

CONTACT POINTS

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Nasal cannula-induced chemical depigmentation

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Key words: depigmentation; nasal cannula; polyvinyl chloride.

Case Report

A 64-year-old male had developed asymptomatic, well-defined depigmentation on the cheek and neck over the past 4 years. No rash, itching or other symptoms had occurred, other than a gradual depigmentation. Topical corticosteroids were not effective in restoring the pigmentation.

The patient has suffered from chronic obstructive pulmonary disease since 1997 and he was being treated with continuous oxygen therapy with 2 l/min of oxygen for 24 hr a day since 2000. He used a nasal cannula for oxygen administration and the depigmentation was seen to coincide with the area contacting the nasal cannula (Fig. 1a). The biopsy was not done as the lesion of the depigmentation was in the face. Based on this clinical finding, he was diagnosed with chemical depigmentation due to the nasal cannula. Instead of allowing the nasal cannula to make direct contact with the skin, he was advised to cover the cannula with cloth. Narrow band ultraviolet B (UVB) therapy was started twice a week with using a UVB machine that was made by Waldmann Medizintechnik, Germany. Repigmentation began to appear after 2 months of treatment and the lesion repigmented almost completely after 4 months (Fig. 1b).

The nasal cannula contained both polyvinyl chloride (PVC) and such

plasticizers as diethylhexyl phthalate, dibutyl phthalate and diethyl phthalate. Para-tertiary-butylphenol-formaldehyde resin known to cause depigmentation was not present in the cannula. The presence of PVC was confirmed by performing Fourier transform infrared (PA-FTIR) spectroscopy and the presence of phthalates was determined by gas chromatography-mass spectrometry (GC-MS). The patient was unwilling to undergo patch testing, either with the nasal cannula or relevant chemicals, after he was warned of the possibility of depigmentation at the patch-test site.

Discussion

Contact depigmentation can occur secondarily to a preceding allergic contact dermatitis or from the toxic effects of depigmenting chemicals. Thus, the depigmented area that is produced may become widespread and it may occur on areas other than those that are in direct contact with the offending chemical (1). Cutaneous chemical depigmentation may result from direct contact or from systemic exposure of various phenolic and catecholic derivatives, and the sulfhydryl compounds (2). Other causative chemicals are monobenzyl ether of the hydroquinone used in rubber, adhesive tapes, diaphragms and rubber condoms (3). For our case, the localization of the depigmented lesions exactly beneath the nasal cannula on the cheek and neck, and the repigmentation induced by avoiding direct contact with the nasal cannula and UVB therapy confirmed the diagnosis that the nasal cannula induced the chemical depigmentation. Further more, chemical analysis showed the nasal cannula used by this patient contained PVC and phthalates.

PVC is one of the most inexpensive thermoplastics and it is the most widely used plastic after polyethylene. It is made by polymerization of the vinyl chloride monomer. The final PVC products, when completely

cured or hardened, are generally considered to be inert and non-hazardous to the skin. There are always a number of additives included in the final PVC products such as plasticizers and stabilizers, as well as molecules of the monomer. Di(2-ethylhexyl) phthalate (DOP), butyl benzyl phthalate and di-*N*-butyl maleate are used as plasticizers for soft PVC (4). These plasticizers may cause contact dermatitis and also contact urticaria.

Chemical depigmentation due to PVC is a very rare condition, and to the best of our knowledge only 2 cases have been previously reported in the English literature. Frenk and Kocsis have reported on a case of depigmentation from adhesive tape which was made of PVC with a natural rubber adhesive base that contained a derivative of dihydroxy diphenyl methane (5). A stethoscope earpiece containing PVC and phthalates was also reported to induce chemical depigmentation on the contacting area (6). Although the exact mechanism of PVC that induces depigmentation has not been elucidated, increasing evidences have suggested that PVC can cause cutaneous chemical depigmentation, especially on an area with long-term contact to the PVC.

We report this case to point out that chemicals other than phenols can also cause depigmentation, and PVC should be added to the list of the chemicals that are capable of inducing depigmentation.

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Fig. 1. (a) Depigmentation in the area of contact with the adult nasal cannula. (b) Repigmentation following treatment.

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Cosmetic dermatitis in an Indian city

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Key words: contact dermatitis; cosmetic dermatitis; patch testing.

The strong desire of individuals to improve their appearance has led to an increased demand for newer cosmetics, contributing to increased incidence of cosmetic dermatitis (1–3). Patch testing helps to confirm and identify the allergen.

Materials and Methods

Fifty cases of suspected allergy to cosmetics were included. Patch testing was done using kit from Systopic Laboratories Pvt. Ltd, New Delhi, India, which included 38 allergens of cosmetic and 12 of standard series. Wherever possible a sample of the suspected cosmetic was added. Reading was done after 48 hrs.

Results

Among males, majority (31.58%) belonged to 41–50 years whereas among females most (38.71%) were 21–30 years of age. Most males (42.11%) had allergy to hair dye compared to females (45.16%) having allergy to face creams. Contact dermatitis was confirmed in 38 cases (76%) by patch testing. Of 2531 patches, 95

Table 1. Showing positive reacting antigens on patch testing

Antigen	Grading of positive reactions									
	Males					Females				
	+	++	+++	T	(%)	+	++	+++	T	(%)
Gallate mix	8		1	9	47.37	9	2		11	35.48
Cetrimide	5		1	6	31.58	5	3		8	25.81
Thiomersal	1	1	1	3	15.79	2	2	3	7	22.58
Paraphenylene diamine	3		3	6	31.58	1			1	3.26
Parabens	1			1	5.26	1	1		2	6.45
Fragrance mix	1			1	5.26	1	1		2	6.45
Quarternium	1			1	5.26	1			1	3.26
Triethanolamine	1			1	5.26	1			1	3.26
Tert butyl hydro quinone						2			2	6.45
Stearyl alcohol						2			2	6.45
Polyoxy ethylene sorbital oleate						1			1	3.26
Benzyl salicylate	1			1	5.26					
Jasmine synthetic	1			1	5.26					
Imidazolidinyl urea	1			1	5.26					
Polyethylene glycol	1			1	5.26					
Butylated hydroxy anisole	1			1	5.26					
Kathon CG						1			1	3.26
Propylene glycol	1			1	5.26				1	3.26

(3.75%) had positive reactions. Table 1 shows the reaction pattern.

Discussion

This study showed the age group to have widened at both extremes, that is, 13–67 years compared to 20–60 years in an earlier study (4), which could be due to increase in use of cosmetics among young and elderly. In the same study (4) the duration of dermatitis prior to consulting the dermatologist was 8 days or longer, in our study it was 1 month or more. Mehta and Reddy (5) in their study on Indian patients reported that bindi, hair dye and face creams were the most common allergens; in this study face creams (30%), hair dye (16%) and soaps (14%) were the suspected cosmetics. Gallate mix positivity was high probably due to the presence of propyl gallate, an antioxidant in creams. Fisher (6) stated that the use of liposome containing creams may unleash a rise in propyl gallate allergy. Direct testing with cosmetic showed positive in 71%, whereas Mehta and Reddy (5) reported a 50% positivity. Dogra and Minocha (7) reported 3.2% positive of 2065 patches, our study showed 3.75% positive.

Once a diagnosis of cosmetic dermatitis is made, patients should be able to purchase safe cosmetics; in India this can only be achieved when declaration of ingredients on the label is made mandatory.

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Allergic contact dermatitis due to orthopedic shoes and a prosthesis for an amputated foot

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Key words: allergic contact dermatitis; chromate; prosthesis; PTBPF resin; shoe leather.

Case Report

A 72-year-old man with an amputation at the third distal of the left foot, which occurred after an accident at work, presented an erythematous oedematous scaly dermatitis involving his stump and extending to the leg (Fig. 1); also the right foot and leg showed mild signs of dermatitis. Eczema had worsened after a previous topical keratolytic treatment for plantar hyperkeratosis.

A cutaneous biopsy from the left leg had been performed; histological picture was consistent with chronic eczematous dermatitis.

A personal history of hand eczema was reported with a documented



Fig. 1. Chronic eczema on the stump lesions at the third distal of the left foot.

sensitization to potassium dichromate, related to his past as a bricklayer.

The patient wore an orthopaedic shoe with a mobile plastic prosthesis covered with leather replacing the front part of the foot (Fig. 2).

We performed patch tests with the Italian standard SIDAPA series, with following results: cobalt chloride (+ D2/+ + D3), nickel sulfate (+ + D2/+ + D3), potassium dichromate (+ + + D2/+ + + D3), *para*-tertiary-butylphenol-formaldehyde resin or PTBPF resin (+ + D2/+ + D3).

The dermatitis healed with oral antihistamines, systemic and topical steroids. No recurrences were observed after replacing the old prosthesis and shoes with new chromate-free and PTBPF resin-free shoes and wearing an extra pairs of socks.

Discussion

Foot eczema due to shoes is fairly common, ranging from 3% to

12.5%, and is usually caused by leather, adhesives, rubber components, linings and dyes (1, 2).

In our case, the clinical pattern of the dermatitis, its preferential location on the amputation stump and the past history of occupational sensitization to potassium dichromate, all pointed to a contact dermatitis due to allergens in footwear.

Potassium dichromate, found in construction materials (primary sensitizers in our patient), is also a tanning agent for leather products (2–5).

Para-tertiary-butylphenol-formaldehyde resin (PTBPF resin) is one of the most common causes of shoe dermatitis because it is widely used in adhesive formulations for leather articles (1, 2, 6).

Cobalt is another frequent allergen and it can be a coallergen with chrome or nickel. Moreover, cobalt compounds may be used as dyes or pigments for footwear, or as catalysts in polyester adhesives (1, 2).



Fig. 2. Shoe leather and orthopaedic foot prosthesis used by the patient.

The relevance of positive reaction to nickel is difficult to evaluate because it is an ubiquitous metal and is rarely a relevant allergen for foot dermatitis (1, 5).

Shoe allergens can be leached out by profuse sweating associated with a hot climate, friction and occlusion, particularly in old shoes (3, 4, 6).

We hypothesize that keratolytic agents may weaken the epidermal barrier and increase allergen penetration, as occurred in our patient.

Sensitization to footwear allergens represents a well-known issue because it is very difficult for patients to avoid leather shoes and to find alternative footwear even after the allergen has been identified (4, 6). Furthermore, some authors demonstrated the presence of potential allergens even in hypoallergenic shoe leather (4).

The problem of allergy to shoes increases in case of orthopaedic foot devices. Contact sensitization to the amputation prosthesis in the disabled is rarely reported (7).

In our patient, despite chromate sensitivity having been previously diagnosed, his prosthesis was covered with leather bonded with an adhesive containing PTBPF resin (as confirmed by the manufacturer), which played an additional role in inducing contact dermatitis (2, 7, 8).

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Allergic contact dermatitis due to diethyl sebacate in a hand cream

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Key words: allergic contact dermatitis; diethyl sebacate; hand cream.

Case Report

A 49-year-old woman visited us with pruritic erythematous macules on the dorsa of hands, where she had applied a hand cream containing 10% urea. The lesions were only observed on the applied area. A

2-day closed patch test was done with the cream as is and petrolatum. A positive reaction was observed to the cream as is at D2 (+) and D3 (+). 21 days later, a second patch test was done using each of the cream's ingredients, provided by the manufacturer. This second test produced a positive reaction to diethyl sebacate 5% pet. at D2 (+), D3 (+) and D7 (+) (Fig. 1). Other ingredients and petrolatum as is were all negative.

Discussion

Diethyl sebacate is widely used in USA and Japan as an emulsifier in cosmetics, hand creams, skin- and hair-care products, and topical medicaments of antimycotic, corticosteroidal, non-steroidal anti-inflammatory ointments, creams and lotions. Diethyl sebacate is added to facilitate the penetration of effective ingredients (1). Until now, 6 cases of allergic sensitization have been reported (1–5). All of these cases were sensitized when using antimycotic medicaments (1–5). Therefore, this is the first report of allergic contact dermatitis from diethyl sebacate in a hand cream.

Previously, patch testing was done with diethyl sebacate 20%–30% in ethanol (1, 2). We confirmed positive reaction to diethyl sebacate to 1% and 10% pet., and 1% and 10% eth (3). Recent 2 cases (4, 5) and the present case showed positive reaction to diethyl sebacate 5% pet. The observation suggests that diethyl sebacate 5% pet. or less than 5% pet. is appropriate for patch testing.

Considering the function of diethyl sebacate in facilitating the penetration of effective ingredients, allergic reactions to it may be more common than is generally realized.

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Allergic contact dermatitis from a degreaser

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Key words: citrus oil, contact dermatitis, degreaser, limonene, occupational, oxidation products, solvent, window installer.

Case Report

A 52-year old installer of windows presented with a dyshidrotic and



Fig. 1. A patch test positive to diethyl sebacate 5% pet. at day 7.

fissured, hyperkeratotic dermatitis of the fingers, which had existed for several months. According to the patient, there was a clear correlation with his work where he came in contact with acrylic glues and several degreasers and detergents.

The patient was patch tested with the European standard series, plastic and glues series (Chemotechnique Diagnostics, Malmö, Sweden), several acrylates (Chemotechnique Diagnostics, Malmö, Sweden) and his own products (acrylate-based glues, degreasers, thinners, organic solvents), the latter being tested with semiopen tests. Only the degreaser 'Reynaers aluminium(086.9181 Alucare, Belgium)' showed a 1+ reaction at D2 and D4.

Because the label of this degreaser indicated 'active component is a solvent obtained from the treatment of citrus fruits and has a lemon smell', further patch testing was done with oxidized *R*- and *S*-limonene (previously called *D*- and *L*-limonene, respectively) (3% in petrolatum), obtained from the Department of Dermatochemistry and Skin Allergy (Department of Chemistry, Göteborg University), both showing a 2+ reaction at D2.

Avoiding this product has led to a clear improvement but not a complete resolution of his hand dermatitis, which was also partly irritant. Unfortunately, we were unable to analyse the degreaser for the presence of oxidized limonene.

Discussion

Limonene, like other monoterpenes, occurs naturally in several botanical species such as in essential oils extracted from trees, plants and fruits. Citrus oil contains a very high (95%) concentration of limonene but different amounts of it are also found in many other essential oils (e.g. tea tree oil), nowadays being very popular as natural remedies (1).

Limonene is used as a degreaser substituting chlorinated hydrocarbons, chlorofluorocarbons and other solvents. It is used in degreasing metals (30% limonene) prior to industrial painting, for cleaning in the electronic industry (50–100% limonene) and printing industry (30–100% limonene), and as a solvent in paints (2). It is also used as

a solvent in histological laboratories (3) and as a flavour and fragrance additive in food, household cleaning products and perfumes. The popularity of limonene for domestic and occupational products and for cosmetics was demonstrated in several studies (4, 5).

Limonene exists as two optical isomers, *R*- and *S*-limonene, and the racemic mixture dipentene. The purity of commercial *R*-limonene is about 90–98%.

Pure *R*-limonene in high concentrations is a strong irritant, but not allergenic. Limonene easily oxidizes upon air-exposure and forms allergenic oxidation products under experimental conditions that mimic normal storage and handling. Because of this, oxidized limonene was proven to be a sensitizer both in animal and human studies, whereas the non-oxidized mother compound did not cause contact allergy (6, 7).

The allergenicity depends on the oxidation products formed, the main allergenic culprit being limonene hydroperoxide. Furthermore, limonene oxide and carvone, two other degradation compounds with allergenic potential were also identified (7, 8).

Allergic reactions to limonene have been described to degreasers used in car mechanics (9), wax polish (10) and hand cleansers (11). However, the purity and the presence of oxidation products in the limonene patch-test material was not considered in those early reports. Contact allergy to oxidized *R*- and *S*-limonene was also found in a large group of hand-eczema patients and thus seems to be an important allergen in hand dermatitis (12).

It is also an important allergen in essential oils (13) and because it is one of the most commonly used fragrance chemicals in scented products (household, cosmetics), it should also be tested in suspected fragrance allergy, all the more because it will not be detected by the main tool for testing fragrance allergy in the standard series, i.e. the fragrance mix (7).

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Balsam of Peru or Balsam of El Salvador?

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Key words: balsam of Peru; El Salvador; history.

It is well known that balsam of Peru or Peruvian balsam is a dark brown, viscous fluid that is still used in the pharmaceutical (e.g. wound healing ointments), cosmetic (e.g. perfumed products), flavoring industries (e.g. sweets, chocolate, drinks, and pastry), and tobacco industry (flavoring of cigarettes) (1). What is not well known is the history behind the name of this resin. Balsam of Peru is extracted from the wounded bark of large trees (*Myroxylon pereirae*), which grow almost exclusively along the coast of El Salvador and not Peru. The misleading name of balsam of Peru comes from the fact that in the 16th century, this balsam was originally packed and shipped to Europe from the port of Callao in Lima, Peru (2–5), one of the main ports of the time in the New World (6). Interestingly, balsam of Peru also was extremely valued for religious ceremonies in Spain and thus was an attraction to robbers in the New World. To distract merchants and pirates from its true origin, the Spanish authorities exported balsam of Peru from Peru around Cape Horn, rather than directly from El Salvador (7, 8). In his seminal monograph on balsam of Peru, Hjorth (9) explains the origin of this misnomer by mistakenly stating that El Salvador belongs to the Viceroyalty of Peru. At that time, Peru had a large political and administrative territory, which only reached to Panama, while El Salvador was part of the General Capitanía of Guatemala (10). We would like to correct this small historic detail since Hjorth's well written thesis is frequently referenced.

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Severe adverse cutaneous reaction to insulin due to cresol sensitivity

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We present the case of an 80-year-old lady known to be sensitive to chlorocresol (4-chloro-3-methyl phenol) who developed severe erythrodermic exfoliative dermatitis with atypical features 2 weeks after commencing subcutaneous insulin. All medications except insulin were stopped, without major improvement. It was noted that the insulin contained m-cresol (m-methyl phenol) so a parabens-based insulin was substituted. There was a significant improvement in her clinical condition within 72 hr. Further patch and intradermal testing to the insulin and m-cresol was planned, but she developed a nosocomial infection and died. We hypothesize that the adverse cutaneous reaction was a systemic manifestation of cresol sensitivity, given the rapid clinical resolution on changing insulins and the previously demonstrated sensitivity to chlorocresol, particularly as cross-reactivity between different low molecular weight methyl phenols is documented. Local injection site reactions and systemic side-effects including nausea, diarrhoea and vomiting have previously been reported with cresol-containing insulins, although to our knowledge, this is the first reported case of a severe cutaneous reaction. It is important to be aware of m-cresol as a potential allergen, as it is contained in most commercially available insulins.

Key words: adverse drug reaction; cresol; insulin.

Case Report

Most adverse cutaneous sequelae to insulin arise from IgE-mediated reactions to protamine, protein contaminants, preservatives or insulin and manifest as localized or generalized urticaria (1). Here, we report a severe cutaneous reaction to insulin which we hypothesize is a manifestation of systemic contact sensitivity to cresol, a preservative found in most insulins.

Conflicts of interest: None

Our patient, an 80-year-old lady with type 2 diabetes, was first seen in 2003 with moderately severe generalized dermatitis that settled rapidly with potent topical corticosteroids. She had a '+' reaction to chlorocresol (4-chloro-3-methyl phenol) on patch testing. There were no further cutaneous episodes until 2 years later when she was started on subcutaneous insulin (Mixtard 30, Novo Nordisk, Bagsværd, Denmark) after an episode of hyperosmolar non-ketotic diabetic coma. She developed severe erythrodermic exfoliative dermatitis 2 weeks after commencing the insulin, with certain atypical features, including dusky areas ranging from 2 to 4 cm in diameter on the limbs, haemorrhagic crust on the lower lip, and punched-out ulcers in the vulva, perineum and lower legs. The clinical differential diagnosis included drug-induced atypical erythema multiforme, dermatitis, vasculitis and an immunobullous disorder. Initial biopsies (Fig. 1) showed a perivascular infiltrate of lymphocytes and eosinophils, several colloid bodies and negative immunofluorescence. All medications except insulin were stopped, including amitriptyline, aspirin, doxazocin, etodolac and furosemide. Bumetanide was given when a diuretic was needed, and intravenous insulin (Actrapid, Novo Nordisk) was administered on several occasions to control the diabetes. There was a slow and incomplete response to oral prednisolone 30 mg OD and a rapid and severe exacerbation on tapering this 3 weeks later. Repeat biopsies were consistent with previous findings. At this stage, it was noted that both the insulins

she was receiving contained m-cresol (m-methyl phenol). A parabens-based insulin was therefore substituted (Monotard, Novo Nordisk). There was noticeable improvement within 72 hr, with significant reduction in erythema and early epithelialization of ulcers. Oral steroids were tapered successfully as she continued to improve. Further patch and intradermal testing to the insulin and m-cresol was planned, but she developed a nosocomial infection during her recovery and died.

We hypothesize that the adverse cutaneous reaction was a systemic manifestation of cresol sensitivity because of the rapid clinical resolution on changing insulins and the previously demonstrated sensitivity to chlorocresol on patch testing, particularly as cross-reactivity between different low molecular weight methyl phenols has been documented (2). Several substances that cause a reaction on patch testing may cause a disseminated cutaneous eruption when administered orally or parenterally. Examples include nickel (3), gentamicin (4), aminophylline (5) and plant products such as Rhus (6). Systemic contact dermatitis may manifest as dermatitis, erythroderma, erythema multiforme, pompholyx and the baboon syndrome (7). Local injection site reactions and systemic side-effects including nausea, vomiting, diarrhoea, headache and sweating have previously been reported with m-cresol-containing insulins (8). However, this is the first reported case, to our knowledge, of a severe cutaneous reaction. It is important to be aware of m-cresol as a potential

allergen, as it is contained in most commercially available insulins.

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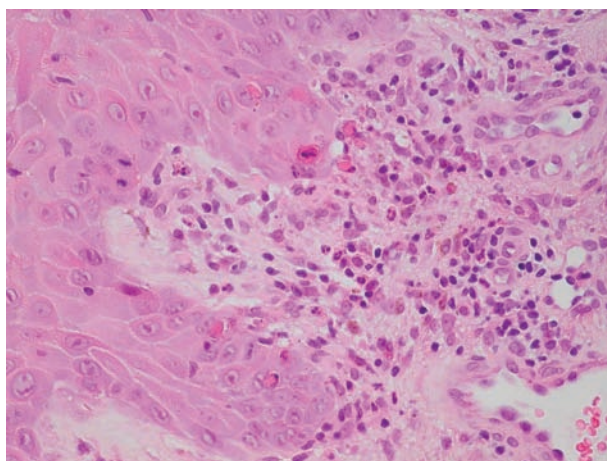


Fig. 1. Histological appearance demonstrating scattered necrotic keratinocytes (magnification: 40×).

Allergic contact dermatitis to glyceryl-hydrogenated rosinatate in a topical plaster

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Key words: allergic contact dermatitis; ester gum; glyceryl-hydrogenated rosinate; topical plaster; transdermal medications

Allergic contact dermatitis caused from transdermal medications are most of the times due to the active agent of the patch and rarely to its other components. We report the case of a patient affected by an eczematous dermatitis due to the resin of an anti-inflammatory medicated patch.

Case Report

A 30-year-old non-atopic woman was referred to our Unit because of the onset of a severe bullous eruption, that was located on the dorsal region of the right wrist and hand. It followed repeated applications of a medicated patch containing ketoprofen, which was prescribed to relieve the symptoms of a tendinitis. The clinical signs were restricted to the site of application of the patch. The symptoms regressed after the suspension of this medication and after 1 month of treatment with antiseptic compresses, topical antibiotics, topical corticosteroid (mometasone furoate) and oral antihistamine. After the healing, the patient was patch tested with the SIDAPA (Italian Society of Allergological, Occupational and Environmental Dermatology) standard series, then with the transdermal patch itself and with its constituents. These included ketoprofen (F.I.R.M.A.m S.p.A, Florence, Italy) (2% pet.), styrene-isoprene-styrene block copolymer (Variati S.p.A, Milan, Italy) (10% pet.), zinc stearate (SIGMA-Aldrich, Milan, Italy) (10% pet.), polyisobutylene (SIGMA-Aldrich, Italy) as is and glyceryl-hydrogenated rosinate (Variati S.p.A, Milan, Italy) (20% pet.). Strong positive reactions (+++) to the patch itself and to glyceryl-hydrogenated rosinate were observed at D2 and D4. Photopatch tests were negative. 5 healthy subjects patch tested as controls with the above mentioned substances showed no reactions.

Discussion

Ketoprofen is a non-steroidal anti-inflammatory drug which is widely

used in the treatment of musculo-skeletal diseases as systemic preparations (oral medications, suppositories and injections) and topical ones (gels, creams, lotions, ointments and plasters). Photocontact dermatitis due to topical ketoprofen is most frequently reported in countries where topical applications are popular and/or sun exposure is likely (1, 2); according to the literature, the causative preparations are creams, gels, lotions and plaster (3). Our case demonstrates that contact allergy to patches containing ketoprofen may also be due to other ingredients rather than to the anti-inflammatory drug itself. In particular, that should be suspected when the eczematous reaction appears during the patch treatment, when sun exposure is unlikely.

Glyceryl-hydrogenated rosinate (INCI name; CAS number 65997-13-9) also known as ester gum is a very strong sensitizer (4). It derives by purified natural rosin from pine trees combined with glycerin to form glycerol esters, which make it more soluble and minimizes tastes. Contact allergy to ester gums have been reported from lipsticks (5), hair-removal strips (5, 6), as well as from hypoallergenic tapes (7) and hydrocolloid dressing (8), but this is the first report of contact sensitization from medicated patch. In our case, in accordance to the literature, no reaction was found for colophony, confirming that the allergens in ester gum (the main one is thought to be glyceryl-1-monoabietate) are different from those in natural colophony (4, 9).

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Airborne occupational contact dermatitis caused by extremely low concentrations of budesonide

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Key words: airborne; allergic contact dermatitis; budesonide; contact allergy; occupational.

Budesonide was recommended to be included in the European standard

patch test series in 2000 (1). The presence of relatively new allergens in the standard series can sometimes help to rapidly show the diagnosis of clinically unspecific skin complaints, the cause of which otherwise probably would have been more difficult to detect. This report describes a case in which the cause of occupational dermatitis could be diagnosed by a positive reaction to budesonide in the standard series.

Case Report

The patient, a female assistant nurse, 48 years old, worked at an internal medicine ward. She was referred due to recurrent urticaria-like lesions, which had started 6 months ago and occurred only at work. The lesions were situated in her face, neck and arms. The patient herself suspected allergy to moulds, as a nearby ward was undergoing renovation because of damage due to damp. She described the skin lesions as fluctuating pruritic red patchy lesions without papules or oozing. She reported no previous skin complaints and no asthma or rhinoconjunctivitis. On clinical examination at our department she had no skin lesions and no dermatographism. Based on the information given by the referring physician and the patient, it was difficult to differentiate between urticaria and eczema. She was tested with the standard patch test series used at our department at the time of her examination, using Finn Chambers[®] (Epitest Ltd Oy, Tuusula, Finland) and Scanpor[®] tape (Alpharma AS, Vennessla, Norway) as adhesive. The tests were left on the back for 48 hr and read on day (D)3 and D7. The reactions were scored according to the International Contact Dermatitis Research Group (ICDRG) criteria. On D3 she had large papular reactions to budesonide 0.01% in petrolatum and hydrocortisone-17-butyrate 1% in ethanol (Chemotechnique Diagnostics[®], Tygelsjö, Sweden). All other tests in the standard series were negative. As immediate contact allergy could also be suspected, at D3 she was tested 'closed' and prick tested with the test preparations used for the patch tests. The tests were negative after 15 min and 60 min, but on D7 she had developed maculae with papular dermatitis on the sites on the arms where the tests had been performed. Thus, 15 min exposure to 0.01% budesonide was

enough to elicit allergic contact dermatitis. Blood tests for the investigation of specific antibodies to latex and moulds were negative and she had normal total IgE level. A more detailed history of her tasks at the ward revealed that she assisted some of the patients with their inhalations. Among medicaments used for the inhalations was Pulmicort[®], which contains budesonide. When reconsidering the time course of her lesions, she noticed that they had occurred when patients treated with Pulmicort[®] were nursed at the ward. Prior to her present work she had no obvious contact with corticosteroids. She was advised to not assist patients with their inhalations and to avoid being in the same room when patients were treated with inhalations with Pulmicort[®]. A visit at her work place was also undertaken. It was found that the masks used for the inhalations were perforated and that the medicaments could easily spread to the surrounding air (Fig. 1). Improvements of the equipment were initiated, and tighter masks and filters were procured. On a second visit at our department 6 weeks later, it was observed that the patient had not experienced any further problems with her skin after having been able to avoid assisting patients with inhalations and she continued working as an assistant nurse at the same ward. On this occasion, she was also patch tested with a tenfold dilution series of budesonide (Chemotechnique Diagnostics[®], Tygelsjö, Sweden) in ethanol ranging between 1% and 0.000000001%. 15 µL of the solutions

were applied to a filter paper disc on Finn Chambers[®] attached to the back with Scanpor[®] tape, left on the back for 48 hrs and scored according to the ICDRG criteria. She reacted positively to all steps of the dilutions series of budesonide, but not to ethanol 99.5%. The reactions to the lowest concentrations covered the whole patch test area and had erythema, infiltration and papules (Fig. 2). The lowest concentration showing a positive reaction corresponds to 0.0000003 µg/cm² or 4.2×10^8 molecules/cm². On a later test occasion she was tested with 0.0000000001% and 0.00000000001% and retested with ethanol 99.5%, but did not react to any of these test preparations.

Discussion

It was concluded that the patient had acquired airborne occupational contact dermatitis caused by budesonide and that her dermatitis could be elicited by extremely low doses of the contact allergen. The allergen was dissolved in the aerosol, which could be seen emitted from the equipment used at the work place for administering the drug to the patients (Fig. 1). The reported locations of the dermatitis supported this conclusion, because areas of the skin not covered with clothes were affected. In a recent (2001) update it was noticed that the number of reports on airborne contact dermatitis are increasing (2). Almost 100 reported allergens causing airborne contact dermatitis were found, among them 1 case of non-occupational airborne contact dermatitis to budesonide (3). Approximately 90% of the



Fig. 1. The equipment used for inhalation of Pulmicort[®] in the assistant nurse's work place at the time of the investigation. The arrows show the patterns of the aerosol seen.



Fig. 2. The dilution series of budesonide.

allergens reported had caused occupational airborne contact dermatitis (2). Recent reports on airborne occupational contact allergy due to pharmaceutical chemicals include tetrazepam, azithromycin, cyanamide and dibenzyl phosphate (4–8). Among adverse skin reactions described to be caused by inhalation of corticosteroids are pruritus, erythema and oedema of the mouth, eczematous lesions, and urticaria (9). Sensitization in patients using inhalations of corticosteroids has been reported (10). Inhalation of budesonide can reactivate skin sites of previously positive reactions to budesonide (11). In the present case, such flare up reactions were judged to be less likely since the lesions according to the patient's description had occurred only on skin not covered by clothes. In a patient treated with inhalations of budesonide and with symptoms suggesting a type I allergy but in which patch testing revealed a severe type IV allergy and no type I allergy has been described (12).

In the case reported here, positive reactions to extremely low concentrations of the allergen were found. Patch testing with serial dilutions of budesonide has shown positive reactions down to 0.0002% on D4 in 6/9 tested patients (13). Lower concentrations were not tested. At the first patch test occasion, this patient did not test negatively to any of the

dilution steps. On the second patch test occasion, the patient did not react to any lower concentration. To the best knowledge of the author, a positive reaction to 0.000000001% of a contact allergen corresponding to 0.0000003 $\mu\text{g}/\text{cm}^2$ is the lowest reported. In studies in which dilution series are tested, the threshold response can be defined as the lowest concentration giving any visible reaction (14). When corticosteroids are tested, the same criteria cannot be used because non-specific reactions such as erythema are very common at early readings (13). The lowest dose reported to give positive reactions varies between 0.00019 and 0.0004 $\mu\text{g}/\text{cm}^2$ for some main allergens in two phenol formaldehyde resins (15, 16) and the perfume contact allergen chloroatranol (14). Even if these results represent reactions to extremely low doses of the allergens tested, the dose eliciting a positive reaction in this case is approximately 1000 times lower. The difference could possibly be even greater considering the difference in criteria for allergic reactions in dilutions series used in the referred studies.

Conclusion

Based on the extremely low dose eliciting a positive reaction found by testing the dilutions series and

supported by the late reactions on the sites of the 'closed' tests with 0.01% budesonide, it can be concluded that this patient was extremely sensitive to budesonide. The possibility of occupational airborne contact allergy to budesonide should be considered in patients who are working where inhalations are administered, and should also be considered even if the lesions might mimic urticaria.

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Ammonium bisulfite contact dermatitis: face eczema due to a bleaching ointment used during hair-dyeing

Contact Dermatitis 2006; 55: 124

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Key words: allergic contact dermatitis; ammonium metabisulfite; antioxidants; bleaching agents; cosmetics; patch-tests; preservatives; sulfites

When contact dermatitis of the face happens after hair-dyeing, paraphenylenediamine (PPD) can often be identified as the responsible allergen, but other allergens should be suspected in some cases.

We report a case of contact dermatitis of the face due to ammonium bisulfite occurring after hair-dyeing.

Case Report

A 41-year-old woman with previous personal allergic rhinitis used to dye her hair with henna for many years without any problem. After applying exactly the same henna dye as usual,

her face started itching while she was still at the hair-dresser's shop. 24 hr later, she noticed itching and erythema over her forehead and temples and next day over her cheeks. After a 3-week course of steroid ointment, she was referred to us for patch-testing with a suspicion of contact dermatitis to her hair-dye. The patient denied any scalp involvement and admitted that the hairdresser had applied two protective ointments over her face during the procedure. The patient was tested (with Curatest) to European standard tray, a preservative and diluent series and the two ointments that had been used. The 48 hr and late readings demonstrated a negative PPD test but a positive test +++/+++ to the Colour Bleaching Ointment Preguard Wella (détachant couleur Preguard Wella). Subsequent patch-testing to the ingredients of the ointment provided by the pharmaceutical company (WELLA, Darmstadt, Germany) identified ammonium bisulfite 2% pet. as the responsible allergen with a +++/+++ positivity at both 48 hr and late readings.

Comments

Sulfites are preservatives used in food and beverages, especially wines, but they are also used in cosmetics and photographic as well as pharmaceutical industry (1). Sodium, potassium, calcium and ammonium sulfites can be used for their antibacterial, antioxidant and bleaching properties. They have been reported to induce asthma, anaphylactoid shock, urticaria and contact eczema (2, 3).

Only one previous case of contact dermatitis to ammonium bisulfite has been described in the literature (4): a 44-year-old woman developed eczema over her eyebrows after using a bleaching ointment containing ammonium bisulfite. The patient was positive to ammonium and sodium bisulfite.

Almost all the other cases described (5) concern sodium bisulfite included in local anaesthetic preparations (3), in topical steroids, in antifungal ointments (3), in an eye-drop preparation, in a dough for a baker (6) and in a photographic product (2). One single case was reported with potassium bisulfite (7). Sulfites are irritant and should not be patch-tested with a concentration above 5% pet. (5). The frequency of a positive test to sulfite

varies between 1.4% (8) and 1.7% (9), but clinical relevance is rarely established.

Knowing the ubiquity of sulfites and the few reports of contact dermatitis to these substances, we think that sulfites are rather weak sensitizers, but dermatologists should be aware that these preservatives may be used as bleaching agents especially in hair care.

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Allergic contact dermatitis due to benzyl alcohol in a hair dye

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Key words: allergic contact dermatitis;
cosmetics; fragrances; patch test.

Case Report

In August 2004, a 40-year-old woman with no previous skin diseases experienced itching followed by dermatitis and oedema on the forehead, periorbital area and behind the auricular folds 5 days after applying a semipermanent hair dye *Récital Préférence les Blondissimes* (L'Oreal, Paris, France). The patient had been using the same hair dye for 2 years without any complication. The lesions gradually disappeared in 2 weeks after frequent shampooing and topical corticosteroid.

Patch tests were performed with the True Test[®] + GEIDC Spanish standard series allergens and a hairdresser series (Hermal-Trolab). Open tests with the 3 components of the hair dye (conditioning colourant, developer cream and shine-enhancing conditioner) were also performed.

Readings at D2 and D4 were positive (+) to paraben mix. Conditioning colourant but neither developer cream nor shine-enhancing conditioner – containing methylparaben – applied as is on the forearm gave a +++ reaction at D2 and D4. Because of this, patch tests with ingredients of the suspected hair dye preparation, kindly provided by the manufacturer, were also performed. Readings at D2 and D4 were positive (+++) to benzyl alcohol (9.5% pet., as provided by the manufacturer). Patch test with benzyl alcohol 1% (Cosmetic series,

Hermal-Trolab) was also positive (++) at D2/D4.

Discussion

Phenylenediamine is the most frequent sensitizer in hairdressers' clients. On the contrary, only 2 of 261 patients with contact dermatitis who frequently underwent hairdressing procedures were sensitized to paraben mix in the study of Guerra et al. and none of them had positive patch test to benzyl alcohol (1).

In the present case, open test with conditioning colourant containing benzyl alcohol as well as patch test with this substance was positive. Benzyl alcohol is an aromatic preservative with anaesthetic and antipruritic actions. Despite its widespread use in topical medicaments and cosmetics, sensitization to this allergen is rare, being considered safe up to 10% for use in hair dyes (2). Nevertheless, benzyl alcohol has been reported as responsible for allergic contact dermatitis due to antibacterial and antimycotic creams, topical corticosteroids, sunscreens, analgesic sprays, sclerosing agents, epoxy adhesives and cutting oils (3).

On the contrary, sensitization to paraben mix was probably not relevant in the present case, because test with shine-enhancing conditioner containing methylparaben was negative. Because of the paraben paradox, patients who have positive patch test reactions to parabens may still be able to use cosmetics containing these substances (4). The positivity to paraben mix may also be explained by cross-sensitivity to benzylparaben, which is included in True Test[®] (5).

To our knowledge, this is the first report of allergic contact dermatitis due to benzyl alcohol in a hair dye.

Hair cosmetic producers provide the hairdresser with a wide variety of chemicals to fulfil stylist and customer desires. Because of this, an increasing number of allergens, which are not always included in standard or even hairdresser series, must be considered, as is the case of benzyl alcohol.

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