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Research Article

Allergic Contact Dermatitis due to Di (2-Ethylhexyl) Phthalate and Polyethylene Glycol Monododecyl Ether

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Abstract

We show a case of allergic contact dermatitis due to a towel on the neck and face in a 62-year-male. This patient used this towel for feeling cool around his neck and face in last summer, and he developed dermatitis on his neck and face about ten days later from using this towel. Scratching test of his usage towel showed positive reactions, but the results of patch testing his usage towel was negative reactions. After investigating his towel, the results of skin tests using some detected substances showed positive reactions against Di (2-Ethylhexyl) Phthalate (DEHP) in scratch test and Polyethylene glycol monododecyl ether in patch test. DEHP is one kind of phthalate esters, and DEHP was used as a plasticizing agent in his towel. Polyethylene glycol monododecyl ether is a kind of detergent. Polyethylene glycol monododecyl ether may be used for this towel washing during processing, and this substance could be residual in the towel. This is a case of immediate and delayed type allergic contact dermatitis, and each origin is different.

Keywords: Allergy; Contact dermatitis; DEHP; Dermatitis; Phthalic esters; Polyethylene glycol; Towel

Introduction

Recently, global warming shows rising average temperature, and there are increasing the number of days with more than 35℃ in Japan. The humidity of summer in Japan is so high, and the sensible temperature is higher and sultry than air temperature. Many groceries for feeling cool are developed every year, and the towel like this case is often having around the neck in summer. The ingredients of these groceries are some chemical substances such as phthalic esters, Isothiazolinone sterilizers and lauryl alcohol. Phthalic esters have been used as plasticizing agents in many products because of its low cost, low temperature flexibility, insulation quality, fire-resistant, good heat light stability and weather resistant. Recently, there are some reports about the toxicity of phthalic esters to human [1-3], and using phthalic esters have been restricted in Japan, EU and USA. Di (2-ethylhexyl) Phthalate (DEHP) was used as plasticizing agents for the flexibility of the towel. DEHP is most frequently used in many kinds of materials, and we previously reported a case of contact urticaria due to Di (2-ethylhexyl) Phthalate (DOP) [4,5]. Polyethylene glycol monododecyl ether is a kind of lauryl alcohol, using as a detergent. This substance may be residual.

Case

A case of 62-year-male developed dermatitis on his neck and face from using a towel. The period of using this towel was about 10 hours a day for 20 days in last summer. 10 days past after his usage towel, his dermatitis started. He stopped using towel after 10 days from his dermatitis developing, because he developed more severe erythema with itching (Figure 1). Our first diagnosis was contact dermatitis due to his towel. The results of patch test using his towel were negative reactions, although scratching test showed positive reactions against his towel. After his dermatitis improved, we investigated his towel and studied skin test with extracted some substances of the towel.

Figure 1: Clinical findings of the dermatitis on the neck and face.

Materials and Methods

Extraction of the Components of the Towel

We suspected his condition was contact dermatitis due to a component in his towel. We extracted the components of his towel with acetone and methanol. The extracted solutions were separated and identified by the LC/MS, GC/MS and DI-Probe-MS. 25 cm^2 towel sample was put in glass bottle with cover with 1 ml acetone and extracted by ultrasound. This extraction sample was sample (sample No. 0). 100 cm^2 towel sample was put in a 500 ml eggplant-shaped flask with 100 ml chloroform and heated for 60 minutes. The solution was heated again by 100 ml methanol for 60 minutes. After filtering with a glass filter (3G160), we concentrated the extract solution to 10 ml by the rotary evaporator. We got extraction sample (sample No. 1) after filtering with glass filter (3G160).

Identification of the Components in the Towel

We analyzed the extract solution and identified the separated chemicals using:

- High performance liquid chromatograph/ mass spectrometry (LC/MS)
- Gas chromatography / mass spectrometry (GC/MS)
- Direct probe mass spectrometry (DI-Probe-MS).

High performance liquid chromatograph/ mass spectrometry (LC/MS)

Sample No. 1 was heated, and solvent was removed. This sample was re-muddled with acetonitrile, and 5 µl of this solution was injected.

Apparatus: EXTREMA, PDA 200-800 nm, FT-ICR-MS 200-2000 m/z. Column: octadecyl group, 2.1 mm id x 150 mm length. Mobile phase A: distilled water, mobile phase B: acetonitrile. Mobile phase mixing ratio: A: B 50:50 (0min) → 0:100 (30 min) → 0:100 (15 min). Detection method: Positive ion detection mode.

Gas chromatography/Mass spectrometry (GC/MS)

One µl of each separated solution (sample No, 0 and 1) was injected. The condition was as followings.

Apparatus: JOEL M Station 700. Column: 5% phenyl methyl silicon (0.25 µm thickness), 0.25 mm id x 30 m length. Carrier gas: Helium 1.5 ml/min. Column temperature: 50 centigrade (3 minutes) → rising 10 centigrade/min → 320 centigrade (10 minutes) → cooling. Ionization mode: Electron ionization (EI) 75 eV.

Direct probe mass spectrometry (DI-Probe-MS)

This investigation was used for detection and identification for dye. Stained samples (sample No, 0 and 1) were heated, and solvent was removed. This sample was re-muddled with acetonitrile, and 200 µl of this solution was injected.

Apparatus: EXTREMA, PDA 200-800 nm, JOEL MStation 700. Column: octadecyl silica gel (5 µm thickness), 6 mm id x 250 mm length. Mobile phase A: distilled water, mobile phase B: acetonitrile. Mobile phase mixing ratio: A: B 50:50 (0 min) → 0:100 (30 min) → 0:100 (15 min). Flow speed: 1.7 ml/min. Probe temperature: 50 centigrade (3 minutes) → rising 64 centigrade/min → 350 centigrade (5 minutes) → cooling. Ionization mode: Electron Ionization (EI) 75 eV.

Results of Investigating the Towel

Analyzed chemicals (Figure 2)

We detected the following substances. Di (2-naphthyl) sulfone, Polyethylene terephthalate oligomer, disperse yellow 232, Polyethylene glycol monododecyl ether, Polyethylene glycol monotetradecyl ether, Polyethylene glycol Alkyl ether, unknown substances and unknown blue substances were detected by LC/MS analysis. Cholesterol, Palmitic acid, Methyl palmitate, Methyl cis-9-octadecenoate, Methyl tras-9-octadecenoate, Methyl 16-methyl heptadecanoate, Dimethyl-p-terephthalate, 2-hydroxyethyl methyl terephthalate, Di (2-ethylhexyl) phthalate (DEHP), Di (2-ethylhexyl) terephthalate (DEHTP) and 1,2 [terephthaloylbis(oxyethyleneoxy) bis tere phthaloyl bisoxylethane were detected by GC/MS analysis. Di (2-naphthyl) sulfone and 1,2 [terephthaloyl bis (oxyethyleneoxy) bis terephthaloyl bisoxylethane were detected by DI-Probe-MS.

Because Cholesterol, Palmitic acid, Methyl palmitate, Methyl cis-9-octadecenoate, Methyl tras-9-octadecenoate and Methyl 16-methylheptadecanoate could be components of lanolin and these are used for the method of processing fibers, we used lanolin and lanolin alcohol for skin testing. Dimethyl-p-terephalate,

2-hydroxyethylmethylterephthalate and 1,2 [terephthaloylbis(oxyethyleneoxy) bisterephthaloylbisoxylethane are impurities of polyester resin. Di (2-naphthyl) sulfone might be dyeing auxiliary. We excluded unknown substances, dyeing auxiliary and impurities of polyester resin for the samples of skin test. The skin test materials were 9 extracts as follows: Extraction Sample 15%pet, Lanolin 30%pet, Lanolin alcohol 30%pet, Dimethyl-p-terephalate 5%pet, Di (2-ethylhexyl) phthalate 5%pet, Di (2-ethylhexyl) terephthalate 5%pet, Disperse yellow 232, Polyethylene glycol monododecyl ether and Blue unknown substances 2%pet.

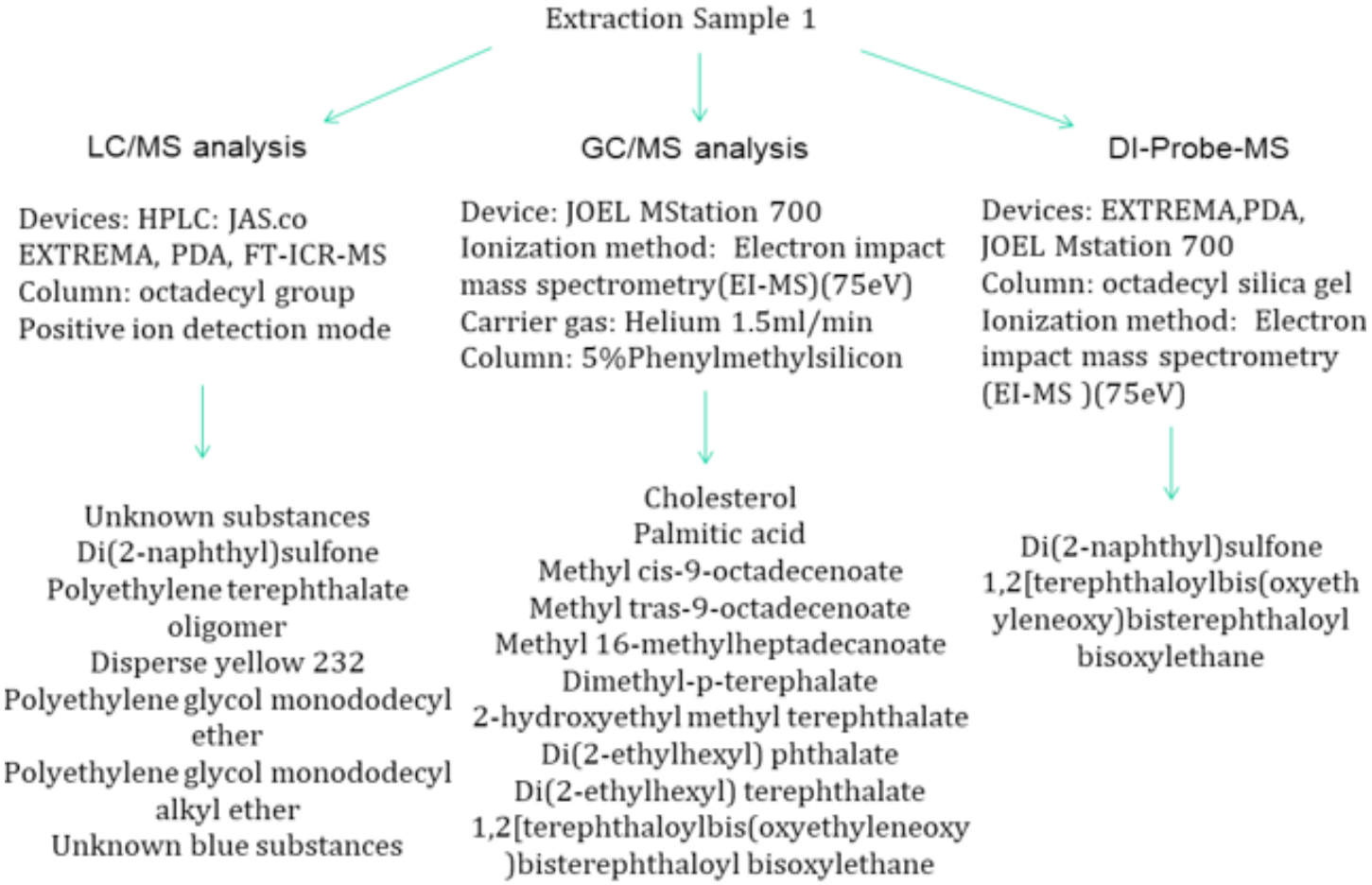

Figure 2: The methods and detected substances

Methods of Prick/ Scratch Test

We performed prick/scratch testing with 9 extracts and our 13 phthalic esters series. We tested histamine hydrochloride 1 % aq as a positive control, distilled water and white petrolatum as a negative control. Readings were made at 20 minutes and at other times if needed after placing samples according to the Lahti's paper [6] as follows: －; not reacted, 2+; 1/2 histamine solution's reaction-sized erythema and 1/2 histamine solution's reaction-sized edema, 3+; a histamine solution's reaction-sized erythema and a histamine solution's reaction-sized edema, 4+; stronger reactions of erythema and edema than histamine solutions-sized.

Methods of Patch Test

Forty-eight-hour closed patch testing on his back with same 9 extracts and our 13 phthalic esters series evaluated by the International Contact Dermatitis Research Group (ICDRG) criteria. We tested white petrolatum as a negative control. Our 13 phthalic esters series are 2-Ethyl-1-hexanol, Bis(2-ethylhexyl) phthalate, Di(2-ethylhexyl) phthalate (DEHP) (DOP), Di-n-hexyl phthalate (DnHP), Dimethyl phthalate (DMP), Diisononyl phthalate(DINP), Diisobutyl phthalate(DIBP), Dicyclohexyl phthalate (DCHP), Dibutyl phthalate (DBP), Bis(butylbenzyl) phthalate(BBP), Diethyl phthalate (DEP), Di-n-octyl phthalate

(DnOP) and Ditridecyl Phthalate (DTDP). Readings of skin test results were made at 20 minutes, 48hours, 72hours and 1week.

Results of prick /scratch testing and patch test (Table 1,2)

Substances/Evaluation hour	48hr	72hr	1week
Extraction Sample 15%pet	-	-	-
Lanolin 30%pet	-	-	-
Lanolin alcohol 30%pet	-	-	-
Dimethyl-p-terephalate5%pet	-	-	-
Di (2-ethylhexyl) phthalate 5%pet	+	+	+
Di (2-ethylhexyl) terephthalate 5%pet	-	-	-
Disperse yellow 232	-	-	-
polyethylene glycol monododecyl ether	-	-	-
Blue unknown substances 2%pet	-	-	-
Histamine chloride 10mg/ml	-	-	-
White petrolatum 100%pet	-	-	-
Distilled water 100%aq	-	-	-

Table 1: The results of scratch test.

Substances/Evaluation hour	48hr	72hr	1week
2-ethyl-1-hexanol 1%pet	-	-	-
2-ethylhexyl 1%pet	-	-	-
DEHP 1%pet	-	-	-
DnHP 1%pet	+	+	+
DMP 1%pet	-	-	-
DIMP 1%pet	-	-	-
DIBP 1%pet	-	-	-
DCHP 1%pet	-	-	-
DBP 1% pet	-	-	-
DnOP 1%pet	-	-	-
DTDP 1%pet	-	-	-
White petrolatum 100%pet	-	-	-
Distilled water 100%pet	-	-	-

Table 2: The results of patch test.

DOP and DHP showed positive reactions in scratch test. PoE-Do showed positive reactions in patch test.

Discussion

We detected Cholesterol, Palmitic acid, Methyl palmitate, Methyl cis-9-octadecenoate, Methyl tras-9-octadecenoate and Methyl 16-methylheptadecanoate, these six substances could be components of lanolin. Lanolin and Lanolin alcohol are often used as finishing agents of fiber or oil of cosmetics, and these are well-known as causing contact dermatitis [7-12]. Sterilizer has been often used as plasticizing agents for the towel like this case. Common sterilizers are 5 Chloro 2 methyl 4 isothiazolin 3 one (CMI), 2 Methylisothiazolin 3(2H) one (MI), 1,2 Benzisothiazol 3 (2H) one (BIT) and 2 Octyl 3(2H) isothiazolinone (OIT). Genrally, these Isothiazolinone sterilizers are used for dishwashing detergent, kitchen cleaner, soap, shampoo, shower foam cosmetics, coating materials, binder and timber. It has been reported that Isothiazolinone sterilizers to possess potential of serious contact dermatitis since 1980'S [13]. Mixture of 5 Chloro 2 methyl 4 isothiazolin 3 one (CMI) and 2 Methylisothiazolin 3(2H) one (MI) is named, Kathon CG. Kathon CG has potential of contact dermatitis, and this is one of Japanese standard allergen.

There were some reports about contact dermatitis or occupational dermatoses due to Kathon CG [14-17]. In our case, the results of skin test usage Lanolin and Lanolin alcohol were negative, and these Isothiazolinone sterilizers were not used in the towel. If you see a case of contact dermatitis like this case, first diagnosis could be lanolin, lanolin alcohol and Isothiazolinone sterilizers are causative agents of dermatitis. Phthalic esters are used for many materials as plasticizing agents in worldwide, but health hazard by phthalic esters are have been reported [18-22]. Dermatoses or allergy due to phthalic esters were reported [23-26], and we first reported a case of contact urticaria due to DOP [4,5]. There were some reports of health risk from phthalic esters [27-30], and phthalic esters are restricted for using in nursery items and toys by Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) in 2007. EU restricts 10 substances (Including 4 phthalic esters, DEHP, DBP, BBP and DIBP) by Restriction on Hazardous Substances (RoHS) [31].

This towel made in one Asian country, and these rules might be not suitable for this country. Our patient had positive reactions against DHP, and this reaction could be cross reaction. The chemical structure of DEHP is resembled to DnHP and differences between DEHP and DnHP are only the structure of alkyl chain. Polyethylene glycol monododecyl ether is a kind of lauryl alcohol, using as a detergent. Polyethylene glycols possess the potential of contact sensitizers, and there are some reports [32-35] of allergic disease or contact dermatitis. We got negative reactions of patch testing usage this towel, although the results of patch

test usage Polyethylene glycol monododecyl ether were positive reactions. These different results could come from the contact time and concentration of allergen. It needs to wash well when you use some materials that applied detergents in manufacturing process, because detergent is easy to persistent in the items. It needs to educate phthalic esters hazards and Polyethylene glycol monododecyl ether allergic potential to user.

Conclusion

We reported a case of contact dermatitis due to immediate and delayed type allergic skin reactions of each different chemical allergen. Only usage test is often not sufficient for pursuit of causative agents of dermatoses.

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