

A clinical and patch test study of adult widespread eczema

LIN-FENG LI AND JING WANG

Department of Dermatology, Peking University The Third Hospital, Beijing, China

The purpose of this study was to investigate the role of contact hypersensitivity (CHS) in adult widespread eczema (WE) and to analyse the aetiology of WE. 108 consecutive adult WE patients were patch tested. 352 patients with suspected localized allergic contact dermatitis (ACD) tested in the same period served as a control. The average age of the patients with WE was significantly greater than the control group (47.6 ± 15.0 v 39.2 ± 14.9 , $p < 0.01$, Student's *t*-test). More male patients were found in the WE group (42.6% vs 25.0%, $p < 0.01$, χ^2 -test). 71 (65.7%) of the WE patients were patch test positive. ACD was diagnosed in 29 out of 108 (26.9% of the WE patients and 40.8% of the PT positive patients) WE patients. ACD was also suspected in another 42 patients (39.8%), who had at least 1 positive PT result but the relevance of PT was hard to determine. In the remaining 37 patch test negative patients, 2 cases of food allergy were diagnosed by clinical findings and open food challenge test. 1 case of atopic dermatitis was diagnosed. 34 patients (31.5%) were diagnosed as unclassified endogenous eczema. Most of the WE patients with ACD (15/29, 51.7%) were ACD from widespread contact with hair dye during bathing. Most of the WE patients with hair dye ACD were male (male:female = 2.75). The total positive rates of PT in the WE group were no different to the control (65.7% vs 61.5%, $p > 0.05$, χ^2 -test). No significant difference was found for the positive rates of common contact allergens. The rate of atopy was no different between the 2 groups either (6.5% v 5.1%, $p > 0.01$, χ^2 -test). These results indicated that contact sensitization was very common in adult WE. Neglected widespread contact with contact allergens, especially hair dye, plays a very important role in our adult WE. The roles of age and sex in WE need to be studied further.

Key words: adult; allergic contact dermatitis; hair dye; patch testing; p-phenylenediamine (PPD); systemic contact dermatitis; widespread eczema. © Blackwell Munksgaard, 2002.

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Widespread eczema (WE) is not rare in dermatology practice. Patients with WE are well known to have impaired quality of life and to need frequent hospitalization. However, the aetiological diagnosis of WE is often very difficult. Widespread contact with allergen, systemic contact dermatitis, skin hyperirritability and the effect of skin microflora have been implicated in the pathogenesis of WE (1–4). Patch testing is a useful tool for the detection of contact hypersensitivity (CHS) and it has been proved useful in the investigation of the cause or exacerbating factors in certain kinds of eczema (4, 5). The main purpose of this study was to investigate the role of contact sensitiza-

tion in WE. Another aim of this study was to analyse other aetiologies of WE.

Patients and Methods

Diagnostic criteria

Allergic contact dermatitis

Allergic contact dermatitis (ACD) was diagnosed by the disease history and clinical examination based on a standard textbook (5).

Eczema

Eczema was diagnosed and classified according to standard textbooks (4, 5). Specific types of eczema,

such as contact dermatitis, atopic dermatitis, asteatotic eczema, seborrhoeic dermatitis, infective dermatitis, dermatophytide, post-traumatic eczema, discoid eczema, gravitational eczema, metabolic eczema, eczematous drug reactions and pityriasis alba were diagnosed accordingly (4), and the remaining unspecified eczema was diagnosed as unclassified endogenous eczema (UEE) (6). Among these, metabolic eczema refers to dermatitis accompanied by diarrhoea (4).

Atopic dermatitis

Atopic dermatitis (AD) was diagnosed by using the U.K. diagnostic criteria for AD (7).

Atopic diathesis

Atopic diathesis was considered when any of the following diseases, allergic rhinitis, allergic asthma, or atopic dermatitis, could be found in the patient's personal history or in blood-related family members within 3 generations.

Study populations

During a 2-year period, 108 consecutive adult patients with WE were patch tested in our contact dermatitis clinics. There were 46 males and 62 females, with an average age of 47.6 ± 15.0 years (mean $\pm$ SD).

Patch testing

Patch testing was performed with the standard series of Beijing Medical University, Beijing, China (6, 8). This includes benzocaine, imidazolidinyl urea, neomycin sulphate, p-phenylenediamine (PPD), potassium dichromate, ethylenediamine dihydrochloride, colophonium, parabens, formaldehyde, epoxy resin, 2-bromo-2-nitropropane-1,3-diol, ammoniated mercury, fragrance mix, nickel sulphate and rubber mix. 'Rubber mix' comprises four mixes. Rubber mix I is a mix of mercaptobenzothiazole, N-cyclohexyl-2-benzothiazole sulfenamide and 2,2'-benzothiazyl disulphide. Rubber mix II contains tetramethylthiuram disulphide and tetramethylthiuram monosulphide. Rubber mix III contains N-phenyl-N'-cyclohexyl-p-phenylenediamine, N-isopropyl-N'-phenyl-p-phenylenediamine and N-N'-diphenyl-p-phenylenediamine. Rubber mix IV is a mix of N-N'-diphenylguanidine, zinc diethyldithiocarbamate and zinc dibutyldithiocarbamate (8). Allergens were applied to the upper back, using Finn Chambers (Beijing Medical University, Beijing, China), and the results were recorded at day(D) 2 and D3 according to ICDRG recommendations (5).

Open food challenge test

Open food challenge test was performed in PT-negative WE patients, as previously described, to detect possible food allergy (9). Briefly, the suspected food was eliminated from the diet until the dermatitis had disappeared and treatment was stopped. Then the suspected food was reintroduced. Recurrence of symptoms within 3 days of food challenge was considered positive (9).

Controls

352 consecutive patients with suspected localized ACD were also patch tested in the same period. There were 88 males and 264 females, with an average age of 39.2 ± 14.9 years (mean $\pm$ SD).

Statistical analysis

The average age in the 2 groups was compared by Student's *t*-test. 2×2 χ^2 -test was used to compare the positive rate to each allergen in each group (10).

Results

The average age of the WE patients was 47.6 ± 15.0 years (mean $\pm$ SD), which was much greater than that (39.2 ± 14.9 years) in patients with suspected localized ACD (Student's *t*-test, $p < 0.01$). 46 out of 108 (42.6%) patients in the WE group were male, which was much higher than that (25%, 88/352) in patients with suspected localized ACD ($p < 0.01$, χ^2 -test).

The final diagnosis and the results of patch testing are shown in Table 1.

ACD was diagnosed in 29 patients (26.9%). 26 of these (89.7%) were diagnosed by patch testing with the standard series. 3 cases (10.3%) were diagnosed by patch testing with the suspected allergen as is.

ACD from Chinese herbal medicine (CHM) was found in 4 cases. 1 was from taking Gentongping pill (containing myrrh) orally for leg pain and 1 was from taking Ganmaochongji orally for a common cold. Both CHMs contain fragrance and fragrance mix patch testing was positive in both patients. The 3rd case was from applying Meifu cream topically and Meifu decoction orally for melasma. The Meifu cream and decoction were made and used in a small hospital and their ingredients could not be obtained. PT showed that she reacted to nickel and both Meifu cream and decoction as is. The 4th patient had ACD from a herbal paste for leg pain: localized ACD had appeared 1 day after application and had become widespread 2

Table 1. Final diagnosis of WE and results of patch testing

Final diagnosis	Patient number (rate)	Sex	Suspected agents	Patch test
ACD from herbal medicine	4 (3.7%)	3F, 1M	Herbal medicine	2 reacted to fragrance, another 2 reacted to herb as is while standard PT was negative
ACD from hair dye	15 (13.9%)	4F, 11M	Hair dye	All reacted to PPD
ACD from metals	3 (2.8%)	2F, 1M	Metals	All reacted to nickel
ACD from rubber	6 (5.6%)	2F, 4M	Rubber	All reacted to at least 1 rubber mix
ACD from cosmetics	1 (0.9%)	F	Facial cream	Reacted to facial cream as is, standard PT was negative
Atopic dermatitis	1 (0.9%)	M	Unknown	Negative
Food allergy	2 (1.8%)	2F	Food	Negative
Suspected ACD	42 (39.8%)	29F, 13M	Unclear	See Table 2
UEE	34 (31.5%)	19F, 15M	Unclear	Negative

weeks later. The name and ingredients of this herbal paste were unclear. Standard PT was negative and she was found to react to the paste as is. 10 patients with suspected localized ACD patch tested with the same paste were all negative and therefore skin irritation could be excluded.

15 cases of ACD were widespread contact dermatitis from PPD in hair dye, which was disseminated through taking showers. Mild dermatitis around the hairline could be seen in all patients. Most of these patients were male (male:female = 2.75) (Table 1).

3 patients were diagnosed as having metal contact allergy. Systemic absorption of nickel in metal jewellery, clothing decorations or watch bands was considered, since all patients presented with localized ACD at the site of metal contact before the appearance of WE, and WE appeared when the localized ACD was getting worse. All the patients were nickel PT positive and systemic contact dermatitis from nickel should therefore be considered.

Similar situations were found in 6 patients with rubber mix allergy. Localized ACD from rubber material could also be observed before the appearance of WE.

ACD from cosmetics was found in 1 patient. WE appeared after applying a face cream made by a beauty parlour for 10 days. The ingredients of the cream could not be obtained from the beauty parlour. PT with the cream as is was positive.

Positive patch test results were also obtained in another 42 patients (38.9%) and ACD was suspected. However, the relationship between the patch test results and WE could not be determined. Among these patients the positive rates of patch testing to 4 common allergens are shown in Table 2. More patients in the WE group reacted to rubber than in the control group.

Positive open food challenge test was found in 2 cases. Atopic dermatitis was diagnosed in 1. Patch testing with the standard series was negative in these patients.

No external factors could be found in the remaining 34 patch test negative patients (31.5%) and no specific type of eczema could be diagnosed. Therefore, they were considered as UEE.

The total positive rate of patch tests and the positive rates to PPD, nickel, fragrance mix and rubber in the WE group and control group are shown in Table 3. No significant difference was found between the 2 groups. 20 patients (18.5%) in the WE group were found to be patch test positive to PPD. Among these, 15 patients had ACD from PPD; 3 patients were found tolerant to PPD. No skin reaction could be observed, although they

Table 2. Positive number (rate) of patch testing to 4 common allergens in 42 WE patients with suspected ACD

Allergen	Suspected ACD (n = 42)	Control (n = 352)	p-value (χ^2 -test)
Rubber mix	14 (33.3%)	57 (16.2%)	< 0.05
Fragrance mix	10 (23.8%)	46 (13.1%)	> 0.05
Nickel	8 (19.0%)	64 (18.2%)	> 0.05
PPD	5 (11.9%)	40 (11.4%)	> 0.05

Table 3. Total positive rate of patch testing and positive rate to PPD, nickel, fragrance mix and rubber mix in WE and control group

Allergen	WE group (n = 108)	Control (n = 352)	p-value (χ^2 -test)
Fragrance	13 (12.0%)	46 (13.1%)	> 0.05
Rubber mix	25 (23.1%)	57 (16.2%)	> 0.05
Nickel	15 (13.9%)	64 (18.2%)	> 0.05
PPD	20 (18.5%)	40 (11.4%)	> 0.05
Total	71 (65.7%)	216 (61.4%)	> 0.05

kept dyeing their hair. The remaining 2 patients did not have any history of hair dyeing.

7 patients in the WE group and 18 patients in the control group were atopic. There was no difference between the 2 groups (6.5% v 5.1%, $p > 0.01$, χ^2 -test).

Discussion

Although WE is not rare in dermatology practice and the life quality of the WE patient is greatly impaired, few systematic studies of WE have been reported. Several cases of WE due to disseminated contact with contact allergens or systemic contact dermatitis from contact allergens have been reported, suggesting that CHS plays an important role in WE (1–4).

In this study, through clinical analysis and PT, ACD was diagnosed in 26.9% of the WE patients, indicating that ACD is very common in WE and that WE patients should be patch tested. ACD was suspected in a further 39.8% of the WE patients with at least 1 patch test positive result. However, the relevance of PT could not be determined. More work should be done to clarify the relevance. In the WE patients with suspected ACD, the positive rate of PT to rubber mix was much higher than in the control group, suggesting that contact sensitization to rubber materials may play a role in WE patients with suspected ACD.

Only 31.5% of the patients were patch test negative and considered as UEE.

In our hands, the average age of the WE patients was greater than the controls and more WE patients were male. Whether this is a general phenomenon or an epi-phenomenon is unknown. More male patients with ACD from hair dye in the WE group may be responsible for these results. Because black is the natural colour of Chinese hair, most Chinese (with only rare exceptions) dye their hair when white hair appears around the fourth decade. People can get their hair dyed in beauty shops, barber shops or even at home. The quality of the hair dye is not well controlled currently. Most people dyeing their hair do so without

being aware of the possible side-effect on their skin. ACD from hair dye is very common in China. The exact roles of age and sex in WE need to be studied further.

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Address:

Dr Lin-feng Li
Department of Dermatology
Peking University the Third Hospital
49 North Garden Road
Haidian District
Beijing 100083
China
Tel: +11861062017691–2660
Fax: +11861062017700
e-mail: zoonli@163.net