

CONTACT POINTS

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Contact arthropod reactions: beware the family cat

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Key words: allergic contact dermatitis; arthropod reactions; bird mites; cat; clothing dyes; *Dermanyssus gallinae*.

Case Reports

Case no. 1

A 40-year-old woman, when seen elsewhere because of an eruption on the trunk and thigh, was treated with systemic prednisone for 14 days, following which she was little better. She was then given triamcinolone acetonide 40 mg intramuscularly (i.m.), together with loratadine and hydroxyzine orally. After another month, she was again given triamcinolone acetonide 40 mg i.m., but the rash persisted. A biopsy showed an angiocentric lymphocytic infiltrate. She was seen in this office, some 5 months after the eruption began. At that time, there was a somewhat erythematous papular eruption localized to the area under her underclothes (panties). There was also an eczematous eruption posterior to the right axilla on the right shoulder and herpes simplex on the skin of the right hip. Medications included warfarin, hydroxyzine, progesterin, diltiazem, norethindrone, digoxin, loratadine, doxycycline and enalapril.

A biopsy done on the papular eruption was interpreted as an arthropod reaction. Patch testing showed ++ reactions to nickel and cobalt, budesonide, at the + level, and + reactions to Disperse Blue 106, Disperse Blue 124, Disperse Blue 35 and Reactive Blue 238.

The patient was advised to avoid dyed fabrics on the upper trunk. She

was also advised as to possible sources of the arthropod reaction, which was localized to the area under her underclothes. Because of the multiplicity of lesions, she was asked to use a repellent and to look for a source, particularly for bird mites. She drove home from the office, and on arriving at her home found the bedroom door open, and the family cat sleeping contentedly in her underwear drawer. The next morning, she found a dead bird infested with bird mites (ostensibly brought home by the family cat) on her front porch. The cat was banished from the bedroom, and the chest of drawers was treated with a pesticide. Following this, the patient made steady improvement and was largely clear 3 weeks later. Her contact dermatitis improved with avoidance, and the herpes simplex was not treated.

Case no. 2

A 58-year-old woman presented with multiple papules with excoriation under her underclothing (panties) and accentuated under the elastic in her underclothing. She also had a few lesions on the legs. The lesions were raised, indurated and excoriated. Some of them were quite firm. She had been treated with a variety of systemic corticosteroids, topical triamcinolone and oral hydroxyzine, cetirizine and fexofenadine. There was a history of an eruption in clothing areas that cleared spontaneously and did not recur.

She denied outdoor exposure to chiggers. She had a cat that was outdoors most of the time although sometimes came indoors. A biopsy confirmed the presence of an arthropod reaction, and the patient was asked to look for sources, especially mites. She was advised about sources of exposure including domestic animals. She took her cat to her veterinarian who found *Dermanyssus gallinae*. The cat was treated with

selamectin, and the patient improved with avoidance.

Discussion

Clearly, without finding the causative organism on the patient in case no. 1 or in her underclothes, one cannot state with certainty that the eruption was caused by bird mites. However, finding bird mites on the patient is often not possible. Finding them in the underwear drawer would have provided cogent evidence, but this was not done as the patient was possessed with a practical rather than scientific spirit. However, there is strong circumstantial evidence. The number of lesions would be unusual for other parasites and especially for those likely to be found on the family cat. Second, the cat was a known hunter, and it had brought in a bird known to be infested with bird mites. Third, the improvement was striking after the cat was banished from the bedroom, the underclothing rewashed and the chest of drawers treated with a pesticide.

In the second case, mites were present on the family cat, which is probably as good evidence as we might expect. Treatment of the cat and avoidance improved the condition, which provides further support.

Mammals may be carriers of bird mites (1), and they may transmit that organism to humans (2) and poultry (3). Furthermore, the tendency for one species, *D. gallinae*, to return to the nest in daytime would make it reasonable for organisms to collect where the cat slept.

Typically, avian mite infestation in humans occurs often in the patient's home near an abandoned bird's nest (4). Such cases have even occurred in hospitals (5–7), infesting patients and sometimes hospital personnel.

The unusual presentation in these cases suggested to many physicians

who had seen them some form of contact reaction, because of the localization under the patient's underclothing. Searching for mites on the host might have to be done at night, as one common organism (*D. gallinae*) tends to feed at night and return to the nest in daytime (2). The sources in both cases seem to have been the family cats. In case no. 1, the localization was a mystery, however, until the patient found the cat sleeping in her underwear drawer.

In case no. 1, the patient also had contact dermatitis from clothing, caused by sensitivity to 3 different textile dyes. This was a minor problem, however, as the eruption was quite mild and the source was uncovered by patch testing. The putative textile reaction in case no. 2 was never investigated, as it had been clear for some time when she was seen.

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Airborne contact dermatitis from a polymercaptan hardener in a finished epoxy resin

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Key words: airborne allergic contact dermatitis; aircraft manufacture; epoxy hardener; occupational; polymercaptan.

Case Report

A 39-year-old employee of an aircraft manufacturer presented with a history of recurrent eczema. The areas of involvement included his forearms, the neck, particularly on the right side, and the lower and upper eyelids. He had not broken out on the hands.

He was fabricating cabinet doors using a combination of aluminium, fibreglass and a layer of wood. The woods included many exotic species, e.g. rosewood, mahogany, teak and several other varieties. He worked with a quickset epoxy used to fill nail holes. The surface of the cabinet doors was sanded after the epoxy had cured. He always wore gloves when working with epoxy, and he had not had a rash on his hands.

Patch testing was negative to sawdust from all woods used (10% pet.). He also did not react to any of the epoxy series (Chemotechnique, Malmö, Sweden) but showed a ++ reaction to the dried adhesive and + reactions to benzoyl peroxide and carba mix. Controls to the finished adhesive were negative. Follow-up patch testing showed +++ to the hardener at 0.1% (pet.) and to the epoxy resin at 0.1% (pet.). Controls were negative at 0.1% and 10%. The manufacturer declared that the epoxy resin was tetraglycidylether of methylene dianiline. The only information released about the hardener was that it was a polymercaptan.

At the last visit, the patient had been given a new job assignment, was no longer exposed and was clear.

Discussion

This case is unusual in several respects. First, contact was airborne. Second, the patient reacted to a

finished epoxy resin. Third, this is a class of epoxy hardeners that is seldom reported. The last may be at least partly due to the fact that sensitivity will not be showed by an epoxy screening series, owing to the class being absent in the series. The category is mentioned in 2 reviews of occupational dermatoses from epoxy systems (1, 2).

Polysulfide (synthetic rubber) sealers are known to cause contact allergy in a number of persons working in the aircraft industry (3–5), but I was unable to confirm that any of these were part of an epoxy system. Polymercaptan hardeners are frequently used in quickset epoxies, as was the case here.

In the case presented, there was undoubtedly free hardener in the final product. To reduce the amount of uncured mercaptan hardener to levels of <8% or <1%, Lee and Neville (6) suggest using a primary or tertiary amine as a co-curing agents. There was no co-curing agent used in this case. The strong reaction to 0.1% hardener, the history of breaking out to the dust from cabinet doors that were sanded and sensitivity to finished resin on patch testing all suggest that there was free hardener in the polymerized epoxy.

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Oral erosions as a manifestation of allergic contact sensitivity to cinnamon mints

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Key words: allergic contact stomatitis; cinnamic aldehyde; mints; oral erosions.

Allergic contact sensitivity is often not considered in the differential diagnosis of erosive oral lesions.

Case Report

A 37-year-old Caucasian woman was referred to the Dermatology Clinic of the National Cancer Institute (NCI) for evaluation of a 1-year history of episodic, painful palatal and buccal blisters and erosions without cheilitis. She presented with a presumptive diagnosis of pemphigus vulgaris (PV), based on a previous positive indirect immunofluorescence (IIF) test on monkey oesophagus (titre 1 : 160). The patient's medical history included basal cell carcinoma, seronegative 'reactive arthritis', asthma and endometriosis. There was no family history of bullous disease.

Initial physical examination found no oral or mucosal lesions. A repeat IIF was negative. Over the next few months, the patient reported episodic oral lesions that resolved spontaneously. On one occasion, she presented with oral erosions clustered on her left and right buccal surfaces, an aphthous ulcer on her tongue and gingival erythema. A repeat of the IIF and enzyme-linked immunosorbent assay (ELISA) for desmoglein III antibodies were negative. Histologic assessment of a biopsy obtained from the periphery of an erosive lesion showed focal ulceration, mild mucosal hyperplasia with focal spongiosis and a moderate lymphohistiocytic infiltrate with eosinophils in the submucosa.

The patient continued to report occasional relapsing and remitting

oral lesions over a 5-month period. At one clinic visit, she presented with grouped vesicles and superficial erosions on the left tonsil. Viral cultures for herpes simplex were negative, and a presumptive diagnosis of herpetiform aphthous stomatitis was made. Colchicine (0.6 mg twice a day) was instituted and the frequency of lesion development appeared to decrease. Over the next few months, the patient remained free of new lesions and the colchicine was discontinued. However, shortly after exposure to cinnamon-flavoured breath mints, the patient developed lesions. In retrospect, she recalled that frequent use of these mints coincided with the initial onset of the oral lesions.

The patient was then evaluated for allergic contact sensitivity. Patch testing was performed in a standardized manner using Finn Chambers[®] (Epitest Ltd Oy, Tuusula, Finland) affixed to the upper back with Scanpor[®] tape (Norgesplaster, Venne, Norway). The patient was patch tested using the North American standard tray, a cosmetic tray (Chemotechnique Diagnostics AB, Malmö, Sweden), crushed cinnamon mints, and Equal[®] sweetener. All patch sites were evaluated at 2 and 4 days. 4 days after application of test substances, positive reactions (all +) to cinnamic aldehyde (1% pet.) (Fig. 1a), crushed cinnamon mints (Fig. 1b), fragrance mix, carba mix, Myroxylon pereirae, and dodecyl gallate were observed.

A voluntary oral provocation test was carried out to determine if the lesions were related to the patient's ingestion of cinnamon mints. The patient challenged herself with the mints on 2 successive days before a clinic visit, and presented with 2 kissing erosions (Fig. 2a,b) on the mobile and fixed gingival surfaces specifically where the mints had been placed. The patient also ingested mints in the clinic and developed bullous oral lesions that evening (approximately 4 hr after the visit). These findings suggested contact sensitivity to cinnamon-flavoured breath mints manifesting as intraoral bullae and erosions. Discontinuation of exposure to the offending mints led to cessation of lesion development.

Discussion

Pemphigus vulgaris is an important consideration in the differential diagnosis of oral erosions. This case illustrates the value of repeating laboratory tests to confirm a diagnosis if results are inconsistent with the clinical picture, especially if the diagnosis may result in exposure to toxic therapies. Atypical causes of oral erosions, including contact sensitivity, should be considered in the differential diagnosis especially if the history and diagnostic tests exclude more common causes such as PV.

This is an unusual presentation of allergic contact sensitivity to cinnamic aldehyde involving the oral

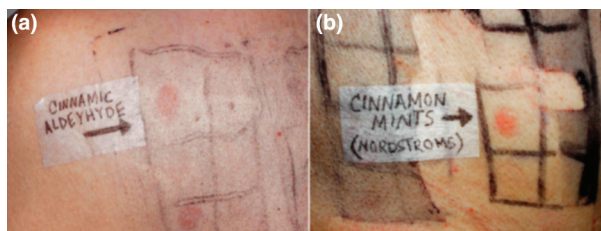


Fig. 1. Patch test results to cinnamic aldehyde (a) and crushed cinnamon mints (b) at day 4.

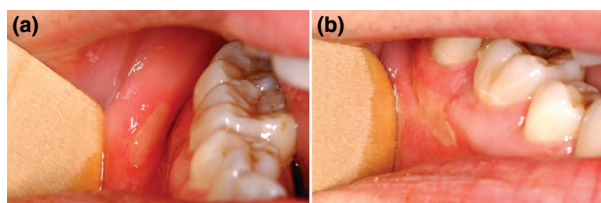


Fig. 2. Abutting oral erosions from provocation on the right mobile gingiva (a) and right hard gingiva (b) where the mint had been located.

mucosa. Previously reported oral manifestations of cinnamic aldehyde sensitivity include stomatitis, cheilitis, lip swelling and erythematous patches with keratosis and/or ulceration, or both (1–4). Cinnamon ingestion has also been associated with chronic lichenoid mucositis, erythema multiforme-like reactions, leukoplakia and squamous cell carcinoma (1, 5–7). Most of these reactions were caused by cinnamon-flavoured gum, cinnamon-flavoured toothpaste, lip-stick and food (5, 8). In aggregate, these cases highlight the importance of a detailed exposure history if there is a suspicion of oral contact sensitivity. This experience also reminds us that exposure to contactants should always be considered as a possible cause of an atypical cutaneous or mucosal reaction.

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Valdecocix-induced systemic contact dermatitis confirmed by positive patch test

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Key words: allergy; Bextra[®]; cyclooxygenase-2 (COX-2) inhibitor; delayed-type hypersensitivity reaction; valdecocix.

Valdecocix is a cyclooxygenase-2 (COX-2) inhibitor prescribed for inflammatory arthritides and other painful conditions. Cutaneous adverse drug reactions are rare^{1,2}.

Case Report

A 67-year-old Caucasian man presented with a maculopapular rash on his trunk and face. For chronic arthritic pain, he had taken

valdecocix for 8 days at a dose of 20 mg/day. Blood tests showed an increased white blood cell count of $11.6 \times 10^3 \text{ mm}^3$ without eosinophilia. On clinical examination, there was a maculopapular rash with cocardi-form purpuric lesions as well as homogeneous erythema of the face and the trunk. 60% of the total body surface was involved (Fig. 1). The mucosa was spared. Valdecocix was discontinued. On systemic treatment with oral methylprednisolone, at an initial dose of 60 mg/day, fexofenadin 180 mg/day and topical treatment with fluocortolone, the skin lesions resolved within a week.

Diagnostic allergy tests were then performed, according to the guidelines of the International Contact Dermatitis Research Group, with the standard series of the German Contact Allergy Group and valdecocix (Bextra[®], Pfizer Pharmaceuticals, New York, NY, USA), celecoxib (Celebrex[®], Pfizer Pharmaceuticals), and sulfamethoxazole 30% aa as well as sulfanilamide 5% pet. Positive reactions were found to valdecocix and



Fig. 1. Maculopapular exanthematous eruption after taking valdecocix for 8 days.

celecoxib after 3 days (Fig. 2). The patient had previously tolerated rofecoxib [Vioxx[®], Merck, Whitehouse Station, NJ, USA], and therefore it had not been patch tested. Prick tests with aqueous valdecoxib and celecoxib were negative. 5 healthy controls patch tested with the same substances were entirely negative.

Lymphocyte-transformation assays (LTA) for valdecoxib, celecoxib, rofecoxib and sulfamethoxazole were performed. Peripheral blood mononuclear cells (PBMC) from the patient and 3 healthy donors were processed for LTA as described previously (3). The incubation period was 5 days. None of the substances induced significant lymphocyte proliferation.

Discussion

Type IV T-cell-mediated reactions to systemic drugs are not rare and can be confirmed by patch testing (4–6). We report a patient with systemic contact dermatitis due to valdecoxib, which presented as a maculopapular rash and was confirmed by patch

testing. Cutaneous adverse drug reactions to valdecoxib have only rarely been described. A case of valdecoxib-induced toxic epidermal necrolysis in a patient allergic to sulfa drugs has been reported (2). However, there are no published reports of positive patch tests to valdecoxib.

In addition to being the first patient with a documented systemic delayed-type hypersensitivity reaction to valdecoxib, our patient demonstrates cross-reactivity between valdecoxib and celecoxib. For the latter substance, positive patch test reactions have been described previously (7). Our patient had never knowingly been exposed to this drug, but had tolerated the COX-2 inhibitor rofecoxib previously.

Therefore, in this patient, cross-reactivity between valdecoxib and celecoxib due to their common benzenesulphonamide moiety exists. Rofecoxib, however, has a distinct molecular structure with a methylsulphon moiety (8), which might be responsible for tolerability in a patient allergic to either substance.

We recommend that each patient allergic to COX-2 inhibitors should be tested for cross-reactivity to other sulphonamides, and vice versa, to prevent severe allergic drug reactions.

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Two cases of facial dermatitis due to chlorphenesin in cosmetics

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Key words: chlorphenesin; contact allergy; cosmetics; facial dermatitis.

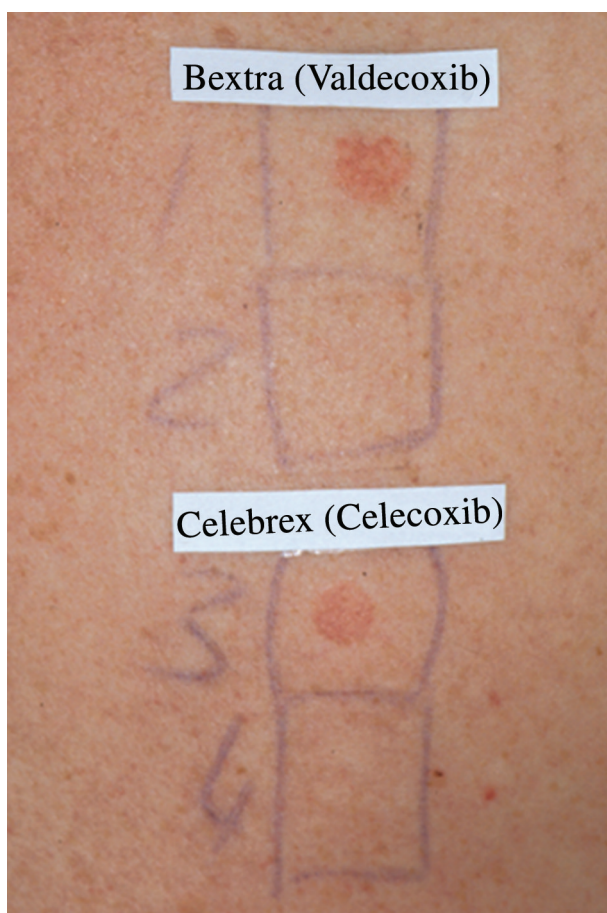


Fig. 2. Positive valdecoxib and celecoxib patch tests at 3 days.

Chlorphenesin (3-(4-chlorphenxy)-1,2-propane-diol) is an antimicrobial agent with antifungal, antibacterial and anticandidal activity. It has been included in preparations to treat dermatophytosis of the feet for more than 60 years and is occasionally added to cosmetics as a biocide and preservative. It is a rare cause of contact allergy.

Case Reports

Case no. 1

A 60-year-old atopic woman developed facial eczema within several hours of applying a foundation make-up. This settled using 1% hydrocortisone ointment and an emollient. Prior to this, she had never had any skin problems or reactions to cosmetics.

Patch testing to our departmental standard series and facial series showed an allergic response to chlorphenesin 1% (pet.), with a ++ reaction at the day 4 reading. We were unable to patch test her directly to the foundation, as she had disposed of it prior to her clinic appointment. However, chlorphenesin was listed as an ingredient in this particular cosmetic. Interestingly, several other foundation make-ups made by the same company do not contain chlorphenesin.

Case no. 2

A 33-year-old Indian woman presented with a 1-month history of facial eczema. This had started on her right cheek and rapidly spread to involve her entire face, neck, upper chest and upper arms. She had attributed this problem to the prior application of a proprietary moisturizing cream. There was no personal or family history of atopy.

She was patch tested to our departmental standard series, facial series and to the moisturizer implicated as the cause of her facial eczema. By day 2, she had a + reaction to chlorphenesin 1% (pet.) and a +++ reaction to the moisturizer (as is). Both reactions persisted to day 4.

The mode of prior sensitization to chlorphenesin in both of the above cases is unknown.

Discussion

Five previous case reports of contact dermatitis from chlorphenesin have

been published, 3 from preparations used to treat foot dermatophytoses (1–3), 1 from a deodorant causing an axillary dermatitis (4) and 1 from a facial moisturizer (5). We can add 2 further cases, in both of which facial dermatitis developed after applying cosmetic preparations in which chlorphenesin was an ingredient.

These are the only allergic patients whom we have detected in the 5 years in which chlorphenesin has been included in our patch test facial series, giving an incidence of 0.02% per year. In view of this very low incidence of allergic contact dermatitis, it will no longer be routinely tested, but will be added if necessary, based on the history. However, the role of this unusual biocide as a potential allergen in cases of cosmetic-associated dermatitis should not be forgotten.

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Cutaneous adverse drug reaction to oral chlorphenamine detected with patch testing

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Key words: alkylamine antihistamine; chlorphenamine; cutaneous adverse drug reaction; positive patch test.

Case Report

A 39-year-old woman took Piriton[®] (Stafford-Miller, Welwyn Garden City, UK) orally (4 mg chlorphenamine) for insect bite reactions. 5 h later, she developed a widespread, erythematous rash, eventually involving most of her trunk and limbs. She remained systemically well, with no involvement of her mucous membranes. The rash settled with a short course of oral prednisolone and emollients.

In 1995, she had been admitted with a similar toxic erythema after taking oral lofepramine and flucloxacillin. Subsequent patch testing (both 20% pet.) confirmed contact allergy to these 2 drugs. In 1996, she described similar rashes occurring in relation to oral paroxetine, venlafaxine and diclofenac. No formal investigations had been performed at that time, but she had been careful to avoid further ingestion of these drugs. At the time of her most recent presentation, she was taking regular temazepam, which she had taken on many previous occasions without clinical reactivity.

In view of this recent and past history, 2 months after the cessation of oral corticosteroids, she was patch tested to chlorphenamine, paroxetine, temazepam, venlafaxine, diclofenac (all at 20% pet.) and the departmental standard series. By day 2, she had already developed a bullous reaction to the chlorphenamine patch that persisted to day 4 (Fig. 1), confirming a delayed hypersensitivity reaction to chlorphenamine. Patch testing to the other drugs was negative (Fig. 1). The original source of sensitization to chlorphenamine is unknown. Patch testing was negative in 15 control subjects with the same chlorphenamine preparation.

Discussion

Drug patch tests can be a valuable investigation in cases of suspected cutaneous adverse drug reactions, but the validity of the results depends on the original clinical picture, drug suspected, adherence to the correct test protocol and inclusion of appropriate controls. Using the published guidelines (1), we have proven that

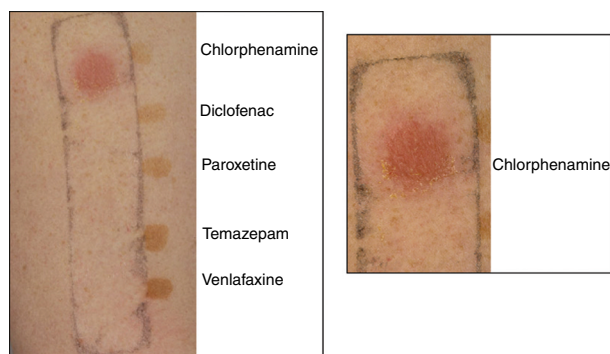


Fig. 1. Patch test results on day 4 (left) with close-up of chlorphenamine (right). All medicaments 20% pet.

our patient had a cutaneous adverse drug reaction to chlorphenamine.

Chlorphenamine maleate, an alkylamine antihistamine, is widely used in the treatment of allergy, hay fever and urticaria. It can be administered by topical, oral and intravenous routes. Topical use is thought to be responsible for sensitization and subsequent contact allergy (2) and allergic contact dermatitis (ACD) from chlorphenamine cream (3) and in eye drops for chronic conjunctivitis (4) has been reported.

In addition, Angelini et al. (5) described 3 positive patch tests to chlorphenamine where the source of sensitization remained elusive. Santucci et al. (6) presented two cases of ACD from topical alkylamines exacerbated by subsequent treatment with injections of chlorphenamine maleate (10 mg) but, interestingly, both cases were later given oral dexchlorphenamine maleate (6 mg) with no adverse effect.

ACD from oral chlorphenamine appears to be rare. The only other published case report we have identified was more than 50 years ago, when Epstein described a woman with an allergic patch test to pheniramine who had previously received the drug by the oral route (7). In addition, our patient was unusual as she was also allergic to oral lofepramine and flucloxacillin, which do not have any structural similarities with chlorphenamine. Our report reminds us that alkylamine antihistamines should be considered in the aetiology of any case of suspected drug allergy.

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Allergic contact dermatitis of the hands and/or feet – common sensitizers

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Key words: allergic contact dermatitis; common allergens; hands and/or feet; patch testing.

Allergic contact dermatitis (ACD) of the hands and/or feet is common, as both are areas of the skin in contact with innumerable contactants (1, 2). Also, difficulties often arise in distinguishing endogenous eczema from contact dermatitis clinically, patch testing being of much diagnostic help in these situations.

Patients and Methods

50 clinically suspected cases of ACD of hands and/or feet (32 male and 18 female) were evaluated by patch testing with the Indian standard series (Systopic Laboratories Ltd, New Delhi, India) using aluminium chamber mounts on Micropore®. Readings were taken on day 2 and day 4 and graded as per international recommendations.

The age of the patients ranged from 10 years to 70 years (mean 36.5). Occupations ranged from semi-skilled (29) and unskilled (2) to housewives (14) and students (5). Clinical presentations were isolated hand dermatitis (11), isolated foot dermatitis (18), both hand and foot dermatitis (10) and, lastly, hand or foot involvement along with dermatitis elsewhere (11). Mean duration of disease was 2.4 years.

Results

Table 1 summarizes the allergens detected, and Table 2 summarizes the different sensitivities by region.

Discussion

The outpatient incidence of hand and/or foot dermatitis was 1.85%, constituting 32.7% of all ACD cases during the period of study (1 December 2000 to 31 May 2001). Overall positivity was 56%: in males, 53% and in females, 61%. Positive males (17) were mostly semi-skilled workers (14) belonging mainly to the age groups 41–50 years (6) and 21–30 years (5). Positive females (11) were mostly housewives (9) and mainly from the age group 21–30 years (5). Of 7 atopics, 3 tested positive. 3 patients who tested positive had a family history of ACD, and the same allergen (nickel) was positive in one family. A 60% heritability of

Table 1. Patch test results in the 28 positively tested patients

Allergen	Vehicle (%)	Male (<i>n</i> = 17)	Female (<i>n</i> = 11)	Total no. of patients with positive reactions
Metals		9	6	15 (53.5%)
Potassium dichromate	0.5 pet.	7	-	7
Nickel sulfate	5.0 pet.	1	6	7
Cobalt chloride	1.0 pet.	1	-	1
Rubbers		6	1	7 (25%)
Mercapto mix	2.0 pet.	2	-	2
Mercaptobenzothiazole	2.0 pet.	2	1	3
Thiuram mix	1.0 pet.	1	-	1
Black rubber mix	0.6 pet.	1	-	1
Antibiotics and other medicaments		7	3	10 (35.7%)
Neomycin sulfate	20.0 pet.	1	-	1
Gentamicin	20.0 pet.	3	1	4
Nitrofurazone	1.0 pet.	2	1	3
Chiniform	3.0 pet.	1	1	2
Benzocaine	5.0 pet.	-	-	-
Cosmetic ingredients		8	5	13 (46.4%)
Myroxylon pereirae resin	25.0 pet.	2	2	4
Fragrance mix	8.0 pet.	4	2	6
Formaldehyde	1.0 aq.	-	-	-
Quaternium-15	1.0 pet.	1	-	1
4-Phenylene diamine base	1.0 pet.	1	1	2
Methylchoro isothiazolinone + methylisothiazolinone	0.67 aq.	-	-	-
Pharmaceuticals used in both medicaments and cosmetics		10	4	14 (50%)
Parabens	15.0 pet.	1	-	1
Colophonium	20.0 pet.	2	-	2
Chlorocresol	1.0 pet.	-	1	1
Lanolin alcohol	30.0 pet.	1	3	4
Ethylenediamine dihydrochloride	1.0 pet.	1	-	1
Propylene glycol	5.0 aq.	3	-	3
Polyethylene glycol 400	100 aq.	2	-	2
Plant antigens		2	3	5 (17.8%)
Parthenium hysterophorus		1	1	2
Xanthium strumarium		1	1	2
Chrysanthemum		-	1	1
Miscellaneous		-	-	-
Epoxy resin	1.0 pet.	-	-	-
<i>p</i> -tert-Butylphenol-formaldehyde resin	1.0 pet.	-	-	-
Control	100 pet.	-	-	-

Table 2. Regional sensitivities in the 28 positive patients

Allergen group	Total number of reactions seen					
	Hand dermatitis (<i>n</i> = 7)		Foot dermatitis (<i>n</i> = 11)		Hand and foot dermatitis (<i>n</i> = 10)	
	Number	%	Number	%	Number	%
Metals	4	57	3	27	8	80
Rubber chemicals	3	42.8	4	36	-	-
Medicaments	3	42.8	3	27	3	30
Pharmaceuticals	1	14	7	63.6	7	70
Cosmetic ingredients	1	14	9	81.8	3	30
Plant antigens	-	-	-	-	5	50

nickel sensitivity was observed in a study by Menne' and Holm (3).

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Allergic contact dermatitis presenting in the emergency department

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Key words: betamethasone valerate; diphenhydramine chloride; emergency medicine; medicaments.

Case Report

On New Year's Eve, a 53-year-old male attended the Emergency Department of our hospital, complaining of severe swelling and redness of the left hand (Fig. 1). Following disinfection with 0.05% chlorhexidine gluconate, the lesion was treated with 1% gentamicin ointment and 0.6% fradiomycin sulfate tulle; subsequently, oral medication with levofloxacin was prescribed, but no alleviation was observed.

4 days later, the topical medicament was replaced with 0.12% betametha-

sone valerate ointment containing 1% gentamicin; however, no significant change was attained. On day 7, a further replacement with 0.05% fluocinonide ointment achieved remarkable improvement of the lesion.

A 2-D closed patch test showed a +++ reaction to diphenhydramine hydrochloride (1% pet.), which had been used topically immediately before

the onset of the current symptoms (Fig. 2), together with a + reaction to betamethasone valerate; however, no response was shown to either vehicle.

Discussion

Diphenhydramine hydrochloride and betamethasone valerate have



Fig. 1. Clinical appearance of left hand 4 days after initial presentation.



Fig. 2. Bullous positive patch test reaction to diphenhydramine chloride.

frequently been employed topically, mainly in over-the-counter drugs and on prescription, respectively, and there have been many reports of associated contact dermatitis. Thus, the US Food and Drug Administration has drafted the rules for topical drugs containing diphenhydramine hydrochloride (1). In a large-scale survey, the positive rate of contact dermatitis attributable to betamethasone valerate was 0.08–5.98% (2).

When aggravating conditions occur concomitantly, as in the present case, even contact dermatitis causes intolerable discomfort. Furthermore, in the present case, the onset happened to coincide with New Year's Eve, leading to limited haematological test availability, the affected hand being the more effective one; unfortunately, allergy had already been induced to the topical drug prescribed for treatment of the suspected contact dermatitis; and finally, the symptoms were severe enough for the patient to be unable to hold chopsticks.

Possible diseases requiring differential diagnosis include cellulitis, circulatory disorders, such as thrombosis, and compartment syndromes. Given that treatments for these diseases are quite different from those for contact dermatitis, recognition of contact dermatitis is important among emergency specialists, because it can be an acute dermatological disease, as in the present case.

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Occupational airborne allergic contact dermatitis due to HBTU

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Key words: airborne allergic contact dermatitis; HBTU; occupational; peptide synthesis coupling reagent.

(*o*-Benzotriazole-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HBTU) is a synthetic intermediate and auxiliary product (peptide synthesis coupling reagent), used in the manufacturing of solid- and solution-phase peptide synthesis. This chemical, even used with protective equipment, is known to be irritant when applied to the skin, ingested or inhaled. Moreover, 2 cases of immediate allergic reactions have been described (1, 2). However, to our knowledge, no allergic contact dermatitis due to HBTU has been reported.

Case Report

A 37-year-old male researcher in chemistry presented with work-related dermatitis, initially limited to the hands and fingers, and improved by corticosteroid creams (class II) with symptom-free periods. Symptoms had progressively worsened until, after 1 year, they had become continuous and had extended to the face, upper part of the back, neck, elbows and ankles. They predominated in air-exposed areas. The patient had allergic rhinitis but no other past medical history. He used to handle several chemical products and, in particular, HBTU powder but with protective equipment such as gloves.

Biopsies of the lesions showed dermal lymphocytic and eosinophilic perivascular infiltration. Acanthosis, spongiotic vesicles, lymphohistiocytes and eosinophils were present in the epidermis.

We patch tested the patient on the upper back with the European standard series, using Finn Chambers on Scanpor® (Epitest, Tuusula, Finland), HBTU (1% pet.) and other

chemicals that he used to handle (*N,N*-dimethylformamide, dichloromethane, acetonitrile and triisopropylsilane). Readings were made at 2 and 3 days, and positivity was evaluated according to internationally accepted criteria (3). Only HBTU was positive (++) at 2 and 3 days. Moreover, symptoms were reactivated during testing.

Currently, the patient still works at the same place, but he tries to avoid handling HBTU powder. Strict avoidance is therefore not possible. Symptoms have partially regressed and are largely controlled by corticosteroid creams.

Discussion

Allergic reactions to HBTU are uncommon. A recent case report described a 29-year-old researcher who presented with occupational contact urticaria, affecting the exposed areas of the face (2). She had positive prick tests to HBTU and *o*-(7-azabenzotriazole-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HATU). Another report (1) concerned occupational rhinitis and bronchial asthma due to *o*-(benzotriazole-1-yl)-*N,N,N',N'*-tetramethyluronium tetrafluoroborate (TBTU) and HBTU. An immediate immunological immunoglobulin E (IgE)-mediated mechanism was suspected, because the patient had positive skin tests. We therefore prick tested with HBTU and other products of the same class (HATU and BOP), even though in our case, a non-IgE mechanism was suspected. As expected, prick tests were negative.

Because HBTU is known to be irritant and hazardous when applied to the skin, ingested or inhaled, we did not consider it ethical to test unexposed subjects and so did not perform patch tests in any control subjects. However, in the present case, airborne allergic contact dermatitis due to HBTU is the most probable diagnosis because of the symptoms of the patient, the results of skin biopsy and the positivity of the HBTU patch test.

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Irritant contact dermatitis from benzalkonium chloride in shampoo

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Key words: benzalkonium chloride; cosmetics; irritant contact dermatitis; shampoo.

Benzalkonium chloride is a quaternary ammonium cationic surfactant and a strong irritant. It is widely used in cosmetics, skin disinfectants, ophthalmic preparations and various other products (1). Cases of allergic contact dermatitis due to benzalkonium chloride have been reported based on the results of patch test with benzalkonium chloride 0.1% aq. (2–4). However, Basketter et al. concluded recently that benzalkonium chloride should not normally be regarded as,

or classified as, a significant skin sensitizer and that many supposed cases of allergic contact dermatitis were likely to be misinterpretations of patch test data (1).

Case Report

A 62-year-old woman was treated for itchy erythematous macules on the face, especially on the forehead and the neck, after using a shampoo containing benzalkonium chloride. The patient was treated with epinastine hydrochloride (20 mg) orally per day and the topical medicaments prednisolone acetate ointment and clobetasone butylate ointment for 1 month.

Patch tests were performed with the cosmetics, shampoo and rinse used by the patient. Patch tests were also performed with the ingredients of the shampoo provided by the manufacturer. There was a positive reaction to both the shampoo at 100 times dilution and benzalkonium chloride 0.1% aq. on D3 (+) and D4 (+), but no reaction to either the shampoo at 1000 times dilution or benzalkonium chloride 0.01% aq. on D2, D3 and D4.

Discussion

Because of the negative patch test result to benzalkonium chloride 0.01% aq., the diagnosis made was irritant contact dermatitis due to benzalkonium chloride in the shampoo, even though a positive reaction to benzalkonium chloride 0.1% aq. was observed on D3 and D4.

Patch test reactions that fade after 2 D are generally considered to be irritant rather than allergic. However, Reiche et al. have refuted this idea by demonstrating prolonged irritant positive reactions with sodium lauryl sulfate (SLS) (5). Löffler and Happel have offered an explanation for the persistent positive patch test reaction (6). They performed irritant patch test with SLS of 0.125, 0.25, 0.5, 1.0 and 2.0%, and demonstrated that SLS caused increased transepidermal water loss even during the regeneration period (D3–D10) (6).

Benzalkonium chloride is also a surfactant and is likely to cause a persistent patch test reaction in the same manner as SLS. Patch tests with surfactants, such as benzalkonium chloride, can cause prolonged irritant reactions. The interpretation of patch test results as irritant or allergic should be performed carefully when surfactants are involved.

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