

CONTACT POINTS

CONTACT DERMATITIS 2005; 53: 114–122

• COPYRIGHT © BLACKWELL MUNKSGAARD

• ALL RIGHTS RESERVED

• CONTRIBUTIONS TO THIS SECTION WILL NOT UNDERGO PEER REVIEW, BUT WILL BE REVIEWED BY THE EDITOR •

Acrylates induced rhinitis and contact dermatitis

Contact Dermatitis 2005; 53: 114

M. C. Torres, T. Linares and M. D. Hernandez
Allergy Department, University Hospital La Fe, Valencia, Spain

Acrylates are a well-known cause of occupational contact dermatitis due to its widespread use in several settings such as dentistry, orthopaedic surgery, graphic industry and cosmetics. We describe the case of a manicurist who developed occupational rhinitis and allergic contact dermatitis induced by the application of acrylic-sculptured nails.

Key words: acrylates; contact dermatitis; occupational; rhinitis.

There are some reports of respiratory involvement in the manufacture ofcianoacrylates. Nevertheless, there is only one report of simultaneous skin and respiratory involvement (1).

We describe the case of a manicurist who developed occupational rhinitis and allergic contact dermatitis induced by the application of acrylic sculptured nails.

Case Report

A 28-year-old manicurist, who had worked making artificial acrylic nails for 1 year, was referred due to work-related nasal pruritus, rhinorrhea, sneezing, bilateral nasal obstruction and dermatitis of her nails folds and fingertips for the past 2 months.

The symptoms appeared 24 hr after working with sculptured nails and persisted 2–3 days without any treatment.

Patch testing was carried out according to the International Contact Dermatitis Research Group recommendations (2) with an acrylate series: acrylic acid, methacrylic acid, ethylacrylate (EA), acrylonitrile, ethyleneglycol dimethacrylate (EGDMA), ethylmethacrylate monomer (EMA), hydroxyethylmethacrylate (HEMA), methylmethacrylate monomer (MMA), methylmethacrylate

polymer and triethyleneglycol dimethacrylate (TREGDMA).

Results were strongly positive after 48 hr and 96 hr with EA, EGDMA, EMA, HEMA, MMA and TREGDMA. There were no immediate responses (20–30 min).

Immediate allergy to common aeroallergens, including house dust mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*), pollens (*Olea europaea*, *Parietaria judaica*, *Lolium perenne*, *Cynodon dactylon* and *Cupressus arizonica*), fungi (*Alternaria alternata*, *Cladosporium herbarum*, *Aspergillus*, *Penicillium*, *Mucor*, *Pullularia* and *Rhizopus*) and dander (cat and dog) were tested by skin prick tests, with negative results. Total immunoglobulin E was 20.9 kU/l.

Baseline lung and nasal function tests (spirometry, peak-flow monitoring 5 times a day during a 2-week working period and rhinomanometry), chest radiography, count blood cells and serum biochemistry were normal.

Nasal involvement was evaluated by a work trial with exposure to acrylates developing strong nasal symptoms. A nasal cytology performed 24 hr after work showed a percentage of eosinophils of 23%. Symptoms were alleviated by treatment with oral and topical antihistamines and only disappeared after changing of activity.

Discussion

This case illustrates that exposure to acrylates may induce occupational allergic contact dermatitis and rhinitis. The immunological background of this type of responses was confirmed by the positive results of patch testing which showed a delayed-type hypersensitivity to acrylates as well as the presence of eosinophil inflammation observed by nasal cytology obtained after exposure.

The mechanism of respiratory hypersensitivity by acrylates is still unknown. A type IV mechanism has been suggested based in the results of patch tests performed in patients with contact dermatitis (3) and a case of rhinoconjunctivitis and asthma (1). Some authors have been described systemic

symptoms during dental appointment using acrylates (4). Systemic reactions 6 hr after application of the patch test to acrylates also have been reported (5).

Nevertheless a type I (immediate hypersensitivity), other mechanisms of hypersensitivity or irritation cannot be excluded (3).

Acrylates are constituted by several monomers and oligomers, which form polymers acrylics. The acrylate monomers are powerful sensitizers, whereas the polymers are nonsensitizing. However, contact with the monomers may occur before polymerization, or some monomers may remain unpolymerized.

The positive patch test reactions to many acrylates may represent concomitant sensitization to several acrylates (1), although cross-reactivity are still a matter of debate. Concomitant sensitization is possible because impurities are contained in acrylates.

References

1. Lindström M, Alanko K, Keskinen H, Kanerva L. Dentist's occupational asthma, rhinoconjunctivitis, and allergic contact dermatitis from methacrylates. *Allergy* 2002; 57: 543–545.
2. Wahlberg J. Patch testing. In: *Textbook of Contact Dermatitis*, Rycroft R J G, Menné T, Frosch P J, Benezra C, (eds). Berlin: Springer-Verlag 1992, 250.
3. Estlander T, Kanerva L, Kari O, Jolanki R, Mölsä K. Occupational conjunctivitis associated with type IV allergy to methacrylates. *Allergy* 1996; 51: 56–59.
4. Devos S A, van der Valk P G M. Immediate contact reaction to 2-hydroxyethyl methacrylate? *Contact Dermatitis* 2000; 43: 364–365.
5. Andersen K E. Systemic symptoms related to patch test with UV curable acrylic monomers. *Contact Dermatitis* 1986; 14: 180.

Address:

Maria Cruz Torres Gorriz
Servicio de Alergia
Hospital Universitario La Fe
Avenue Campanar 21
46009 Valencia
Spain
Tel: +34 6351 47902
Fax: +34 9619 73089
e-mail: mtorres_gorriz@hotmail.com

Occupational contact dermatitis to 1,2-benzisothiazolin-3-one and 5-chloro-2-methylisothiazolin-3-one/2-methylisothiazolin-3-one in paint manufacturers

Contact Dermatitis 2005; 53: 115–116

N. J. Hardcastle and D. J. Gawkrödger

Department of Dermatology, Royal Hallamshire Hospital, Sheffield, S10 2JF, UK

Key words: 1, 2-benzisothiazolin-3-one; 2-octyl-4-isothiazolin-3-one; 5-chloro-2-methyl-4-isothiazolin-3-one/ 2-methyl-4-isothiazolin-3-one; allergic contact dermatitis; biocides; occupational; paint; varnish.

Case Reports

3 male employees of a paint and varnish manufacturer were referred with hand dermatitis that became more extensive, over a 6–12-month period. All had worked for the company for several years. Patients 1 and 2 were product makers who mixed chemicals to make water-based varnishes and paints. Patient 3 was an industrial chemist who developed new varnishes, sealants and wood dyes. He weighed and mixed chemicals on an open bench. The products being manufactured contained the biocides 1,2-benzisothiazolin-3-one (BIT) and 5-chloro-2-methylisothiazolin-3-one/ 2-methylisothiazolin-3-one (MCI/MI, Kathon CG).

Patients 1 and 2 developed hand dermatitis, which spread to the face and wrist in one and to the trunk and limbs in the other. Neither of them had a history of skin disease or

atopy. Both wore rubber gloves to the wrists, aprons, safety shoes and respirator facemasks at work. In patient 1, the eruption responded to a moderate potency topical steroid and disappeared when he moved to the packing department and had no contact with chemicals. In patient 2, the eruption, which had abated when on holiday, resolved when he was transferred to work as a driver.

Patient 3, who had had psoriasis and hay fever, presented with a 12-month history of an eruption affecting the antecubital fossae and wrists. He wore eye protection in the laboratory and a lab coat to the elbow, but he only started wearing protective gloves once the eruption started. Results of patch testing to the British Contact Dermatitis Society standard series, an oil/coolant series and additional biocides are summarized in Table 1.

Discussion

Isothiazolinones are biocides with bactericidal, algicidal and fungicidal activity, added to industrial and household products to prevent spoiling. BIT is reported to have a sensitization rate of 1.2% (1). The 3 men developed contact allergies to one or more biocides to which they were exposed in the manufacture and development of paint and varnish products.

Sensitization to BIT has been reported in workers employed in carpet making, paint and air freshener manufacturing, pottery, printing, metalworking and water softening (2–6). All 3 of our patients were allergic to BIT, but the 2 product makers were also positive to MCI/MI. Like BIT, MCI/MI is used in metalworking fluids, paints, glues and plastics but is also contained in cosmetics, whereas BIT is not in Europe. Cross-sensitivity might explain these findings, which have been reported

before in workers exposed to BIT, but it is generally felt that separate sensitization is the explanation (3, 5). Our patients handled a product that contained MCI/MI.

We found no evidence that our patients handled 2-octyl-4-isothiazolin-3-one, but they may have had past exposure. Contact dermatitis to 2-octyl-4-isothiazolin-3-one has previously been described in paint manufacture (7, 8) and in a postgraduate student who worked with the product (9).

References

1. Schnuch A, Geir J, Uter W, Frosch P. Patch testing with preservatives, antimicrobials and industrial biocides. Results from a multicentre study. *Br J Dermatol* 1998; 138: 467–476.
2. Taran J M, Delaney T A. Allergic contact dermatitis to 1,2 benzisothiazolin-3-one in the carpet industry. *Australas J Dermatol* 1997; 38: 42–43.
3. Damstra R J, Van Vloten W A, Van Ginkel C J W. Allergic contact dermatitis from the preservative 1,2 benzisothiazolin-3-one (1,2-BIT; Proxel): a case report, its prevalence in those occupationally at risk and in the general dermatological population and its relationship to allergy to its analogue Kathon CG. *Contact Dermatitis* 1992; 27: 105–109.
4. Cooper S M, Shaw S. Occupational hand dermatitis due to 1,2 benzisothiazolin-3-one in the water-softener manufacturing industry. *Contact Dermatitis* 1999; 40: 221.
5. Muhn C, Sasseville D. Occupational allergic contact dermatitis from 1,2-benzisothiazolin-3-one without cross-sensitization to other isothiazolinones. *Contact Dermatitis* 2003; 48: 230–231.
6. Chew A-L, Maibach H I. 1,2-benzisothiazolin-3-one (Proxel): irritant or allergen? A clinical study and literature review. *Contact Dermatitis* 1997; 36: 131–136.
7. Jee S H, Chao K Y, Sun C C, Wang J D. Outbreak of contact dermatitis related to Acticide EP paste in a paint manufacturing factory. *J Formos Med Assoc* 1996; 95: 628–631.
8. Mathias C G, Andersen K E, Hamann K. Allergic contact dermatitis from 2-n-octyl-4-isothiazolin-3-one, a paint

Table 1. Patch test reactivities in the 3 subjects

	1,2-benzisothiazolin-3-one (0.1% pet.)		2-octyl-4-isothiazolin-3-one (0.1% pet.)		MCI/MI (0.01% aq)		Fragrance-mix (8% pet.)	
	D2	D4	D2	D4	D2	D4	D2	D4
Patient 1	+	++	–	?+	–	+	–	–
Patient 2	+	+	+	+	+	+	+	+
Patient 3	+	+	–	–	–	–	–	–

mildewcide. *Contact Dermatitis* 1983; 9: 507–509.

9. Young H S, Ferguson J E, Beck M H. Contact dermatitis from 2-octyl-4-isothiazolin-3-one in a PhD student. *Contact Dermatitis* 2004; 50: 47–48.

Address:

Prof. D. J. Gawkrödger
Department of Dermatology
Royal Hallamshire Hospital
Sheffield, S10 2JF
UK

Tel: +44 114 271 2203

Fax: +44 114 271 3763

e-mail: david.gawkrödger@sth.nhs.uk

Allergic contact dermatitis from sodium stearoyl lactylate, an emulsifier commonly used in food products

Contact Dermatitis 2005; 53: 116

Charlotte D. Jensen and Klaus E. Andersen

Department of Dermatology, Odense University Hospital, University of Southern Denmark, Odense and National Allergy Research Centre, Gentofte, Denmark

Key words: allergic contact dermatitis; contact allergy; cosmetics; emulsifier; sodium stearoyl lactylate.

We report a case of cosmetic allergy to the emulsifier, sodium stearoyl lactylate (SLL) (CAS 25383-99-7), in an Ostrich oil cream. Emulsifiers are basic ingredients in lotions and creams, because of their ability to mix water with fatty substances such as oils, fats and waxes by reducing the surface tension of both components. SLL is used in cosmetic products but is more common as an additive in processed foods (E481). Besides the ability to mix oil and water, emulsifiers are added to food products because of a variety of functions such as foam stabilization,

Table 1. Patch test results of controls

	Negative	+?	+
SLL 2% pet.	15	10	–
SLL 5% pet.	11	14	1

SLL = sodium stearoyl lactylate.

Table 2. Results of 4 epicutaneous tests of the case patient

	1995		2000		2004		2005	
	D2–3	D5–7	D2–3	D5–7	D2–3	D5–7	D2–3	D5–7
Dichromate	–	+	++	++	NT	NT	++	++
Colofonium	–	–	+	+	+	+	+	+
Nickel	–	–	–	–	+	+	+	–
Cobalt	–	–	–	–	+	+	+	–
Compositae mix	NT	NT	+	+	NT	NT	++	+
Ostrich oil cream					++	++	NT	NT
SLL 5% pet.							++	++
SLL 2% pet.							+	+

SLL = sodium stearoyl lactylate; NT = not tested.

aeration of bread products and crystallization control. SLL is made by combining lactic acid and stearic acid, and subsequent reaction with sodium hydroxide makes the sodium salt. SLL is used in foods as a dough conditioner to improve the texture of baked goods, as a stabilizer and whipping agent in egg whites and artificial whipped cream and as an emulsifying agent in salad dressings, soups and coffee whiteners.

Case Report

A 61-year-old woman with a 20-year history of palmoplantar pustulosis and chronic hand and foot dermatitis was admitted to our hospital, in 2004, with an acute deterioration and spreading of her dermatitis. After symptomatic treatment, she was patch tested with her own cosmetic products, and an Ostrich oil cream produced a strong positive reaction. The ingredients were kindly provided by the manufacturer, and the only positive reaction was to a preparation of the emulsifier, SLL 5% pet. A later retest with a 2% pet. preparation produced a + reaction. A use test on the lower arm with 2 daily applications of SLL 5% pet. showed small papules and itching after a few days and was clearly positive on D18.

To examine the irritant potential of SLL, 51 controls were patch tested (Table 1), 25 with 2% SLL pet. and 26 with 5% SLL pet. The 2% preparation produced 15 negative responses and 10 doubtful, probably irritant, responses. The 5% preparation showed 11 negative and 14 doubtful reactions, and 1 control had a + reaction on D3. These results show that SLL has irritant potential. The reproducible patch test and use test reactions are considered to be of allergic nature, because of the clinical picture, patient history and patch tests in controls.

The patient had a known and relevant dichromate allergy (Table 2), and an epicutaneous test in 2000 showed no other reactions than doubtful reactions to colofonium and compositae mix. When the patient was patch tested in 2004, colofonium produced a weak positive reaction, suggesting a true allergy, although of unknown relevance. Weak positive reactions were also seen to nickel and cobalt. These reactions, however, were only reproduced as doubtful at a retest 1 year later, while the positive reactions to colofonium and dichromate were reproduced. In 2000, compositae mix had shown a doubtful reaction, but when retested in 2005, a ++ reaction was produced.

Discussion

This is to our knowledge the first case of contact allergy to the emulsifier SLL. Our case patient has been patch tested a total of 4 times over 10 years (Table 2) showing the course of her contact allergy. An increase in the number of positive patch test reactions is seen, however, with some fluctuations in the patch test results. This patient seemingly belongs to a group of patients who have sensitive, labile skin that easily contract new allergies. This is confirmed by the sensitisation to a rare sensitizer such as SLL.

Address:

Charlotte Devantier Jensen
Department of Dermatology
Odense University Hospital
Sdr. Boulevard 29
5000 Odense C
Denmark
Tel: +45 65413239
Fax: +45 66123819
e-mail: charlotte.devantier.jensen@ouh.fyys-amt.dk

Patch testing with phenylmercuric acetate

Contact Dermatitis 2005; 53: 117–118

J. Geier¹, H. Lessmann¹, W. Uter² and A. Schnuch¹

¹Information Network of Departments of Dermatology, University of Göttingen, Germany

²Department of Medical Informatics, Biometry and Epidemiology, University of Erlangen/Nürnberg, Germany

Phenylmercuric acetate (PMA; CAS no. 62-38-4) has been used as a preservative in eyedrops, as disinfectant, as a paint preservative, formerly as fungicide in agriculture and possibly as fungicide in leather processing. Contact allergy to PMA has been reported (1, 2). However, the diagnostic quality of the patch test preparation PMA 0.05% pet. is not satisfying (3). Many doubtful, erythematous reactions occur, resulting in a negative reaction index (RI), and the vast majority of the positive reactions are not stronger than +, resulting in a high positivity ratio (PR) (1, 4). This could point towards a relatively high irritancy of the patch test preparation with irritant reactions presenting as macular or infiltrated erythema, i.e. ? or + reactions, even at day 3 (D3). The German Contact Dermatitis Research Group (DKG) conducted a multicentre study in order to find out whether the irritancy of the PMA patch test preparation can be diminished by reducing the test concentration. Hence, PMA 0.05% pet. and 0.01% pet. were tested in parallel in two DKG test series, namely the ophthalmic drug series and the leather series.

Table 1. Patch test reactions at D3 to phenylmercuric acetate (PMA)

Reaction at D3	Test concentration	
	0.05%	0.01%
Negative	905	1137
?	81	2
+	97	9
++	18	1
+++	6	0
Irritant	44	2
Total	1151	1151

Materials and Methods

From December 2002 to June 2004, a total of 1151 patients have been patch tested with both PMA concentrations in the above-mentioned test series, which were applied selectively in case of suspected exposure to (one of) the allergens included. Tests were performed according to DKG guidelines (5). Patch test preparations were obtained from Hermal, Reinbek and Germany. Data were collected and processed by the Information Network of Departments of Dermatology (IVDK), according to the routine procedure (6). Data analysis was done on the basis of D3 patch test reactions at the IVDK centre using SAS[®] 8.2 software (SAS Institute, Cary, NC, USA), according to current guidelines (7).

Results

PMA 0.05% pet. caused positive reactions in 121 patients (10.5%), and doubtful or irritant reactions occurred in 125 patients (10.9%). Hence, the RI was -0.02. With 97 + reactions among a total of 121 positive reactions, PR was 80% [95% -confidence interval (CI):

72%–87%]. In contrast, only 10 patients (0.9%) reacted positively to PMA 0.01% pet., and of these, 9 had a + reaction. Hence, PR was 90% (95% - CI: 55%–100%). Doubtful or irritant reactions occurred in 4 patients (0.35%), yielding an RI of 0.43 for PMA 0.01% pet. Test reactions observed at D3 are listed in detail in Table 1. Of the 10 patients reacting positively to PMA 0.01% pet., only 4 had a concomitantly positive test reaction to PMA 0.05% pet., while in the other 6 patients, the patch test with PMA 0.05% pet. remained negative. The proportions of positive reactions to the two test concentrations differed significantly (exact McNemar's test; $P < 0.0001$). Of the 24 patients with a strong reaction (+++, +++) to PMA 0.05% pet., 22 did not react to PMA 0.01% pet. at all. An additional comparison of test reactions to PMA and 2 other organic and inorganic mercury compounds (thimerosal and mercury amide chloride) revealed no agreement beyond chance, irrespective of the PMA test concentration (see Table 2). With both, thimerosal and mercury amide chloride, Cohen's kappa was 0.14 only for PMA 0.01% pet. and not higher than 0.24 for PMA 0.05% pet., indicating poor agreement only. Reliable data on clinical relevance of positive test reactions to PMA were not available.

Discussion

Reduction of the PMA test concentration from 0.05% to 0.01% pet. resulted in a dramatic decrease of any kind of patch test reactions. As the proportion of doubtful and irritant test reactions was reduced to an even greater extent than positive reactions, the RI of the lower test

Table 2. Cross tabulation of dichotomized test reactions at D3 to mercury amide chloride 1% pet. and thimerosal 0.1% pet. versus phenylmercuric acetate (PMA), 0.01% pet. and 0.05% pet., respectively.

		Mercury amide chloride (1% pet.)			Thimerosal (0.1% pet.)		
		Neg., ?, irr.	Pos.	Total	Neg., ?, irr.	Pos.	Total
PMA 0.01% pet.	Neg., ?, irr.	1007	27	1034	458	36	494
	Pos.	7	3	10	4	4	8
	Total	1014	30	1044	462	40	502
		Cohen's kappa: 0.14 (95% - CI: -0.01 to 0.29)			Cohen's kappa: 0.14 (95% - CI: 0.00–0.28)		
PMA 0.05% pet.	Neg., ?, irr.	987	11	998	414	23	437
	Pos.	93	20	113	48	17	65
	Total	1080	31	1111	462	40	502
		Cohen's kappa: 0.24 (95% - CI: 0.15–0.34)			Cohen's kappa: 0.25 (95% - CI: 0.06–0.37)		

Neg., negative; Pos., positive; irr., irritant.

concentration was markedly higher (+0.43 versus -0.02). At first sight, one might draw the conclusion that PMA 0.01% pet. is more suitable for patch testing than PMA 0.05% pet. However, a real improvement of the diagnostic quality would be achieved only if irritant, false-positive reactions were diminished, but cases of true contact allergy still be detected by patch testing with the lower PMA concentration. Patients allergic to PMA, with a positive reaction to the lower test concentration, would be expected to react positively to the higher concentration also, presumably with a stronger reaction. As can be seen from Table 2, this was definitely not the case: only 4 of 10 patients with a positive reaction to PMA 0.01% pet. also reacted to PMA 0.05%, while the other 6 patients remained completely negative. Hence, morphologically positive (at least infiltrated, erythematous) reactions to PMA 0.01% pet. may be false positive and have to be interpreted as cautiously as those to PMA 0.05% pet. The fact that there is little agreement between positive test reactions to PMA at both concentrations and other mercury compounds can be interpreted as supporting evidence that by far not every positive reaction to PMA is truly allergic.

Conclusion

Reduction of the PMA patch test concentration from 0.05% pet. to 0.01% pet. does not improve the diagnostic quality. Further studies with graded concentrations between these extremes could possibly achieve a better test preparation. However, the problem of irritancy in patch testing is not necessarily exclusively a problem of the correct test concentration. Inherent irritant properties of a substance might compromise the diagnostic quality anyway, irrespective of the concentration, e.g. like with iodopropynyl butylcarbamate (8, 9). Admittedly, we have no reliable data on the current extent of PMA use, but according to our information, the general exposure to PMA seems to be declining. No disinfectants currently used in healthcare still contain mercury compounds, and in 2004, only 5 brands of eyedrops (of 3 manufacturers) on the German market are preserved with phenylmercuric salts, of all them being replaceable by preparations with the same active ingredient but with a different preservative (10).

Hence, only few cases of contact allergy due to PMA are to be expected in the future. This perspective prompted the DKG to abandon the search for an optimized PMA test concentration. Instead, the DKG removed PMA from all test series and recommended that, in patients with suspected PMA allergy, the incriminated products and PMA 0.05% pet. (which is still commercially available) should be patch tested on a case-by-case basis, and the results should be interpreted with care.

References

- Herbst R A, Uter W, Pirker C, Geier J, Frosch P J. Allergic and non-allergic periorbital dermatitis. patch test results of the Information Network of the Departments of Dermatology during a 5-year period. *Contact Dermatitis* 2004; 51: 13–19.
- Torresani C, Caprari E, Manara G C. Contact urticaria syndrome due to phenylmercuric acetate. *Contact Dermatitis* 1993; 29: 282–283.
- Iden D L, Schroeter A L. The vehicle tray revisited: The use of the vehicle tray in assessing allergic contact dermatitis by a 24-hour application method. *Contact Dermatitis* 1977; 3: 122–126.
- Geier J, Uter W, Lessmann H, Schnuch A. The positivity ratio – another parameter to assess the diagnostic quality of a patch test preparation. *Contact Dermatitis* 2003; 48: 280–282.
- Schnuch A, Aberer W, Agathos M, Brasch J, Frosch P J, Fuchs T H, Richter G für die Deutsche Kontaktallergie-Gruppe. Leitlinien der Deutschen Dermatologischen Gesellschaft (DDG) zur Durchführung des Epikutantests mit Kontaktallergenen. *Hautarzt* 2001; 52: 864–866.
- Uter W, Schnuch A, Geier J, Frosch P J. Epidemiology of contact dermatitis. The Information Network of Departments of Dermatology (IVDK) in Germany. *Eur J Dermatol* 1998; 8: 36–40.
- Uter W, Schnuch A, Gefeller O. Guidelines for the descriptive presentation and statistical analysis of contact allergy data. *Contact Dermatitis* 2004; 51: 47–56.
- Brasch J, Schnuch A, Geier J, Aberer W, Uter W. Iodopropynylbutyl carbamate 0.2 % is suggested for patch testing of patients with eczema possibly related to preservatives. *Br J Dermatol* 2004; 151: 608–615.
- Schnuch A, Geier J, Brasch J, Uter W. The preservative iodopropynyl butylcarbamate: frequency of allergic reactions and diagnostic considerations. Results from the IVDK. *Contact Dermatitis* 2002; 46: 153–156.
- Rote Liste 2004 Service GmbH, ed. *Rote Liste*. German Drug Inventory. Cantor Verlag, Aulendorf, Germany 2004.

Cutaneous adverse drug reactions to Fluticasone propionate and Deflazacort in an asthmatic patient

Contact Dermatitis 2005; 53: 118–119

M. T. Ventura¹, G. F. Calogiuri¹, R. Buquicchio¹, E. Di Leo¹ and A. Ferrannini¹

¹Department of Internal Medicine, Immunology and Infectious Diseases (MIDIM), University of Bari Medical School, Policlinico, Bari, Italy

Key words: adverse drug reaction, asthmatic patient, corticosteroid cross-reactivity, Deflazacort, Fluticasone propionate, glucocorticoids, urticaria.

It is demonstrated that glucocorticosteroids (GCSs) might be responsible for allergic symptoms correlated to both a cell-mediated (IV type) and immediate (I type) hypersensitivity classification (1–3). We describe the first case of adverse reaction to inhalant Fluticasone propionate (Fp) in a patient with allergic bronchial asthma and a clinical history of anaphylactoid reactions for aspirin (ASA) and no steroidal anti-inflammatory drugs (NSAIDs).

Patients and Methods

Female patient, 57-year-old, affected by allergic asthma with sensitization to Grass, Parietaria and Olive pollen, treated with β_2 -agonists and inhalant GCSs (Beclomethasone dipropionate). During a therapy with a mixture of propyphenazone, dihydroergotamine and caffeine, the patient presented a generalized urticaria and asthmatic symptoms.

In addition, the patient referred a strong generalized itch and facial erythematous reaction few minutes after the administration of an undetermined intravenous corticosteroid after an asthmatic crisis. The recommended therapy was Formoterol and Fp. Following the consumption of Fluticasone for 2 weeks, the patient referred oral dryness, palate itch and dysphonia.

The presence of a strong dermographism did not allow us to perform prick tests or intradermal tests for GCSs. Patch tests (PTs) were applied to the skin on the back and were removed after 72 h of occlusion. The following GCSs were used after being placed on Finn Chambers on Scanpor (Merck – Milan, Italy): Budesonide 0.1% and Tixocortol pivalate 1% petrolatum (Lofarma – Milan, Italy), Clobetasol valerate 1% in ethanol, ethanol 0.1% in watery solution (F.I.R.M.A. – Florence, Italy), Fp ointment and Flixotide as it is. The results were interpreted as truly positive (allergic) or falsely positive (toxic) reactions. During the last reading of PTs, in order to investigate both an immediate-type and cell-mediated type reaction, oral challenge tests (OCTs) were performed with 3 different GCSs with an interval of 14 days between each other: Prednisone pills (2.5 mg, 5 mg, 10 mg, 15 mg and 25 mg), Deflazacort drops (5, 10, 20 and 30 drops) and Betamethasone pills (0.5 mg, 1 mg, 2 mg and 4 mg) with an incremental dosage on every hour in a critical care unit.

Results

Patch tests resulted negative for Budesonide and Tixocortol pivalate after readings on 2nd, 4th and 7th days, while ethanol and Clobetasol propionate were responsible for an irritative erythematous reaction considered doubtful. The application of Fp ointment in occlusion and in the open on the forearm was responsible for an urticarial reaction. Due to the strong dermographism of our patient, instead of the ethanol as a vehicle for the drug, we have used the commercial Fp ointment and the aerosol itself. In the following 24 hr, the patient developed urticaria on the site where we had sprayed Fluticasone and in the area of the PT with Fp ointment.

Concerning the OCT, Prednisone was well tolerated; by contrast, after the consumption of 5 drops of Deflazacort 5, asthenia, dyspnoea and generalized urticaria appeared in the patient. During the third OCT, the patient showed an immediate adverse event after the administration of 4 mg of Betamethasone (total dosage: 7.5 mg). In the light of these findings, an immediate-type allergy to GCSs was diagnosed. Nevertheless,

the complexity of the anamnesis does not allow us to exclude an allergic contact dermatitis (ACD) to GCSs.

Discussion

According to Kamm and Hagmeyer (4), the presence of bronchial asthma, a positive clinical history for allergic or pseudoallergic reactions to ASA and NSAIDs and the repeated administrations of GCSs should be considered as risk factors for an allergic immediate-type reaction to GCSs.

In addition, Doms-Goossens (5) has suggested that patients with a history of adverse immediate-type reaction to systemic GCSs could show an ACD to topical GCSs. This phenomenon would also be possible after a topical GCS inhalator. Subjects with asthma and allergic rhinitis should be considered exposed to a double (I and IV types) allergic mechanism due to the chronic use of inhalant and systemic GCSs. Lauerma (6) identified specific IgE for Budesonide in a subject treated with inhalant Budesonide and with erythematous-oedematous lesions of the skin.

The present case represents the first report of an adverse reaction to inhalant Fp in an asthmatic patient, even though this topical GCS is rarely considered to induce allergic contact sensitization. In the literature, few cases of ACD or urticaria-angioedema to Deflazacort are reported (7). Concerning the OCT, because the patient had never before assumed Deflazacort, the adverse reaction might be associated to a phenomenon of allergic cross-reactivity with other GCSs (8). Interestingly, the patient developed allergic reactions towards GCSs, which showed the site on C9 occupied (a fluorine atom in Betamethasone and Fluticasone, a hydrogen atom in Deflazacort), according to Wilkinson's hypothesis (9). In fact, for their particular chemical structure, both Fluticasone and Deflazacort are GCSs not completely comparable with the classification suggested by Coopman and Doms-Goossens (10).

References

1. Matura M, Goossens A, Matura M. Contact allergy to corticosteroids. *Allergy* 2000; 55: 698–704.

2. Burdorf T, Venemalm L, Vogt T, Landthaler M, Stolz W. IgE mediated anaphylactic reaction induced by succinate ester of methylprednisolone. *Ann Allergy Asthma Immun* 2002; 89: 425–428.
3. Ventura M T, Muratore L, Calogiuri G F, et al. Allergic and pseudoallergic reactions induced by glucocorticoids: a review. *Current Pharmac Design* 2003; 9: 1956–1964.
4. Kamm G L, Hagmeyer K O. Allergic type reactions to corticosteroids. *Ann Pharmacother* 1999; 33: 451–460.
5. Doms Goossens A. Clinical aspects of contact allergy to corticosteroids. *Dermatology* 1994; 189 (Suppl. 2), 54–55.
6. Lauerma A I, Kistaala R, Makinen-Kiljunen S, Haathela T. Allergic skin reaction after inhalation of budesonide. *Clin Exp Allergy* 1993; 23: 232–233.
7. Gomez C M, Higuero N C, Moral de Gregorio M H, Nunez Aceves A B, Lara M J, Sanchez C S. Urticaria-angioedema by deflazacort. *Allergy* 2002; 57: 370–371.
8. Ventura M T, Calogiuri G F, Matino M G, et al. Alternative glucocorticoids for use in case of adverse reaction to systemic glucocorticoids: a study on 10 patients. *Br J Dermatol* 2003; 148: 139–141.
9. Wilkinson S M. Corticosteroid cross-reaction: an alternative view. *Contact Dermatitis* 2000; 42: 59–63.
10. Coopman S, Degreaf H, Doms-Goossens A. Identification of cross-reaction patterns in allergic contact dermatitis to topical corticosteroids. *Br J Dermatol* 1989; 121: 27–34.

Address:

M. T. Ventura
Department of Internal Medicine
Immunology and Infectious Diseases
University of Bari, Policlinico
Piazza G. Cesare n° 11
70124 Bari
Italy
Tel: + 39 080 5592789
Fax: + 39 080 5478875
e-mail: mt.ventura@allergy.uniba.it

Hypersensitivity from dental acrylates in a patient previously sensitized to artificial nails

Contact Dermatitis 2005; 53: 119–120

P. Jung, R. Jarisch and W. Hemmer

FAZ – Floridsdorf Allergy Centre, Vienna, Austria

Key words: 2-HEMA; acrylates; allergic contact dermatitis; dental materials; sculptured nails.

Case Report

A 63-year-old female patient planned to restore her teeth (central incisor, lateral incisor and the canine of the first and second quadrant). A temporary crown composed of dimethacrylates and mono-, di-, triglycerin-dimethacrylate-phosphates was fabricated. This crown was attached to the damaged teeth using dimethacrylate-based cement, and it was covered for aesthetic reasons with a UV-cured adhesive lacquer, containing 2-HEMA and BIS-GMA.

The night after this intervention the patient experienced painful blisters, oral erythema and oedema of the inner lip on the adjacent mucosa. When symptoms persisted she visited her dentist. This was 8 days after the intervention. The dentist cleaned the provisional crown and again covered it with the 2-HEMA-containing adhesive lacquer. The symptoms aggravated severely and she visited the dentist 2 days after the second intervention. The dentist prescribed oral corticosteroids that gave only partial relief.

Patch testing using standard series and acrylate series showed 1+ reaction to nickel, 1+ reaction to fragrance mix, 2++ reaction to EGDMA, 1+ reaction to 2-HEMA after 48 and 72 hr. Testing with MMA, TREGMA, BISGMA and diurethandimethacrylate was negative. The patient has been wearing for years artificial fingernails of the 'acrylic' type without complaints. However when questioned she admitted having had an eczematous reaction to sculptured nails of the 'photobonded' type 3 years before.

Comment

Acrylic materials are found in dental and cosmetic products (1, 2). Eczematous allergic reactions to acrylates in artificial fingernails are well known (3–6) and nail designers as well as subjects wearing sculptured fingernails are concerned. Occupational allergic contact dermatitis due to acrylates in dental personnel is frequently reported (2). Sensitization in patients, however, is rare.

The present case demonstrates that severe contact allergy to acrylates in dental materials can occur in patients, who have been previously sensitized

to acrylic nails. Macedo et al. (6) described a case of a dentist, in whom sensitization by artificial fingernails caused contact dermatitis from acrylic compounds used at work.

Patch test results, clinical aspect and history of our patient make it very likely that 2-HEMA in the UV-cured lacquer was the putative allergen, which is also regularly used in photobonded nails (3), which were not tolerated by the patient. However, it cannot be excluded that other involved acrylates may have played a cross-reacting role too.

Interestingly, our patient tolerated sculptured nails of the 'acrylic' type composed of acrylate monomer liquid mixed with a polyacrylate powder. In contrast, 'photobonded' nails, which strongly resemble dental composite resins (3) and, unlike acrylic nails, typically include 2-HEMA (5), were not tolerated. However, the 'acrylic' (4, 5) as well as the 'photobonded' type (3, 6) may lead to allergic eczematous skin reactions.

Previous sensitization to acrylates in artificial fingernails may lead to severe complaints in patients when re-exposed to acrylates during dental treatment and should therefore be taken into consideration.

References

1. Rosenberg R, Scher R. Nail cosmetics: adverse reactions. *Am J Contact Dermat* 1993; 4: 71–77.
2. Kanerva L, Estlander T, Jolanki R, Tarvainen K. Occupational allergic contact dermatitis caused by exposure to acrylates during work with dental prostheses. *Contact Dermatitis* 1993; 28: 268–275.
3. Hemmer W, Focke M, Wantke F, Götz M, Jarisch R. Allergic contact dermatitis to artificial fingernails prepared from UV light-cured acrylates. *J Am Acad Dermatol* 1996; 35: 377–380.
4. Fisher A A. Permanent loss of finger nails from sensitization and reaction to acrylic in a preparation designed to make artificial nails. *J Dermatol Surg Oncol* 1980; 6: 70–71.
5. Constand L, Hecke E V, Naeyaert J M, Goossens A. Screening for contact allergy to artificial nails. *Contact Dermatitis* 2005; 52: 73–77.
6. Macedo N A, Carmona C, Pineyro I. Contact dermatitis from acrylic nails. *Contact Dermatitis* 1995; 32: 362.

Address:

Peter Jung, MD
Floridsdorf Allergy Centre
Franz Jonas Platz 8/6
A-1210 Vienna, Austria

Tel: +43 1 270 25 41
Fax: +43 1 270 25 42 78
e-mail: jung@faz.at

Compositae dermatitis in a herbal medicine enthusiast

Contact Dermatitis 2005; 53: 120–121

C. Cusack and C. Buckley

Waterford Regional Hospital, Waterford, Ireland

Key words: compositae dermatitis; herbal products.

A 41-year-old woman presented in late September 2004 with a 5-month history of regular flares of a periorbital rash with associated eyelid erythema, eye discomfort and lacrimation.

She is now a full-time housewife having worked as an accountancy lecturer until 2 years ago. She has a keen interest in herbal medicine with regular ingestion of chamomile, calendula, echinacea, arnica and sunflower seed derivatives. She gave a history of regular ingestion of chamomile tea and echinacea as a prophylaxis against colds. She has no previous dermatological, medical or family history.

She experienced a significant flare subsequent to a walk in the park in early October 2004 for which a course of oral prednisolone, flucloxacillin and a mild emollient were commenced. Examination revealed marked perioral erythema and less inflammatory dermatitic areas with impetiginization on the sides of neck and lower cheeks. She lives in the city-centre with no occupational or recreational exposure to plants.

Standard battery, cosmetic and plant series patch tests were performed while off corticosteroids. The plant series used was the standard plant battery (PL-1000, authorized by the ICDRG) (Chemotechnique Diagnostics, Malmö, Sweden). All series were negative at 48 hr. However, a strongly positive, 3+ reaction to parthenolide was recorded at 72 hr. Her reaction to sesquiterpene lactone mix remained negative.

She presented with a further flare in November 2004, within 1 day of visiting a florist. On examination 1 week later, her facial skin remained erythematous. She was advised to avoid all food supplements and scented products and was commenced on azathioprine 2 mg/kg/day.

Photopatch testing conducted in December 2004 was negative. Patch testing in February 2005 with her own herbal products which included chamomile, calendula, echinacea, arnica and sunflower seed derivatives yielded a strongly positive (3+) reaction to German chamomile (*Chamomilla recutita*) 2.5% pet. When informed of this reaction, she admitted to drinking several chamomile infusions per day. Testing with her regularly used cosmetic creams was negative. None of these products contained Compositae extracts. A relapse in January 2005 secondary to the inadvertent use of chamomile shampoo necessitated re-introduction of azathioprine at 2 mg/kg/day. Azathioprine has been withdrawn since late February 2005. She now avoids all herbal-based products and has had no further flares.

Discussion

The Compositae group with its numerous sesquiterpene lactones is a particularly common allergen; at least 180 species of Compositae cause contact dermatitis worldwide (1–3).

Our patient reacted to parthenolide, which is found in *Tanacetum parthenium* (feverfew) and several other Compositae plants. Interestingly, none of her products contained parthenolide, but it is a potent sesquiterpene lactone that cross-reacts with other Compositae species (4). Subsequent patch testing revealed chamomile sensitivity.

This case illustrates the phenomenon of Compositae sensitization from herbal-based remedies. The incidence of this phenomenon is unknown but a number of reports document its occurrence (5, 6). Local and systemic contact dermatitis from chamomile tea has been reported in isolated cases (7–9).

This case highlights the importance of patch testing with constituents of suspected products when a Compositae allergy is suspected clinically. Similarly, supplemental testing with a Compositae mix or feverfew

extract dramatically increases detection of Compositae allergy (10, 11).

In summary, this case illustrates the phenomenon of sensitization secondary to the use of herbal-based products and also highlights the importance of testing with suspected products and parthenolide to increase detection of a Compositae allergy.

References

1. Menz J, Winkelmann R K. Sensitivity to wild vegetation. *Contact Dermatitis* 1987; 16: 169–173.
2. Hausen B M. A 6-year experience with Compositae mix. *Am J Contact Dermat* 1996; 7: 94–99.
3. Paulsen E, Andersen K E, Hausen B M. An 8-year experience with routine SL mix patch testing supplemented with Compositae mix in Denmark. *Contact Dermatitis* 2001; 45: 29–35.
4. Hausen B M, Osmundsen P E. Contact allergy to parthenolide in *Tanacetum parthenium* (L.) Schulz-Bip. (feverfew, Asteraceae) and cross-reactions to related sesquiterpene lactone containing Compositae species. *Acta Derm Venereol* 1983; 63: 308–314.
5. Ery Paulsen. Contact sensitization from Compositae-containing herbal remedies and cosmetics. *Contact Dermatitis* 2002; 47: 189.
6. Ernst E. Adverse effects of herbal drugs in dermatology. *Br J Dermatol* 2000; 143: 923–929.
7. Pereira F, Santos R, Pereira A. Contact Dermatitis from chamomile tea. *Contact Dermatitis* 1997; 36: 307.
8. Rodriguez-Serna M, Sanchez-Motilla J M, Ramon R, Aliaga A. Allergic and systemic contact dermatitis from *Matricaria chamomilla* tea. *Contact Dermatitis* 1998; 39: 192–193.
9. Rycroft Richard J G. Recurrent facial dermatitis from chamomile tea. *Contact Dermatitis* 2003; 48: 229.
10. Goulden V, Wilkinson S M. Patch testing for Compositae allergy. *Br J Dermatol* 1998; 138: 1018–1021.
11. Jovanović M, Poljački M, Anwar W et al. Sesquiterpene lactone mix patch testing supplemented with dandelion extract in patients with allergic contact dermatitis, atopic dermatitis and non-allergic chronic inflammatory skin diseases. *Contact Dermatitis* 2004; 51: 101–110.

Address:
C. Cusack
Waterford Regional Hospital,
Waterford
Ireland
Tel: +353 51 842150
Fax: +353 51 842290
e-mail: caitriona_55@hotmail.com

Fixed drug eruption on the tongue due to clarithromycin

Contact Dermatitis 2005; 53: 121–122

J. C. Martínez Alonso¹, A. Callejo Melgosa¹, M^a. J. Fuentes Gonzalo² and C. Martín García¹

¹Allergy Unit, Hospital Virgen de la Concha, and ²Family Medicine Department, ZBS, Zamora, Spain

Key words: azithromycin; clarithromycin; erythromycin; fixed drug eruption; oral challenge; patch testing.

Clarithromycin is a macrolide antibiotic, active on a wide spectrum of pathogens, used for cutaneous and respiratory system infections with an optimal tolerability profile (1). The most common adverse effects involve the GI tract, but few cases of adverse skin reactions to this drug have been reported.

Case Report

A 68-year-old woman began oral treatment for acute upper respiratory infection with clarithromycin 250 mg, 2× daily. 4 days later, she developed an erythematoviolaceous patch over the dorsum of the tongue. Examination revealed a well-defined, oval, hyperpigmented patch, 2 cm × 2 cm, on the posterior third of the dorsum of the tongue. No other area of the oral mucosa was affected, and there were no cutaneous lesions. Lesion improved in 15 days just with discontinuation of the drug.

Patch testing was performed on normal skin with commercial clarithromycin (KlacidTM, Abbott, Madrid, Spain), 2 other macrolide antibiotics, azithromycin (ZitromaxTM, Pfizer, Madrid, Spain) and erythromycin (PantomicinaTM, Abbott), all tested at 10% pet., but negative results were obtained.

An oral challenge test with 250 mg of clarithromycin was performed showing after 4 hours a pigmented patch on his tongue associated with an erythematous halo around it. The pigmented patch was resolved completely over a period of 2 months. Following this, we performed a

double-blind oral challenge test with azithromycin and erythromycin in order to find an alternative treatment, but the patient tolerated these drugs without problems.

Discussion

Fixed drug eruption due to clarithromycin although very unusual, has been described, but with cutaneous involvement exclusively (2, 3). To our knowledge, this is the first report of fixed drug eruption with mucosal involvement alone induced by clarithromycin.

Clarithromycin has also been associated with leukocytoclastic vasculitis (4, 5), Henoch-Schönlein purpura (6), maculopapular rash-type hypersensitivity reaction (7, 8) thrombocytopenic purpura (9) and bronchospastic reaction (10).

References

1. Guay D R, Patterson D R, Seipman N, Craft J C. Overview of the tolerability profile of clarithromycin in preclinical and clinical trials. *Drug Saf* 1993; 8: 350-364.
2. Rosina P, Chieragato C, Shena D. Fixed eruption from clarithromycin. *Contact Dermatitis* 1998; 38: 105-122.
3. Hamamoto Y, Ohmura A, Kinoshita E, Muto M. Fixed drug eruption due to clarithromycin. *Clin Exp Dermatol* 2001; 26: 48-49.
4. Gavura S R, Nusinowitz S. Leukocytoclastic vasculitis associated with clarithromycin. *Ann Pharmacother* 1998; 32: 543-545.
5. de Vega T, Blanco S, Lopez C, Pascual E, Sanchez M, Zamarron A. Clarithromycin-induced leukocytoclastic vasculitis. *Eur J Clin Microbiol Infect Dis* 1993; 12: 563.
6. Goldberg E I, Shoji T, Sapadin A N. Henoch-Schönlein purpura induced by clarithromycin. *Int J Dermatol* 1999; 38: 706-708.
7. Igea J M, Lazaro M. Hypersensitivity reaction to clarithromycin. *Allergy* 1998; 53: 107-109.
8. Vangala R, Cernek P K. Hypersensitivity reaction to clarithromycin. *Ann Pharmacother* 1996; 30: 300.
9. Oteo J A, Gomez-Cadinanos R A, Rosel L, Casa J M. Clarithromycin-induced thrombocytopenic purpura. *Clin Infect Dis* 1994; 19: 1170-1171.
10. Gangemi S, Ricciardi L, Fedele R, Isola S, Purello-D'Ambrosio F. Immediate reaction to clarithromycin. *Allergol Immunopathol* 2001; 29: 31-32.

Address:

Allergy Unit, Hospital Virgen de la Concha
Avda Requejo 31-33
49022 Zamora, Spain
Tel: +34 980 548221
Fax: +34 980 512838
e-mail: med023218@nacom.es