in patients with stasis eczema, burns and other chronic dermatitis (1, 2).

PEGs are condensation polymers of ethylene glycol, extensively used as vehicles in topical medicaments, suppositories, insect repellents, cosmetics, toothpastes, spermicidal, etc. Considering their widespread use, sensitization to PEG is infrequent (3).

We report 5 cases of contact dermatitis to Furacin®. They referred local eczematous lesions 24–48 hr after application. 1 patient, who applied Furacin® to a burn on her forearm, presented eczematous lesions on her forearm, but curiously the application skin area was free of lesions. She referred another

eczematous episode on her eyelids, nose and lips after application of Furacin® to a burn on a finger of her hand. Again, no lesions appeared on her finger and hand.

Patch tests were carried out with Furacin® as is, nitrofurazone (1% in pet.) and PEG (4% in pet.). These resulted positive to Furacin® in all patients, to nitrofurazone in 4 patients and to PEG in 3 patients.

They were diagnosed of ACD to Furacin®. 4 patients were sensitized to nitrofurazone and 3 to PEG. Finally, 2 patients were sensitized to both nitrofurazone and PEG.

The combination of a potent allergen as nitrofurazone with PEG, a vehicle that enhances the bioavailability of topical medicaments, and its use on a damaged skin constitute all predisposing factors to develop an ACD. De Groot et al. (4) described a case of ACD to furazolidone. Furazolidone 2% patch test was negative in pet. but positive in PEG-400 and in alcohol (both vehicles were patch tested separately with negative results), showing how PEG enhanced the cutaneous penetration of furazolidone.

Although PEG has been described as an infrequent sensitizer by some authors (3), others have found different results. Bajaj et al. (5) found an incidence of PEG allergy of 5.3% in 120 suspected cases of topical medicaments sensitivity; Braun et al. described 4% positive reactions to PEG-300 in a group of 92 dermatological patients (6).

Several authors reported ACD to Furacin®. Braun et al. (1) studied 40 cases of sensitivity to Furacin®. 12 patients had a positive reaction to PEG, only 1 of them reacted to PEG alone; Guijarro et al. (7) reported a case of ACD to Furacin® with positive patch tests to nitrofurazone and PEG, as 2 of our patients; Stenveld et al. (8) described a case of ACD in a patient with chronic leg ulcers treated with Furacin® and other topical preparations containing PEG and propylene glycol, who was sensitized to both vehicles.

We want to point out the location of cutaneous lesions in 1 patient. The treated skin (the burn) was free of eczematous lesions. The patient denied the application of a topical corticosteroid or immunosuppressor on this area. We hypothesized that epidermal Langerhans' antigen-

presenting cells or lymphocyte functional capability was decreased due to the burn, as it has been demonstrated with ultraviolet radiation (9). Facial lesions could be explained by indirect contact through the hands.

Our results show the importance of patch testing with the individual constituents of topical medicaments. Sensitization to PEG may not be so infrequent. Lastly, as Furacin® is a very frequent cause of ACD, it should be used cautiously, mainly in patients with chronic dermatitis.

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Contact urticaria to *Cannabis sativa*

Contact Dermatitis 2006; 54: 127

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Key words: *Cannabis*; contact urticaria; occupational.

Case Report

A 29-year old technician working for the Forensic Science Service was referred to the clinic for rhinitis, headaches and urticarial wheals occurring within minutes following contact with *Cannabis* plants at work. She worked with *Cannabis* plants, stripping, grinding and growing them for 6 years. Her symptoms began 2 years after commencing this line of work and were gradually worsening with quicker onset post exposure. She was symptom-free during 2 episodes of maternity leave. She was non-atopic and otherwise fit and well. She did not use *Cannabis* recreationally.

Examination in clinic was unremarkable. Patch testing was carried out to the British Contact Dermatitis Society Standard Battery cosmetic, plant series and cannabis resin, leaf, flower and stem. This revealed a positive reaction only to Thiomersal. However, contact urticaria testing to dried and fresh cannabis leaf, flower and resin was positive. She has subsequently been moved away from cannabis plants and resin and remains symptom-free.

Discussion

The Cannabinaceae family consists of 3 species, *Cannabis sativa*, *Humulus lupulus* L and *Humulus japonica* (1). The *C. sativa* plant provides the fibre hemp from its stem, cannabis resin from its flowering tops, and birdseed and fishing bait from its seeds (1). It is mainly cultivated for its resin, which has mood-altering properties. Delta9-tetrahydrocannabinol (THC) and cannabidiol are major constituents of the resin. THC, the psychoactive

constituent, is present in high concentrations in marijuana but in low concentrations in industrial hemp, which is used for the manufacture of clothes, cosmetics and other materials (2). *H. lupulus* L provides hops and is used in the brewing industry for production of beer and other similar alcoholic beverages.

4 types of hypersensitivity reaction exist. Our patient developed contact urticaria, which is a Type I hypersensitivity reaction to cannabis. The wheal-and-flare reaction that appears when certain agents come in contact with the skin maybe of 2 types: immunologic (allergic) or non-immunologic (non-allergic) (3). We believe our patient developed immunologic urticaria as it occurred with a history of previous exposure without symptoms, with increased sensitization upon further exposure. Usually, a low proportion of exposed subjects are affected in immunological urticaria and it is more common in atopic individuals. It is usually mediated through IgE. However, IgG and IgM may also play a role in the activation of the innate pathway in immunological urticaria (3). Non-immunologic urticaria occurs without prior sensitization. It is the most common and potentially the least serious form of contact urticaria as severe systemic reactions are not evoked. It affects atopics and non-atopics equally. A probable cause is thought to be a direct influence of allergen on dermal vessels or a non-antibody-mediated release of vasoactive substances such as histamine, bradykinin or prostaglandins (3).

Several cases of Type I hypersensitivity to *Cannabis* have been reported but remain an uncommon finding in dermatological literature (4, 5). We would therefore like to highlight the role of this unusual allergen to our colleagues.

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Use of patch test in fixed drug eruption due to metamizole (Nolotil®)

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Key words: fixed drug eruption; metamizole; patch test.

Fixed drug eruption (FDE) is an adverse cutaneous drug reaction. It may present as localized or generalized and can be classified as bullous or macular. FDE is characterized by itching erythematous violaceous macules in the areas repeatedly exposed to a specific medication, leaving residual hyperpigmented lesions once the drug has been withdrawn. It has been attributed to over 120 different drugs.

Clinical Case

We present the case of a 39-year-old Vietnamese woman who came to the dermatology clinic due to slightly descamative erythematous brownish maculae on hands, feet and back. The patient had a known allergy to acetylsalicylic acid and to piroxicam. She stated that the lesions first appeared 5 days earlier, with itching erythematous-violaceous maculae on her back and acral areas after the

intake of 1 metamizole (Nolotil[®]) pill. Her case was diagnosed as FDE secondary to metamizole intake, and topical treatment with 0.1% triamcinolone acetonide and hydroxyzine 25 mg PO every 12 hr (BID) was initiated. Skin lesions progressively improved.

Patch tests with the standard and NSAID batteries performed 2 weeks after the acute episode were both negative. Liquid Nolotil[®] (metamizole) was applied occlusively on the back in the area where the FDE presented initially, with a positive skin reaction (++) after the application (Fig. 1).

Nolotil[®] applied on the arm, an area free of FDE lesions when the patient came to the clinic, was negative. 10 further tests with Nolotil[®] were all negative. The patient rejected the oral provocation test with metamizole, as she was breastfeeding a 2-month-old infant.

1 month later, occlusive 1% metamizole in Vaseline[®] was applied to the back area where the FDE first appeared and gave a positive skin reaction (++). 10 controls were also made, with negative results.

Discussion

Metamizole is one of the most frequently used analgesics in medical practice. Cases of urticaria-angioedema, erythroderma (1), generalized

acute exanthematic pustulosis (2), toxic epidermic necrolysis (3) and FDE (4) have been related to metamizole use.

The FDE diagnosis is based on clinical evaluation and the oral provocation test (5). To make the aetiological diagnosis of FDE in some situations, however, the topic provocation test has been used instead of the oral provocation in the areas where the lesions appeared for the first time (6).

The presence of intraepidermic memory CD8⁺ T cells has been demonstrated in high concentrations in the residual lesions of FDE. These CD8⁺ T cells become activated when the oral provocation test with the drug is made, and they release interferon- γ and tumour necrosis factor- α , which reactivate the lesion and produce epidermic injury (7). We believe this mechanism could be produced in the same way with the occlusive topical application (patch test) of the drug.

In some cases of FDE, due to metamizole, the topical provocation test with this drug has been reported to be positive in the area where the lesion first appeared (4, 6, 8). In 2 cases, the occlusive patch test produced a generalized FDE (6, 8). Gonzalo-Garijo et al. (8) thus suggested doing the patch test with metamizole with the lowest possible dose, between 1% and 10%, in an attempt to prevent possible general-

ized side effects. For localized FDE, we suggest the occlusive application of 1% metamizole in Vaseline[®], using the open patch only in cases of severe generalized FDE.

We recommend the patch test as the first diagnostic step in FDE cases due to metamizole, especially when the patient rejects the oral provocation test or when the test can produce unwanted side effects.

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Fig. 1. Skin-positive reaction ++ of the patch test with Nolotil[®] at the site where the fixed drug eruption lesion first appeared.

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