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Sofa dermatitis: Value of patch test with 2-(thiocyanomethylthio)benzothiazole

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Abstract

Background: In 2008, numerous cases of allergic contact dermatitis caused by leather chairs (sofa dermatitis) were reported, with dimethylfumarate being the culprit allergen. However, octylisothiazolinone, methylisothiazolinone and cobalt have also been associated with cases of sofa dermatitis. An antifungal agent, 2-(thiocyanomethylthio)benzothiazole (TCMTB), has also previously been described as a contact allergen in leather.

Materials and Methods: Seven patients were referred to the Department of Dermatology of the Cliniques universitaires Saint-Luc, Brussels, Belgium with suspicion of allergic contact dermatitis caused by leather sofas. They were patch tested with the European Baseline Series, additional series (according to the patients' history and clinical aspect of the eruption), dimethylfumarate (4/7 patients) and with TCMTB.

Results: All seven patients presented a positive reaction to TCMTB and only one presented a concomitant positive reaction to dimethylfumarate. All patients showed clinical improvement after avoiding contact with their leather sofa.

Conclusion: 2-(Thiocyanomethylthio)benzothiazole (TCMTB) is probably an underestimated allergen present in leather chairs (responsible for the so-called 'sofa dermatitis'), and more generally in leather objects. It is, therefore, important to test with TCMTB 0.1% petrolatum in case of contact dermatitis related with leather products.

KEYWORDS

2-(thiocyanomethylthio)benzothiazole, allergic contact dermatitis, antifungal, antimicrobial, CAS 21564-17-0, leather, preservative, sofa dermatitis

1 | INTRODUCTION

Sofa dermatitis refers to eruptions described in patients suspected of allergic contact dermatitis (ACD) caused by chairs or sofas. The clinical lesions were mainly located on the posterior areas of the thighs, back and sometimes also of the arms/forearms. The allergen reported as being responsible for an epidemic of cases in 2007 was dimethylfumarate (DMF).¹ A few other cases of sofa dermatitis have been described with octylisothiazolinone (OIT), methylisothiazolinone and cobalt. We report a case series of seven patients in which 2-(thiocyanomethylthio)benzothiazole (TCMTB; CAS no. 21564-17-0), an antimicrobial and antifungal agent used in leather products,²⁻⁴ was responsible for sofa dermatitis.

2 | PATIENTS AND METHODS

2.1 | Patients

Between 2019 and 2022, seven patients (16–67 years old) were referred to the Dermatology Department of the Cliniques universitaires Saint-Luc, a tertiary hospital in Brussels, Belgium, following the development of skin reactions suspected to be related to contact with their sofa/chairs. All patients suffered from erythematous-squamous lesions, initially located on the posterior sides of the thighs. Four patients (patients 4–7) had more diffuse involvement with lesions on the back and sometimes also on the posterior areas of the arms/forearms, but all of them presented a relative sparing of the anterior part



FIGURE 1 Clinical aspect of allergic contact dermatitis caused by leather sofas (sofa dermatitis; patients 1–7). The pictures were taken few weeks before the patch testing.

of the body. These same four patients had also palmoplantar involvement, for some of them with a hyperkeratotic aspect. No patient presented lesions on the face. The clinical characteristics of each of these seven patients are shown in Figure 1. The demographic data of all patients are summarized in Table 1. In all of these patients, ACD to the chair and/or leather was suspected. Note that patients 1 and 2 had previously reported and been diagnosed with contact allergy to TCMTB contained in their leather car-seats, belts and shoes.³

2.2 | Patch testing

Patients were patch tested using the European Baseline Series (Chemotechnique Diagnostics, Vellinge, Sweden and/or Allergeaze, SmartPractice, Phoenix, AZ). Depending on the patients' history and the clinical aspect of the dermatitis, additional series were also tested, that is, plastic and glues series (patients 1–5), rubber series (patients 1–5), (meth)acrylate series (patient 2) and dye series (patient 2; all allergens being obtained from Chemotechnique Diagnostics and/or Allergeaze). Four patients were tested with DMF 0.1% (patients 3–6), one patient was tested with acetophenone azine 0.1% (patient 5) and all patients were tested with TCMTB (obtained in 90% purity from Toronto Research Chemicals, North York, ON, Canada), prepared at 0.1% in petrolatum (pet.) by the Department of Occupational and Environmental Dermatology in Malmö. Patch tests were applied on the upper back and occluded for 2 days with IQ Ultra test chambers from Chemotechnique Diagnostics; they were fixed with Fixomull

stretch (BSN Medical, Hamburg, Germany). Readings were performed on days (D) 2 and D4 according to the European Society of Contact Dermatitis (ESCD) criteria.⁵ All patients were tested outside of the eczema flare-up period and after a minimum of 15 days without topical corticosteroid application.

2.3 | Skin biopsies

Given the severity and extension of the clinical lesions, the atypical appearance and the unexpected location, skin biopsies were performed to exclude other diagnoses such as psoriasis or mycosis fungoides in three patients (patients 5–7) who were those with the more extensive skin eruptions.

3 | RESULTS

3.1 | Patch tests

All patch test results are summarized in Table 1. All seven patients tested positively to TCMTB 0.1% pet. One patient (patient 6) also reacted positively to DMF 0.1% (+). Two patients presented a concomitant positive reaction to cobalt and chromium (patients 3 and 6), and one of whom also reacted to OIT (+) (patient 6). One patient presented multiple sensitizations to rubber derivatives [N-cyclohexyl-2-benzothiazyl sulfenamide, dibenzothiazyl disulphide, 2-(4, morpholinylmercapto)

TABLE 1 Patch test results of seven patients with allergic contact dermatitis from 2-(thiocyanomethylthio)benzothiazole.

Patient	Age	Sex	Personal products (D2/D4) ^a	European baseline series ^b (D2/D4) ^a	P&G series (D2/D4) ^a	Rubber series (D2/D4) ^a	Acrylates series (D2/D4) ^a	Dyes series (D2/D4) ^a	TCMTB (D2/D4) ^a	DMF (D2/D4) ^a	AA (D2/D4) ^a
1	16	F	Leather belt +++/+++ Leather shoe sole +++/+++	—/—	—/—	—/—	NT	NT	+/+++	NT	NT
2	35	F	Leather car seat —/+	—/—	—/—	—/—	—/—	—/—	+/+++	NT	NT
3	65	F	Leather car seat —/—	Chromium +++/+++ Cobalt +++/+++	—/—	—/—	NT	NT	+/+++	—/—	NT
4	21	M	Different shoe soles —/—	—/—	—/—	—/—	NT	NT	?+/+	—/—	NT
5	37	M	Shoe sole Adidas —/+ Ahoe sole Berkelmans —/+ Leather shoe sole —/+++	Colophonium +++/+++ MP —/+ Mercapto mix +++/+++ MBT +++/+++ Textile dye mix +/+	—/—	N-cyclohexyl-2-benzothiazyl sufenamide +++/+++ MBTS +++/+++ MOR +++/+++ PBN —/+ N-(cyclohexylthio) phthalimide +/+	NT	NT	+/+++	—/—	—
6	45	M	Leather seat car seat —/—	Chromium +++/+++ cobalt +/+ OIT +/+	NT	NT	NT	NT	+/+	+/+	NT
7	67	M	NT	MP +/+ FMI +/+ Oakmoss absolute +/+	NT	NT	NT	NT	+/+++	NT	NT

Note: —, negative; ?+, doubtful; + to +++, positive patch test reaction.

Abbreviations: AA, acetophenone azine; DMF, dimethylfumarate; F, female;

FMI, Fragrance Mix I; M, male; MBT, 2-mercaptobenzothiazole; MBTS, dibenzothiazyl disulphide; MOR, 2-(4-morpholinylmercapto)benzothiazol; MP, myroxylon pereirae; NT, not tested; OIT, octylisothiazolinone; P&G series, plastic and glues series; PBN, N-phenyl-2-naphthylamine; TCMTB, 2-(thiocyanomethylthio)benzothiazole.

^aThe readings were performed on day (D) 2 and D4.

^bDuring the time of the investigation, OIT was a recommended addition to the European baseline series, not formally part of it. However, it was tested in all seven patients.

benzothiazol, *N*-phenyl-2-naphtylamine, *N*-(cyclohexylthio) phthalimide] but also to mercapto mix (++++) and mercapto benzothiazole (++++) (patient 5). As reported previously, patient 2 presented a positive reaction with a piece of leather from his car seat.³ Patients 1 and 5 presented positive reactions with samples of other leather products (shoes and/or belt).

3.2 | Skin biopsies

Histopathological examinations of the skin biopsy specimens were suggestive of eczema with epidermal acanthosis and focal parakeratosis. The epithelial layers included spongiosis and exocytosis of lymphocytes.

The superficial dermis contained a moderate to dense perivascular inflammatory infiltrate, mainly composed of lymphohistiocytic cells accompanied by few polymorphonuclear eosinophils in two patients.

4 | DISCUSSION

In 2007, DMF was responsible for an important number of cases of ACD caused by leather products, in particular by sofas imported from China. DMF was notably present in small sachets labelled 'mouldproof agent' used as antimicrobial and antifungal agents during storage and transport of these leather products.⁶ Patients presented localized or more extensive dermatitis on the back and in posterior sides of the thighs. Following this epidemic of ACD, in 2012, DMF was banned from use in Europe at concentrations greater than 0.1 mg/kg⁷ and the term 'sofa dermatitis' was used to describe skin reactions suspected of ACD caused by a sofa or all other type of seats. As in the present case series (patients 5–7), in some cases of ACD to DMF, the severity and clinical extension of the skin reaction suggested other diseases including drug-induced reactions, lymphoproliferative disease, paraneoplastic skin disorder, mycosis fungoides or psoriasis. However, skin biopsy confirmed the diagnosis of eczema, so an ACD was suggested, and patch tests were performed.⁸

Given the clinical aspect of sofa dermatitis, our patients were patch tested with the allergens previously reported in the literature for this condition, but also for TCMTB, which is used for its biocidal properties, notably in leather products. According to the Biocidal Products Regulation (BPR; EU No 528/2012), TCMTB is currently approved for use only in two types of products: PT9 (fibre, leather, rubber and polymerized materials preservatives) and PT12 (slimicides). Therefore, in Europe, it can be found in different types of products such as, leather, imitation leather, in the process of paper and cardboard manufacturing.⁹

The use of TCMTB as a biocide during the leather-tanning process started in the 1990s when pentachlorophenol was banned as a leather fungicide in the European Union (EU).¹⁰

Since the ban of use of DMF, other biocides have been used during the leather-tanning process, in particular isothiazolinones derivatives. Methylisothiazolinone (MI) has been reported as the allergen responsible of ACD caused by leather-care products used by patients

to clean their leather sofas.¹¹ More recently, OIT, another isothiazolinone derivative, has also been implicated in sofa dermatitis^{12–16} notably caused by car seats.¹⁶ The latter type of chair was responsible for ACD in two of our patients (patients 1 and 2). Patients reported the purchase of a new car with leather seats followed within a few weeks by the appearance of skin lesions.³ MI and OIT were tested in all patients in this case series, but unfortunately, not all patients were tested with a piece of their sofa due to fear of damaging it. But in case of skin lesions suggestive of 'sofa dermatitis', not only chairs, but all seats should be suspected (e.g. armchairs, sofas, chairs, office chairs, car seats, golf carts, etc.). For the other patients in our series, a regular contact (more than 1×/day) with a leather chair/armchair was identified. The dermatitis of all the patients sensitized to TCMTB improved and/or healed after the avoidance of contact with their sofa and all other leather products. As previously reported, patient 2's car seat leather was analysed by gas chromatography–mass spectrometry (GC–MS) and confirmed the presence of TCMTB.³ The concentration of the latter was determined at 250 mg/kg in the sample analysed (by liquid chromatography). Among analyses carried out in 2011 by liquid chromatography on several leather samples (*n* = 40), Font et al. found TCMTB in 90% of the samples analysed, at concentrations up to 440–540 mg/kg. Note that in comparison, only 8% of the samples contained OIT with a lower concentration (44–230 mg/kg).⁴ In the present series, not all patients reported that their chair/sofa was recently purchased. Therefore, sensitization of these patients is possibly explained by a release of the allergen after progressive wear and tear.

In 2018, a Swedish and French Competent Authorities proposed to restrict the use of some skin sensitizers in textile and leather products in the EU.¹⁷ However, the proposed restriction did not cover the active ingredients in biocidal products, which are within the scope of the BPR. This was supported by the Committee for Risk Assessment (RAC) and the Committee for Socio-economic Analysis (SEAC). The opinion by RAC and SEAC must be adopted by the European Commission. Our case series illustrates the need for more stringent restrictions within BPR regarding the use TCMTB in order to protect consumers and workers against skin sensitization to TCMTB.

It is often difficult to obtain the exact composition of leather products, especially as some products are manufactured outside of Europe (with different legislations) and imported. In Europe, TCMTB in substances and mixtures (chemical products) is classified as skin sensitizer (category 1, H317 may cause an allergic skin reaction; harmonized classification) according to the European Classification, Labelling and Packaging (CLP) Regulation.¹⁸ Today, however, there is no obligation to label the presence of TCMTB in solid materials or articles. In order to know the composition of these leather products, chemical analyses (by chromatography analyses) are necessary. However, these techniques require expert skills and are not routinely performed since they are not available in all Contact Allergy Units. Moreover, to date, not all centers have TCMTB for patch testing (suitable preparations are not commercially available) leading to an under-diagnosis.

In our case series, one patient with diffuse eruption and palm-plantar involvement also presented positive reaction to 2-mercaptobenzothiazole (MBT), mercapto mix and other rubber

derivatives (patient 5). In the series of Nardelli et al., among the patients sensitized to TCMTB, 69% presented a positive reaction to mercapto mix and 57% to MBT.² These authors suggested a cross-reaction between MBT and TCMTB based on concomitant patch test reactivity. Cross-reactivity could be suggested because MBT is the main product of the degradation of TCMTB. This has been reported by studies on metabolites in rat urine and/or microbial transformation in wastewater.^{19,20} However, among our case series, only one (among the seven TCMTB sensitized patients) reacted to MBT or other MBT-mix substances. This does not seem to support a cross-reactivity phenomenon. To date, no human study has yet investigated whether the concomitant positive patch tests to TCMTB and MBT is due to cross-reactivity or concomitant/multiple exposure. Further investigations are thus necessary to confirm cross-reactivity in humans.

In the present case series, some patients presented concomitant positive patch tests to other allergens; however, these patients had no prior history of contact dermatitis. Therefore, the associated positive patch test reactions to chromium, cobalt and/or OIT are more likely due to concomitant (co-)sensitization.

In this case series, the diagnosis would have been missed in more than 50% of cases, if TCMTB had not been tested. However, TCMTB is not present in commercial products for patch testing. Since TCMTB is found in 90% of leather objects,⁴ given the diffuse and severe clinical aspects in some patients and sensitization due to commonly occurring exposure to undeclared TCMTB in leather products, we recommended the availability of this molecule in commercial patch test preparations.

5 | CONCLUSION

We report a series of seven patients with skin reactions suspected of ACD from leather sofas (sofa dermatitis) and with positive patch test reactions to TCMTB 0.1% pet., a biocide used in leather products. All patients showed clinical improvement after avoiding contact with their sofa and with all leather objects. Diagnosis in more than half of the patients would have been missed if TCMTB had not been tested. It is recommended to test this allergen diluted at 0.1% in pet. As TCMTB has been contained in several leather products, it appears important to test this agent in every suspected case of ACD due to sofas or chairs in order to avoid missing any new source of sensitization. We also recommend that a preparation of TCMTB for patch testing shall be made available.

AUTHOR CONTRIBUTIONS

Anne Herman: Conceptualization; methodology; investigation; writing – original draft; data curation; writing – review and editing. **Liliane Marot:** Writing – review and editing; formal analysis. **Marie Baeck:** Writing – review and editing; validation.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

PATIENT CONSENT

Patients in this manuscript have given written informed consent to the publication of these case details.

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