

Pigmented contact dermatitis in the axillae caused by hydroperoxides of limonene



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INTRODUCTION

Limonene is a fragrance terpene that is derived from peel oil of citrus fruits.¹ It is commonly used in household cleaning agents, cosmetics, personal care products, and fragrances for its fresh lemon aroma.¹ Limonene on its own has low sensitization potential.^{1,2} However, upon exposure to air, limonene undergoes auto-oxidization to form different oxidation products, of which, hydroperoxides of limonene is a potent sensitizer and is known to cause allergic contact dermatitis.^{1,2} We report an unusual case of pigmented contact dermatitis caused by hydroperoxides of limonene.

CASE REPORT

A 57-year old Chinese man presented with a 1-year history of mildly pruritic hyperpigmented rashes in his bilateral axillae. The rashes would appear 1 to 2 days after application of his roll-on antiperspirant. He had used the same brand of antiperspirant for 3 decades. The rashes responded to topical steroids but recurred with reuse of the antiperspirant. The antiperspirant would turn a darker shade of pink if left open for extended periods (Fig 1). He denied any other topical applications. He had no history of atopy, with no significant medical history. He worked as a construction site manager.

Clinically, the patient had hyperpigmented patches with minimal erythema and scaling mainly on the edges of the axillary folds (Fig 2). Although his axillary vault showed mild erythema, he did not have any active plaques or scaling on examination. There were no other rashes elsewhere. Fungal microscopy and culture of skin scrapings from the



Fig 1. Pigmented contact dermatitis of the axillae caused by hydroperoxides of limonene. Patient's older antiperspirant (Bottle 1, left) and newer anti-perspirant (Bottle 2, right). The older antiperspirant (left) was noticeably a darker shade of pink than the newer antiperspirant (right).

axillae were negative. Patch tests were performed using allergens from our local standard, cosmetic, bakery series from Chemotechnique Diagnostics (Vellinge, Sweden), and old and newer batches of his deodorant “as is.” Patches were applied to the back using IQ Ultra chambers (Chemotechnique Diagnostics) and removed at 48 hours, with readings taken at 72 hours. Readings were per International Contact Dermatitis Research Group recommendations.³ Seventy-two-hour readings found weak positive reaction (+) to hydroperoxides of limonene 0.3% in petrolatum and strong positive reactions (++) to both older and newer antiperspirants (Fig 3, A and B). Limonene was listed as an ingredient of his deodorant. There were no other concomitant positive reactions to fragrances or other haptens. He was given avoidance advice and on his latest follow-up the hyperpigmented patches had nearly resolved.

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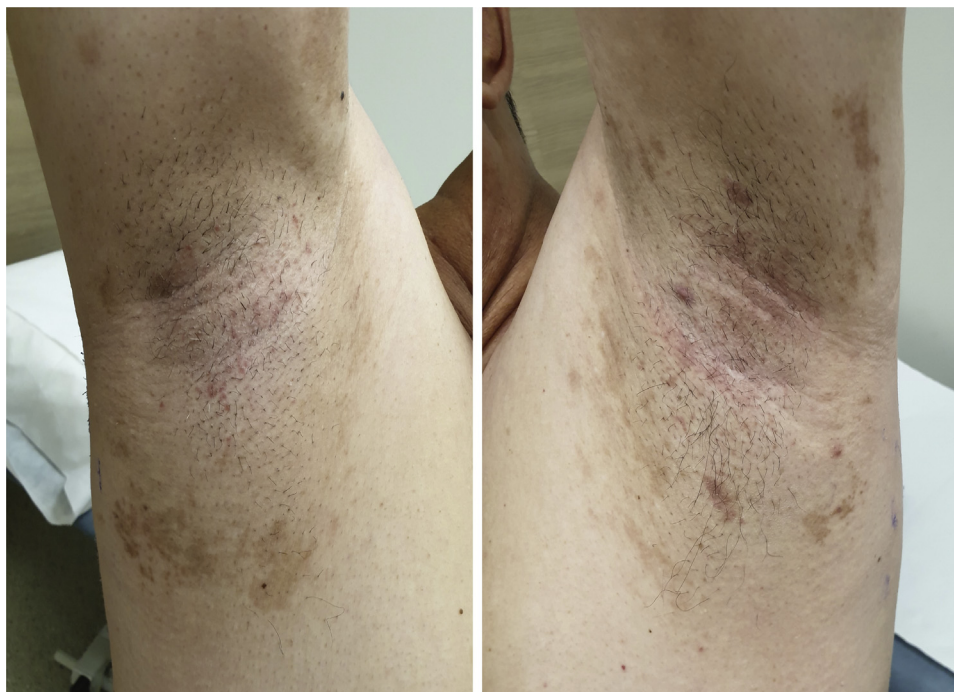


Fig 2. Pigmented contact dermatitis caused by hydroperoxides of limonene. Hyperpigmented patches at the periphery of the patient's bilateral axillae.

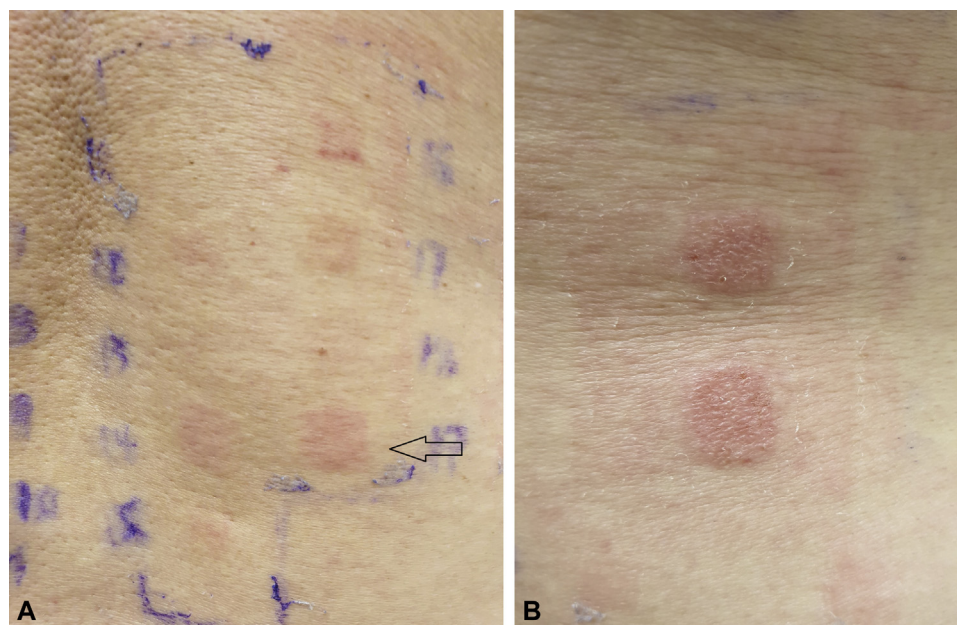


Fig 3. Pigmented contact dermatitis caused by hydroperoxides of limonene. Patch tests showed **A**, weak positive reaction to hydroperoxides of limonene 0.3% in petrolatum (*arrow*). **B**, Strong positive reactions to the older antiperspirant (top) and newer antiperspirant (bottom).

DISCUSSION

Hydroperoxides of limonene have emerged as an important cause of contact allergy in recent years.² Positive patch test rates to hydroperoxides of limonene 0.3% in petrolatum in a multicenter study

in the United Kingdom was reported to be 5%, whereas positive patch test rates to stabilized limonene were only at 0.2%.⁴ In a survey undertaken in the United Kingdom, limonene was found to be an ingredient in up to 98% of women's fragrances and

more than half of household cleaning products and detergents.⁵ It can also be found in high concentrations in solvents and industrial degreasing agents.^{1,6} Experimental studies have found that the concentration of hydroperoxides of limonene in essential oils increase significantly with time regardless of storage or handling conditions.⁷ However, the determination of hydroperoxides of limonene in fragrances and commercial products can be challenging because of low thermal stability and the complexity of mixtures in fragrances.⁸

Patch tests to hydroperoxides of limonene 0.3% petrolatum have been reported to yield predominantly weak-positive reactions, and our patient's patch test reaction is in keeping with these studies.^{6,9} Although the reasons for this are unknown, patch testing to hydroperoxides of limonene 0.3% in petrolatum can be challenging because of the frequency of irritant and doubtful reactions at this concentration.¹ The patient's stronger reaction to the actual antiperspirant itself may be related to a higher concentration of hydroperoxide of limonene, although unfortunately we were unable to investigate this further by means of liquid chromatography.

Our patient had mainly hyperpigmented macules with minimal dermatitis. To our knowledge, this is an unusual presentation of contact allergy to hydroperoxides of limonene in the form of pigmented contact dermatitis. He did not react to the other components of fragrances that are known to cause pigmented contact dermatitis such as eugenol and fragrances, even though they were found in his antiperspirant. Our patient's antiperspirant contained both limonene and linalool, although he was only found to be allergic to hydroperoxides of limonene. Because citrus fruits are a well-known cause of phytophotodermatitis with a prominent hyperpigmentary component occasionally without much of a dermatitic reaction, it may not be unexpected for hydroperoxides of limonene to be a potential cause of pigmented contact dermatitis.

We suspect that the patient may have had an allergic reaction to his antiperspirant only recently, possibly because of a change in antioxidants in the antiperspirant. However, we were unable to obtain

any samples or ingredients list from decades ago for comparison. Limonene has also been reported to oxidize before its addition to a product during the manufacturing process or later during storage and handling of the product.¹⁰ The addition of an antioxidant such as butylated hydroxytoluene may prevent the degradation of limonene, although this addition is only efficient until the antioxidant has been consumed.¹⁰ Butylated hydroxytoluene was listed as an ingredient in the patient's antiperspirant. The reported change in color of his older products may be indicative of oxidization of the product and limonene when left exposed to air. Interestingly, he did not show a stronger allergic response to the older product. Clinicians should be aware of hydroperoxides of limonene as a cause of pigmented contact dermatitis.

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