

Research letters

Allergic contact dermatitis to nonmethacrylate nail allergens in the UK

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DEAR EDITOR, The soaring demand for acrylic nails has resulted in a rapid increase in the frequency of allergic contact dermatitis (ACD) to (meth)acrylates.^{1,2} However, traditional nail varnish remains widely used. Nail varnish is a mixture of film formers and includes nitrocellulose, adipic acid–neopentyl glycol–trimellitic anhydride copolymer (AA) and phthalic anhydride–trimellitic anhydride–glycols copolymer (PA). Resins such as tosylamide formaldehyde resin (TSFR), a polymer formed from the reaction of toluene sulfonamide and formaldehyde, allow the film to adhere to the nailbed.

TSFR was historically a frequent nail varnish allergen and is present in the updated 2019 BCSA facial series. Allergic contact dermatitis (ACD) to AA and PA has been described only rarely, despite widespread use of nail varnish. The most recent edition of Fisher's Contact Dermatitis does not index PA at all.³ Few cases of patients with ACD to nail varnish have been described in the US and UK literature.^{4,5} More recently, AA, PA and TSFR were shown to be responsible for ACD in a single-centre UK audit.⁶ The authors suggested that AA and PA had become a more frequent cause of nail varnish contact allergy than TSFR, and recommended including AA and PA in the facial, fingertip and vulval series.

No large-scale multicentre audits have previously been performed on the incidence of ACD to these nail allergens, and therefore we conducted a retrospective audit of seven dermatology centres in the UK and Ireland. Data were collected retrospectively in six centres (Birmingham, Bath, Uxbridge, Newport, Leeds and Cork) and prospectively in one centre (Leicester). Patients with suspected contact dermatitis had been patch tested over a mean period of 43 months (range 9–60) between November 2013 and August 2018 to AA 1% in petrolatum (pet.), PA 1% pet. and TSFR 10% pet. In Leicester, AA, PA and TSFR were included in the baseline series, and therefore consecutive patients with suspected contact dermatitis were tested. The other six centres included these allergens as part of their cosmetic series (Leeds), face series (Cork, Bath, Uxbridge, Newport) or both (Birmingham).

AA and PA were prepared by Boots Contract Manufacturing (Boots, Nottingham, UK). TSFR was obtained from Chemotechnique Diagnostics (Malmö, Sweden). Readings were carried out according to the European Society of Contact

Dermatitis guidelines on days 2 and 4 by dermatologists experienced in interpreting patch tests.⁷

In total, 8053 patients with suspected contact dermatitis were patch tested to TSFR, 7440 to AA and 5490 to PA. Overall, 52 patients tested positive to at least one nail allergen, with a total of 76 positive reactions: 30 patients tested positive to AA, 27 patients to PA and 19 to TSFR.

In the six centres where AA, PA and TSFR were part of a facial or cosmetics series, the proportion of patients with a positive patch test to PA was 0.56% (range 0–1.84%), to AA 0.43% (range 0–1.15%) and to TSFR 0.26% (range 0–0.99%). In Leicester, where 1016 consecutive patients were tested, the proportions of patients with a positive patch test to AA, PA and TSFR were lower: 0.3%, 0.2% and 0.1%, respectively (Table 1). Thirty out of 52 patients (58%) had positive reactions to only one of the nail allergens (AA or PA or TSFR). Seventeen of these 30 patients (57%) did not react to any other allergens in the baseline or/and additional series (Table 1; numbers in brackets).

Nine of the 16 patients (56%) who tested positive to TSFR only (negative to AA and PA) did not have any other cosensitivities: they did not react to any other allergens in the baseline and/or additional patch test series. In the majority of these nine patients (seven of nine) the results were clinically relevant. Smaller but clinically significant proportions of the 52 patients tested positive to only one of the other nail allergens (AA or PA): 13% (seven of 52) and 12% (six of 52), respectively (Table 1; numbers in brackets). Therefore a diagnosis of ACD to nail cosmetics would have been missed in 25% of the patients had they been tested to TSFR alone.

Cosensitizations were reported in 25 of 52 patients (48%) with a positive patch test to the nail allergens. These included 2-HEMA (2-hydroxyethylmethacrylate) and other (meth)acrylates, limonene, linalool, methylisothiazolinone, colophonium, *Myroxylon pereirae*, cobalt, chromium and formaldehyde.

This large multicentre audit suggests that allergy to PA and AA is being missed, leading to undiagnosed cosmetic allergy with associated morbidity and a lack of information for regulators. Development of a commercial patch test preparation for PA and AA should be a priority. Until a commercial manufacturer prepares patch test materials for PA and AA, we recommend screening patients with facial dermatitis using nail varnishes containing PA and AA, tested 'as is' painted on a test chamber, and allowed to dry before application to the patient's back. Once available, we suggest that PA and AA should be included in an updated British Society for

Table 1 Number and percentage of patients who patch tested positive to at least one nail allergen and the number and percentage of patients who patch tested positive to only one nail allergen per centre and in total

	Allergic contact dermatitis to:			Total number of patients	Total number of positive patch test reactions	Proportions of patients with positive patch tests
	AA 1% pet.	PA 1% pet.	TSFR 10% pet.			
Leicester						
At least one	3	2	1	5	6	AA 0.3%, PA 0.2%, TSFR 0.1%
Only one	2	1 (1)	1			
Newport						
At least one	4	4	0	4	8	AA 0.84%, PA 0.84%, TSFR 0%
Only one	0	0	0			
Bath						
At least one	2	3	2	5	7	AA 0.58%, PA 0.88%, TSFR 0.58%
Only one	0	1	2			
Leeds						
At least one	4	4	1	7	9	AA 0.12%, PA 0.12%, TSFR 0.03%
Only one	2	2 (1)	1			
Uxbridge						
At least one	7	9	6	13	22	AA 1.15%, PA 1.48%, TSFR 0.99%
Only one	0	2 (2)	4 (1)			
Birmingham						
At least one	10	5	6	15	21	AA 0.6%, PA 1.84%, TSFR 0.37%
Only one	4 (4)	0	5 (5)			
Cork						
At least one	0	0	3	3	3	AA 0%, PA 0%, TSFR 0.38%
Only one	0	0	3 (3)			
All centres						
At least one	30	27	19	52	76	AA 0.40%, PA 0.49%, TSFR 0.24%
Only one	8/52; 15%	6/52; 12%	16/52; 31%			

AA, adipic acid–neopentyl glycol–trimellitic anhydride copolymer; PA, phthalic anhydride–trimellitic anhydride–glycols copolymer; pet., petrolatum; TSFR, tosylamide formaldehyde resin. Several patients in each centre patch tested positive to more than one nail allergen. The number of patients who did not report any other sensitizers in either the baseline or additional series is noted in brackets.

Cutaneous Allergy facial and cosmetic series, with subsequent reaudit.

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Identification of a founder mutation in *KRT14* associated with Naegeli–Franceschetti–Jadassohn syndrome

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Dear Editor, Naegeli–Franceschetti–Jadassohn syndrome (NFJS; MIM 161000) is a rare, autosomal-dominant ectodermal dysplasia.¹ Affected individuals present with a heterogeneous spectrum of ectodermal abnormalities. The most distinctive features are absent dermatoglyphs, reticulate hyperpigmentation of the skin, palmoplantar keratoderma and decreased sweating. Other features may include abnormalities of the teeth, hair, nails and skin.¹

Histopathologically, affected skin areas show mild hyperkeratosis, and in areas of hyperpigmentation an accumulation of melanosomes is observed in the upper part of the epidermis.² Lugassy et al. identified three distinct mutations in the *KRT14* gene, which encodes the intermediate filament keratin 14 (*KRT14*), in four families with NFJS and one family diagnosed with dermatopathia pigmentosa reticularis (DPR; MIM 125595).² DPR shares clinical characteristics of NFJS. Recently, Burger et al. comprehensively summarized the clinical and genetic spectrum of the NFJS/DPR cases that have been published to date, and showed inter- and intrafamilial phenotypic heterogeneity associated with *KRT14* mutations.¹ However, there is a consensus that NFJS and DPR represent a continuous phenotypic spectrum of the same entity.^{1–3} Here, we report the detection of a *KRT14* mutation in a large kindred group with NFJS from Germany.

The family (Figure 1a) was referred to the genetic counselling unit at the University Hospital of Bonn with suspected NFJS. The index patient (Figure 1a; III:1, aged 21 years) and her sister (Figure 1a; III:2, aged 18 years) presented with absent dermatoglyphs, anhydrosis, hyperpigmented lenticular-sized spots in the axillary and inguinal regions, and mild palmoplantar keratoderma (Figure 1b, c). No other ectodermal abnormalities were observed. The index patient had developed blistering and peeling skin a few hours postpartum (Figure 1d), which had healed within the first weeks of life without scarring or recurrence. Nine further family members presented with clinical signs of NFJS (Figure 1a).

Diagnostic DNA analysis was performed. Written informed consent was obtained from all participants, in accordance with

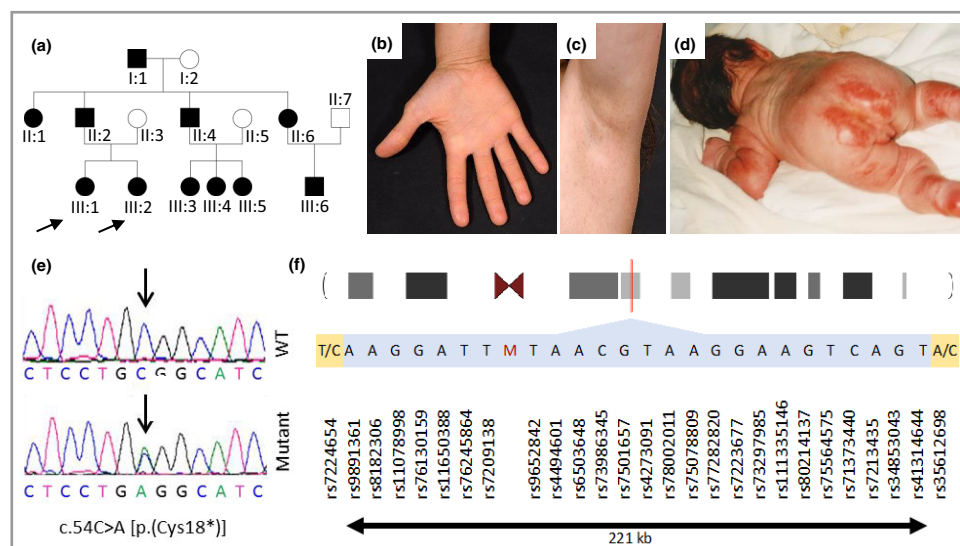


Figure 1 Pedigree, clinical presentation and genetic analyses. (a) Pedigree of the German family with 11 affected individuals. All affected family members are shown in black; circles and squares denote female and male individuals, respectively. Mutation and haplotype analyses were performed in individuals III:1 and III:2, as indicated by arrows. (b, c) Clinical presentation of III:1 at the age of 21 years, with (b) absent dermatoglyphs and (c) reticulate hyperpigmentation in the axilla. (d) Skin erosions and blistering in III:1 postpartum. (e) Sequencing of *KRT14* revealed a c.54C>A substitution, leading to a premature stop codon at position 18 [p.(Cys18*)]. The mutated sequence is shown in comparison with the wildtype (WT) sequence. (f) Illustration of haplotypes on chromosome 17 in the investigated affected individuals from both families. Shared haplotypes are highlighted in blue shading, nonoverlapping haplotypes are highlighted in yellow shading. M indicates the localization of the mutation.