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CONTACT DERMATITIS

Allergic contact dermatitis from allyl isothiocyanate in a Danish cohort of 259 selected patients

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Allyl isothiocyanate is present in many plants. Allergic contact dermatitis from allyl isothiocyanate is well known but infrequently reported. The aim of this study was to investigate the prevalence of contact allergy to allyl isothiocyanate in patients with suspected contact dermatitis from vegetables and food. 259 such patients were tested at the Department of Dermatology, Gentofte Hospital, Denmark, from 1994 to 2003. Only 2 patients (0.8%) had a positive reaction (+) to allyl isothiocyanate and 43 patients (16.6%) had a ?+ reaction. One of the patients with a positive reaction provided samples of margarine, salad cream, oil and mayonnaise. These were analysed with high-performance liquid chromatography, and a moderate concentration of allyl isothiocyanate (2.5 ppm) was detected in the sample of margarine. This patient was a professional sandwich maker presenting with fingertip dermatitis mimicking 'tulip fingers' or allergic contact dermatitis from garlic and onions. In conclusion, allergic contact dermatitis from allyl isothiocyanate occurs in only a limited number of cases, despite frequent exposure. The large number of ?+ reactions raises the question as to whether the recommended patch test concentration is too low.

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Individuals working professionally in food preparation may risk acquiring an occupational dermatosis as the result of exposure to irritants and allergens in foodstuffs, including vegetables. The Cruciferae (or Brassicaceae) plant family includes about 3200 species, of which several are vegetables used in the kitchen, for example broccoli, cress, cauliflower, radish, cabbage, rape and mustard. It is a characteristic of species from the Cruciferae family that they contain glucosinolates, which generate isothiocyanates, or so-called mustard oils, on hydrolysis (1). These mustard oils primarily contain allyl isothiocyanate and to a lesser extent benzyl and phenyl isothiocyanate. Isothiocyanates possess both a highly irritant and an allergenic potential. Generally, reports on dermatological problems from members of the Cruciferae plant family are sparse, though well known (2–7). Kohl and Frosch (2) reported a case of irritant contact dermatitis induced by a self-made mustard compress left on the skin. Mitchell and Jordan (3) described a case of allergic contact dermatitis provoked by radish in a waitress, and Dannaker and White (4) reported a case of allergic contact dermatitis caused by mustard in a salad maker. Other case reports include examples of allergic contact dermatitis from broccoli (5, 6) and cauliflower (7). Moreover, immediate-type allergy, manifested as contact urticaria and angio-oedema, has also been described (8–10).

The literature on allergic contact dermatitis from members of the Cruciferae family is limited to case reports and small series of patients. The aim of this study was: (i) to investigate the frequency of contact allergy to allyl isothiocyanate in a Danish cohort of patients with suspected contact dermatitis from vegetables and other foods; (ii) to determine the content of allyl isothiocyanate in food products provided by a patient with contact allergy to this compound; and (iii) to describe this patient with allergic contact dermatitis from allyl isothiocyanate (*case report*).

Materials and Methods

Patients

We retrospectively identified all patients patch tested with a series of food allergens, including allyl isothiocyanate, during the years 1994–2003 in the Department of Dermatology at Gentofte Hospital. Patients were selected for testing when a contact allergy to food products was suspected and included chefs, sandwich-makers and housewives. They represent a highly selected group among the patients referred to the department for investigation.

Patch testing

Patch testing was performed with a series of allergens related to food products (Table 1), used at the Department of Dermatology at Gentofte Hospital, including allyl isothiocyanate. Allyl isothiocyanate (Merck, Darmstadt, Germany) 0.1% in petrolatum (pet.) and Finn Chambers® (Epitest, Tuusula, Finland) on Scanpor® tape (Alpharma AS, Norgesplaster Facility, Vennesla, Norway) was used for patch testing. Test material was removed after 2 days, and reactions were recorded on days 3, 4 and 7. Reactions were read and interpreted according to International Contact Dermatitis Research Group guidelines (11).

Determination of allyl isothiocyanate in food products

One patient with a positive reaction to allyl isothiocyanate provided samples of food products to which she was exposed. Allyl isothiocyanate content was determined in samples of margarine, salad cream, oil and mayonnaise. 10 ml of acetonitrile was added to approximately 2 g of test material, weighed accurately and the mixture shaken for 40 min and then filtered. The content of allyl isothiocyanate in the filtrate was determined by high-performance liquid chromatography (HPLC), using a reversed phase C18 column and mobile phase composed of 0.2 M disodium-hydrogenphosphate-acetonitrile-water (5 : 65 : 50). HPLC of 20 µl filtrate and calibration solutions of allyl isothiocyanate were performed in isocratic mode and detection at 190–350 nm using diode array detection. Allyl isothiocyanate was determined at its λ_{max} 244 nm. The spectrum match (190–350 nm) as well as the match of HPLC retention time was used for the correct identification of allyl isothiocyanate in the samples (Fig. 1). The recovery of allyl isothiocyanate from all samples, spiked to 4 ppm with this compound, was >98%. The detection limit of allyl isothiocyanate by the present method was approximately 0.5 ppm.

Table 1. Series of allergens related to food products

Allergen	Test concentration and vehicle
Butyl hydroxytoluene	2.0% petrolatum
Butyl hydroxyanisole	2.0% petrolatum
Allyl isothiocyanate	0.1% petrolatum
Clove oil	2.0% petrolatum
Onion	10.0% ethanol
Shallot	10.0% ethanol
Garlic	10.0% ethanol
Sodium metabisulfite	1.0% petrolatum
d-α-tocopherol	5.0% petrolatum
Lettuce	As is
Leek	As is

Results

Patients

A total of 259 patients patch tested with allyl isothiocyanate were identified. This group was comprised of 73% female and 27% male patients.

Patch testing

2 patients (0.8%) developed a positive reaction (+), defined as redness and homogeneous infiltration in the test area to allyl isothiocyanate. The majority (196) of the 259 patients had a negative test (75.7%). 43 patients (16.6%) were classified as having a ?+ reaction. A group of 15 patients (5.8%) was interpreted as having an irritant reaction, and 3 patients (1.0%) developed a follicular reaction. Below, we describe the findings in one of the patients with a positive reaction. The 2nd patient with a positive reaction was lost to follow-up.

Determination of allyl isothiocyanate

The patient with + reaction (described below) provided a sample each of margarine, salad cream, oil and mayonnaise, to which she was exposed during her work. The margarine sample was found to contain 2.5 ppm allyl isothiocyanate. Allyl isothiocyanate could not be detected in the other products provided by the patient.

Case report

The patient providing food products for analysis was a 44-year-old female sandwich maker with no prior history of atopy. She presented with hand eczema of 8-month duration. Symptoms included hyperkeratosis and fissuring of fingertips and pulps, onycholysis and scaling of the palms and on the dorsum of the hands (Figs 2 and 3). The right (dominant) hand was most severely affected. Her job required repeated contact with a wide

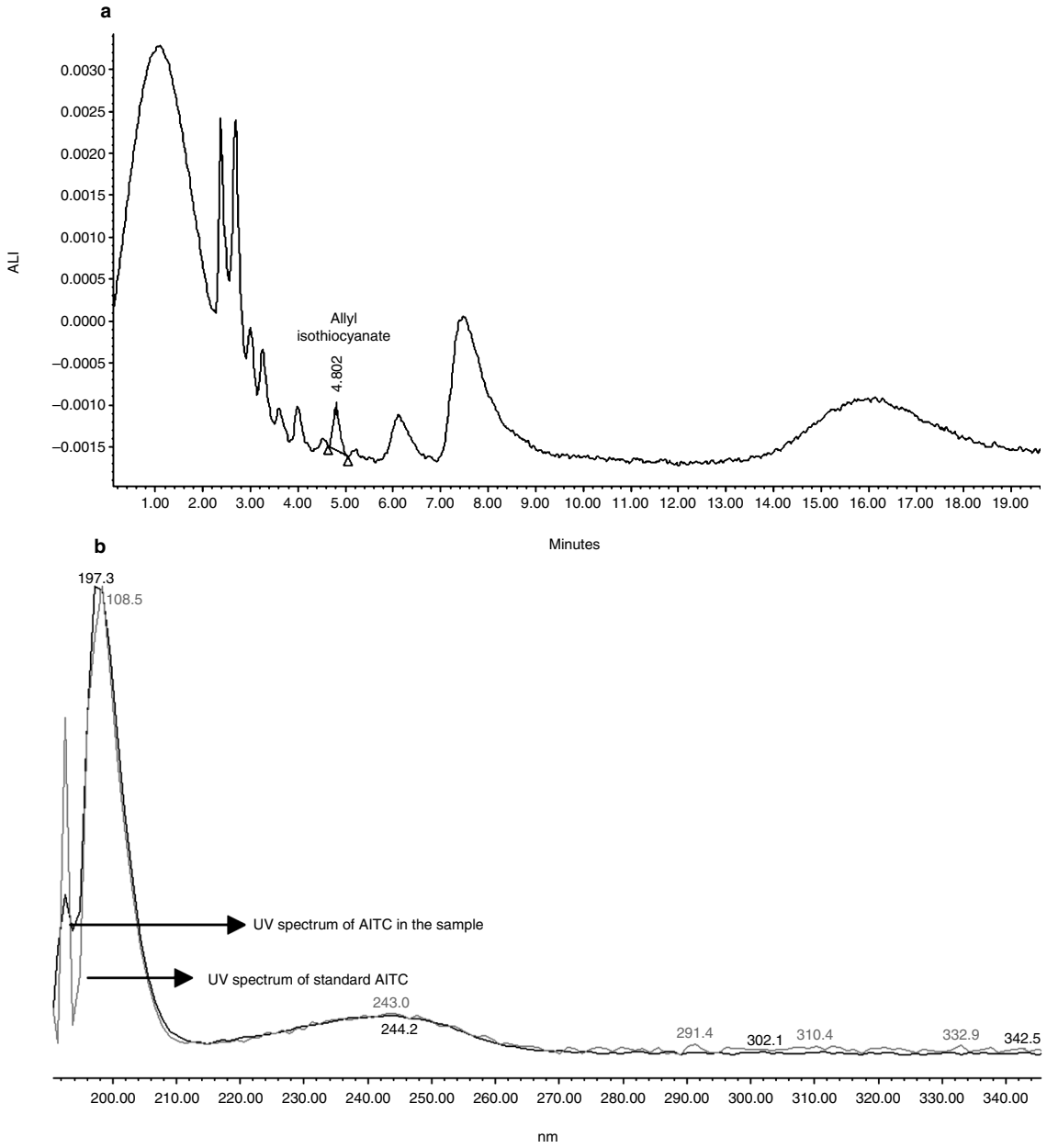

Fig. 1. High-performance liquid chromatography (HPLC) (a) of the extract of margarine preparation and spectrum match (b) of the standard allyl isothiocyanate (AITC) with that of HPLC peak at 4.8 min.

range of food products. Rubber gloves were used intermittently.

Patch testing was performed with standard series and food allergens and showed a ?+ reaction to thiuram mix in 3 recordings, a + reaction to methyldibromo glutaronitrile and a + reaction to allyl isothiocyanate 0.1% in pet. Extensive prick testing with the European standard series, natural rubber latex, extract of rubber gloves, fresh vegetables, fresh fish and fresh meat yielded no positive reactions.

Eczema on the dorsum of the hands regressed as the patient stopped using rubber gloves. Methyldibromo glutaronitrile was found in a shampoo used by the patient. The patient did not describe dermatitis of the face and neck. Because of the eczema, the patient stopped working as a sandwich maker and also avoided direct contact with vegetables and food products known to contain isothiocyanates domestically. Subsequently, the eczema has healed.

Discussion

In this retrospective study, we present data on 259 selected patients consecutively patch tested with

Fig. 2. Fingertip dermatitis due to contact allergy to allyl isothiocyanate.

allyl isothiocyanate during a 10-year period. In the majority of the previously reported cases of allergy to members of the Cruciferae family, patch testing was conducted with the suspected vegetable or food product as is (4–7). So far, literature describing patch testing with allyl isothiocyanate presents mostly single (2, 3, 12) or a very limited number of cases (13, 14).

Despite the considerable number of cases tested in this study only 2 patients were positive. It seems that, although contact with vegetables belonging to the Cruciferae family and products manufactured from rape and mustard (i.e. vegetable oil, margarine and salad cream) occurs frequently both domestically and occupationally, sensitization and allergic contact dermatitis occur in only a very limited number of cases. An alternative explanation could be that the present test concentration fails to detect all true allergic patients. In our study, 43 patients developed a ?+ reaction and 3 patients developed a follicular reaction, supporting the possibility that we might be missing some true-positives. A further possibility is that we are not missing any true allergic patients, but instead observing a number of weakly irritant reactions.

Fig. 3. Fingertip dermatitis due to contact allergy to allyl isothiocyanate.

The literature regarding correct test concentration is sparse. Initially, a concentration of 1% allyl isothiocyanate in alcohol was recommended (15). However, Gaul (14) patch tested a suspected allergic individual with allyl isothiocyanate 0.01, 0.1 and 1% in pet., applying the material for only 24 h. Testing with the 0.01% dilution was negative. Patch testing with 0.1% allyl isothiocyanate resulted in a vesicular reaction and testing with the 1% solution produced a severe positive reaction. 12 controls showed no reaction to 0.1% allyl isothiocyanate. As a result, the authors concluded that 0.1% was a suitable patch test concentration to avoid an irritant reaction. Kohl and Frosch (2) reported a clearly demarcated irritant reaction with superficial necrosis using allyl isothiocyanate 5%. The remaining studies describing patch testing with allyl isothiocyanate have used a 0.1% dilution (3, 12, 13). A conclusive answer to the optimal test concentration is still required.

Another possible explanation of the lack of positive test results is that we are not really testing individuals at risk of having contact allergy to allyl isothiocyanate. We believe this not to be the case, considering the highly selected study population chosen.

Allyl isothiocyanate was detected at a concentration of 2.5 ppm in the margarine sample provided by one of the patients with a positive reaction. Margarine is comprised of a mixture of vegetable oils (for example rape oil, sunflower oil and palm oil) and to a lesser extent animal fats together with water and milk. Rape is very likely the constituent of the margarine responsible for the positive test result. The detected concentration indicates that even a modest concentration of allyl isothiocyanate is sufficient to induce allergic contact dermatitis in some patients. The patient also reported having repeated contact with cress. This, as well as occasional contact with other vegetables from the Cruciferae family, might have contributed to the dermatitis. The patient was extensively examined for other possible causes of her symptoms, including further patch testing and prick testing (*case report*). This further testing failed to explain her symptoms in other ways.

The patient presented with a morphologically distinct eczema involving mainly the fingertips and pulps. This is also characteristically seen in patients presenting with contact dermatitis from certain flowers (tulip and alstroemeria), garlic and onions. 'Tulip fingers' presenting as fissuring,

scaling and hyperkeratotic eczema on the fingertips, especially the thumb, index finger and middle fingers of the dominant hand, typically arises in florists or nursery workers handling tulips and tulip bulbs (16–18). The causative allergen is *tulipalin A* (α-methylene-γ-butyrolactone) which is also found in alstroemeria (Peruvian lily or Inca lily) (19). Contact with garlic can induce a variety of dermatological problems including irritant contact dermatitis, protein contact dermatitis and also allergic contact dermatitis involving the fingertips (20). Likewise, Sinha et al. (21) reported fingertip dermatitis caused by exposure to garlic or onion. Our case with fingertip dermatitis due to allergy to allyl isothiocyanate should be remembered when investigating causes of fingertip dermatitis.

In summary, this study found allergic contact dermatitis from allyl isothiocyanate to be infrequent in spite of clearly widespread exposure. It is possible that the recommended patch test concentration fails to detect all true allergic patients, and further studies are needed to determine the optimal patch test concentration. Also, the case of allergic contact dermatitis described indicates that exposure to even a modest concentration of allyl isothiocyanate in a susceptible patient can induce contact allergy. In addition, allergy to allyl isothiocyanate should be considered when fingertip dermatitis is present.

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