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Compositae sensitization in Danish children and adolescents

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Abstract

Background: Compositae plant sensitization in children is relatively frequent. From 1995–2006, we found a prevalence of 1.8% sesquiterpene lactone (SL) mix/parthenolide patch test positives among consecutive eczema patients <18 years.

Objectives: To report the results of patch test screening for Compositae sensitization in patients <18 years in the last 13 years.

Methods: Children and adolescents <18 years, diagnosed with Compositae sensitization between 2007 and 2019, were included.

Results: Among 388 children tested, 12 (3%) were Compositae-sensitized, and 11 (2.8%) had positive reactions to SL mix. Compositae mix 5% pet. elicited positive reactions in six of seven patients tested, and dandelion extract 2.5% pet. in six of 10 patients tested. The mean age of the five girls and seven boys was 9.4 years and 11.7 years, respectively. Eleven children had a personal and one a family history of atopy, and 11 children had hand eczema. Only two were mono-sensitized to Compositae.

Conclusions: SL mix is a suitable screening agent among children and adolescents in our area, well supplemented with Compositae mix 5% and dandelion extract. The study emphasizes the importance of Compositae screening in children with a personal and/or family history of atopy, hand eczema or widespread airborne dermatitis, summer exacerbation, and plant exposure.

KEYWORDS

allergic contact dermatitis, Asteraceae, children, Compositae, Compositae mix, dandelion, patch testing, sesquiterpene lactone mix

1 | INTRODUCTION

In recent decades, Compositae sensitization in children with eczema has been reported as frequent in selected patch test populations.^{1–4} Large-scale clinical studies with either sesquiterpene lactone mix (SL mix) or Compositae mix 5/6% pet. (CM 5/6) as screening agents have detected prevalences of between 1.3% (SL mix) and 4.2% (CM6%).^{2,4} Furthermore, case reports and case series have pointed to dandelion (*Taraxacum officinale* [L.] F.H.Wigg) as an important allergen in Compositae-sensitive children.^{5–8}

We have previously reported a prevalence of 1.8% SL and/or parthenolide patch test positives among consecutive eczema patients

<18 years of age, patch tested from 1995–2006.⁷ Here we report the result of patch test screening for Compositae sensitization in patients of the same age group in the period 2007–2019.

2 | METHODS

Children and adolescents <18 years of age, who were diagnosed with Compositae sensitization in the period January 1, 2007–December 31, 2019, were included in the analysis. Dependent on age, some were patch tested with the baseline series and others with a modified, shorter baseline series. From 2014, a baseline series for children was

introduced. This included, among others, metals (nickel, chromium, cobalt), fragrance mix I and II, preservatives, rubber chemicals, and SL mix. SL mix was the only Compositae screen in the series.

At the beginning of the study period, the baseline series included SL mix 0.1% pet. (Trolab, Almirall Hermal, Reinbek, Germany) and parthenolide 0.1% pet. (Chemotechnique Diagnostics, Vellinge, Sweden) as Compositae screening agents. They were supplemented with Compositae mix (CM) 2.5% pet. (Chemotechnique Diagnostics) and parthenolide 3 $\mu\text{g}/\text{cm}^2$ (TRUE Test, AllergEaze, SmartPractice, Phoenix, Arizona) in 2015. Additional Compositae allergens and extracts were added, dependent on the baseline series used and the patient's exposure. The supplementary allergens included Compositae mix 5% pet., which was replaced by Compositae mix II 5% in 2014 (Chemotechnique Diagnostics). The patch test materials were applied to the back for 2 days, using Finn Chambers on Scanpor tape (SmartPractice). Readings were performed on day (D) 3 or D4 and D7, according to the latest recommendations.⁹

3 | RESULTS

From January 2007–December 2019, 388 children and adolescents <18 years of age were patch tested with the SL mix, and 12 (3%) were sensitized to Compositae. Among the 12 patients, 11 had positive patch test reactions to SL mix, yielding a detection rate of 2.8% (11/388). The 12 patients comprised five girls with a mean age of 9.4 years, and seven boys with a mean age of 11.7 years. Ten of the 12 children/adolescents had or had had, atopic dermatitis, while one had hay fever and one had a family history of atopy. The results of patch testing with Compositae allergens and extracts are shown in Table 1. Among the seven children with positive reactions to CM 5%, three were tested with the old CM 5% pet. and four with CM II 5%

pet. Only two children had no other contact allergies; however, patient 2 had a positive reaction to the outside of a goalkeeper's glove, which may have been contaminated with Compositae plant debris (Table 1). Altogether, five children had one other contact allergy, four had two other contact allergies (the reactions to parts of an insulin pump and glucose sensors in patient 12 was attributed to isobornyl acrylate), and one had three other contact allergies. The distribution of these allergies is shown in Table 2.

Concerning clinical features, patient 12, who was sensitized to isobornyl acrylate from glucose sensors and an insulin pump, was the only one who did not have hand eczema. Patient 6 had primarily facial dermatitis at the time of testing. The remaining 10 patients had, at least partly, volar involvement of the hands. Two of these had had an airborne contact dermatitis reaction after exposure to Compositae. Patient 7 was the only one with an occupational exposure: she handled lettuce in a bistro kitchen. The Compositae sensitization was considered of current and/or previous relevance in 11 patients, the only exception being patient 12 with isobornyl acrylate contact allergy.

Summer exacerbation was reported in nine patients. Persons without summer exacerbation included patient 12 with isobornyl acrylate sensitization and patient 7 with occupational exposure; however, the latter recalled dorsal hand eczema as a child.

4 | DISCUSSION

It has long been recognized that SL mix is an inadequate screening mix for Compositae sensitization, especially compared to the original CM 6% pet.^{10–13} The prevalence of positive patch test reactions to the former, among consecutive patients at patch test clinics, is between 0.49% and 1.9% in European studies.^{14,15} In the present

TABLE 1 Distribution of positive reactions to Compositae screening agents and additional Compositae extracts and plants among consecutive children and adolescents tested at a Danish university hospital

Patient no.	Sex/age (years)	Test year	SL mix	PTH	CM5% CMII5%	CM 2.5%	Dandelion 2.5% pet.	Other
1	M/9	2008	++	++	NT	NT	++	Pos. Yarrow, tansy, chamomile
2	M/9	2011	++	++	++	NT	++	NT
3	M/10	2011	+	–	–	NT	–	NT
4	F/8	2014	++	NT	++	NT	+	Pos. Chrysanthemum and feverfew
5	M/17	2015	++	++	++	++	++	Pos. iceberg lettuce as is
6	M/14	2015	++	++	NT	NT	++	Pos. tansy, chamomile
7	F/17	2017	+	–	+(+++ at second test)	?+-F.	NT	Pos. iceberg lettuce “as is”
8	F/3	2017	+	NT	NT	+	+	NT
9	F/5	2018	+	+	NT	?+-F.	–	Neg. yarrow
10	M/12	2019	–	–	+	NT	?+-	Pos. tansy, chamomile, sunflower
11	M/11	2019	++	–	NT	+	?+-F.	Neg. CM compounds
12	F/14	2019	++	?+-	+	?+-	NT	NT

Abbreviations: ?+-, doubtful positive; CM, Compositae mix 5% pet. and Compositae mix II 5% pet. (used from 2014) and Compositae mix 2.5% pet.; F., follicular reaction; Neg., negative; NT, not tested; Other, other Compositae extracts or plants tested; Pos., positive; PTH, parthenolide 0.1% pet. or 3 $\mu\text{g}/\text{cm}^2$; SL mix, sesquiterpene lactone mix 0.1% pet.

TABLE 2 Distribution of contact allergies other than Compositae in 12 Compositae-sensitive children

Patient no.	Sex/age (years)	Other contact allergens
1	M/9	Cobalt chloride
2	M/9	Goalkeeper's glove
3	M/10	Cobalt chloride
4	F/8	Nickel sulfate
5	M/17	Cobalt chloride
6	M/14	Cobalt chloride, quaternium 15, formaldehyde
7	F/17	Colophonium, carba mix
8	F/3	Potassium dichromate, fragrance mix I
9	F/5	0
10	M/12	Fragrance mix I, falcarnol
11	M/11	0
12	F/14	Gold sodium thiosulfate, Isobornyl acrylate, Medtronic insulin pump (plastic; Medtronic Ltd. Abbott Diabetes Care, Alameda, CA, USA), Medtronic glucose sensor (plastic), Freestyle Libre sensor (plastic and adhesive)

study, the prevalence of positive SL mix reactions of 2.8% in children and adolescents is possibly the highest ever reported. This may, of course, reflect the relatively small number of children tested. Giordano-Labadie et al reported a prevalence of SL mix-positive of 1.7% in 114 children, Lubbes et al 1% in 995 children/adolescents, and Simonsen et al 1.3% in 1522 children and adolescents.^{1,4,16} There seems to be a slight increase in the number of Compositae-sensitive children detected in the last 5 years (Table 1). This was also reflected in the Danish multicentre study (including our department) of 1522 children and adolescents: the prevalence of SL mix positives was 1.3% in the period from 2012–2016, which was higher than the 0.8% positives in the period from 2003–2011 ($n = 2542$).^{4,17}

Most of the SL mix-positive reactions were considered relevant; this was also supported by the positive reactions to other Compositae allergens/extracts (Table 1). However, we have previously seen a few adolescents with possible cross-reactivity between *p*-phenylenediamine and SL mix and, the relevance of the SL mix reactions was unknown.¹⁸ Furthermore, in recent years an unexplained association between positive patch test reactions to isobornyl acrylate and SL mix has been reported from all over Europe, and this may cause possibly irrelevant reactions to SL mix, as exemplified in patient 12 in the present study.¹⁹

With regard to CM 5%, a Swedish multicentre study reported the results of inclusion of this mix in the baseline series for 1.5 years: 31 of 2818 patients (1.1%) had positive patch test reactions to CM 5% compared to 26 to the SL mix (0.9%). The conclusion was that CM 5% was not suitable as a supplement to the SL mix, but might be used as a substitute.²⁰ Belloni-Fortina et al used CM 5% as a screening agent in children and reported the following prevalences: 0.3% (321 children <3 years of age), 1.6% (2614 children <11 years of age), and 2.6% (641

children/adolescents <17 years of age).^{3,21,22} In the present study, almost all children tested with CM 5% had positive reactions, supporting the suitability of the mix as a screening agent. In the Swedish study,²⁰ two cases of alleged active sensitization were noted, but lowering the concentration of CM 5% to 2.5% means that some cases of sensitization will be missed: two children with doubtful reactions to CM 2.5% had positive reactions to CM 5% (Table 1). Because of these findings, we interpret doubtful reactions to CM 2.5% in both children and adults as possible markers of Compositae contact allergy and supplement with CM 5%/CM II 5%.²³ Of course, we cannot rule out that the prevalence of Compositae sensitization in children would be even higher if all children were screened with CM II 5%.

In a German retrospective multicentre study on Compositae sensitization in cooks, florists, and a large control group,²⁴ no case of active sensitization to either CM 5% or CM II 5% was reported. However, in 15.5% of the patients, the application time was one day, and only D3/D4 readings were analyzed. The data are thus not comparable with those of the Swedish study and, therefore, they cannot rule out a risk of sensitization.

Dandelion extract is definitely a useful supplementary allergen as more than half of the patients tested had positive, and two doubtful positive, reactions to the extract, but it is not as useful as SL mix and CM 5% in our area. In an American case series including three children with Compositae contact allergy, dandelion extract elicited positive reactions in all children, whereas SL mix and CM 5% was positive in only two children.⁸ The main allergen of dandelion, taraxinic acid, which is an eudesmanolide sesquiterpene lactone, apparently does not cross-react with the eudesmanolide sesquiterpene lactones of the SL and Compositae mixes.

Exposure varies and, therefore, patch testing should be based on the individual child's history. In the countryside, exposure to weeds may be important, but ornamental plants and lettuce may also sensitize (Table 1). Parthenolide seems to be less important and should not be tested on its own when CM 5% is available (Table 1).

Based on the literature, many Compositae-sensitive children have positive patch test reactions to SL mix.^{6,7} This probably reflects that the reactions are true expressions of plant sensitization as opposed to positive patch test reactions to Compositae mixes, which may be caused by cross-reactivity to colophonium and fragrance terpenes.²⁵

Previous studies of patch test populations in Europe, the USA, and India have shown either an equal distribution of Compositae sensitization in the two genders or a preponderance of females.^{26–29} The slightly higher number of boys in the present study, however, is in accordance with the findings of Belloni Fortina et al³: they reported that positive reactions to CM 5% were significantly higher in boys and ascribed this to greater outdoor exposure.

Even though the mean age was about 11 years for all children, the youngest was 3 years old and several of the children had had symptoms of Compositae contact allergy for some time prior to patch testing. Simonsen et al, in their first nationwide multicentre study of patch testing in Danish children, reported that SL mix ranked 2nd out of five allergens eliciting positive patch reactions most frequently in 1–4 year-old children, and as 4th of 5 among 5–8 year-old children.¹⁷

This emphasizes the importance of a high level of suspicion of Compositae sensitization, especially in toddlers and kindergarten children.

The clinical features of Compositae dermatitis are best assessed in patients without endogenous eczema or other contact allergies. In the present study, however, the majority of the patients had, or have had, atopic dermatitis, while the remaining had a family history of atopy, including even the patient with unknown relevance of the SL mix reaction and isobornyl acrylate contact allergy.

This association between atopy and Compositae sensitization is in accordance with previous case reports and case series.^{5-7,30,31} Furthermore, Belloni Fortina et al, in their study of 641 children and adolescents <17 years of age, reported a significantly higher prevalence of Compositae sensitization in patients with atopic dermatitis compared with children without atopic dermatitis, and the later study on 2614 children <11 years of age from the same group confirmed this finding and also found a significantly higher prevalence of Compositae sensitization in boys, as mentioned above.^{3,22}

The most common clinical feature in the present study was hand eczema, often localized to the palms. Hand eczema was also a common feature in the published case reports and partly in case series.^{5-7,21,30,31} Belloni Fortina et al,²¹ in their study of Italian children with Compositae sensitization, reported that the Compositae dermatitis was localized to air-exposed skin, mainly face and hands, in all children. Whether the hand eczema is the cause or the result of Compositae sensitization is not clear, but, considering the disposition to endogenous eczema in these children, the most likely explanation is that the impaired skin barrier of atopic dermatitis results in atopic hand eczema and secondary plant sensitization. This is also supported by the occurrence of more than one contact allergy in most patients, although genetic disposition to polysensitization may also play a role here (Table 2).³² Netterlid et al reported on patch testing in children with allergic rhinitis and/or asthma, and one child with widespread atopic dermatitis since early childhood as well, was diagnosed with Compositae sensitization. She had summer exacerbation of both dermatitis and rhinitis, ascribed to pollen, but the dermatitis improved after allergen avoidance.³³

As mentioned above, the majority of the children had more than one contact allergy, although only one was polysensitized (≥ 3 or more contact allergies). The occurrence of cobalt sensitization without nickel sensitization in atopic individuals has been reported previously. The reason for this is not clear, but possible exposure in children include leather shoes.^{34,35}

5 | CONCLUSIONS

The present study confirms the association between a personal and/or family history of atopy and Compositae sensitization in children and adolescents. The presence of hand eczema is an important clinical feature, although it is not clear whether the hand eczema is the cause or the result of Compositae sensitization.

The prevalence of SL mix patch test reactions is surprisingly high (2.8%) in children and adolescents, confirming SL mix to be a useful

screening agent in our area.²³ However, CM/CM II 5% are very good supplementary allergens, and we cannot rule out an even higher prevalence of Compositae sensitization if either of these had been used as a screening mix. Because of a potential risk of sensitization with CM 5%,²⁰ we prefer to use both this and the newer CM II 5% as an additional allergen only. The study also confirms that dandelion extract is an important allergen, which should be tested when Compositae contact allergy is suspected in children. In general, the history of exposure is a key factor for the choice of further Compositae patch test materials. Compositae sensitization may be suspected in children, even toddlers, with (i) a personal and/or family history of atopy; (ii) localized eczema of hands and/or face or more widespread, recalcitrant, possibly airborne, dermatitis; (iii) summer exacerbation, which may sometimes be attributed to pollen in patients with hay fever, thus delaying the diagnosis; and (iv) possible exposure through feeding of pets with lettuce or dandelion, living in a rural area, or participating in outdoor activities.

CONFLICTS OF INTEREST

Klaus E. Andersen is advisor for SmartPractice. Evy Paulsen has previously been principal investigator for SmartPractice.

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