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CALCIUM PANTOTHENATE IS PRESENT IN COSMETICS AND MAY CAUSE ALLERGIC CONTACT DERMATITIS

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KEY WORDS

Allergic contact dermatitis; case report; cosmetics; calcium panthotenate (CAS no. 137-08-6); vitamin B5; panthenol (CAS no. 81-13-0); panthenyl ethyl ether (CAS no. 667-83-4); pantothenic acid (CAS no. 79-83-4); calpanate; Pantholin.

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Calcium pantothenate (IUPAC name: calcium;3-[[(2R)-2,4-dihydroxy-3,3-dimethylbutanoyl]amino]propanoate; molecular formula $C_{18}H_{32}CaN_2O_{10}$; CAS no. 137-08-6; syn. calpanate; Pantholin; Pancal; UNII-568ET80C3D; Cris Pan; Ca-HOPA; Calpan) (1) is the calcium salt of pantothenic acid (CAS no. 79-83-4), the water-soluble vitamin B5 (2). It is used in cosmetics due to its anti-static and hair conditioning properties (3).

CASE REPORT

In 2008, a 53-year-old female nurse's aide with a family history of rheumatoid arthritis (a sister) and lupus erythematosus (one daughter), presented with recurrent itchy eyelid eruptions. Patch tests with the Spanish Contact Dermatitis Research Group (GEIDAC) baseline series (TRUE Test and supplementary allergens supplied by AllergEaze, SmartPractice, Calgary, Canada), were performed and a positive result to nickel sulfate of unknown clinical relevance was obtained. A skin biopsy was performed (Online supplemental Fig. 1.a-1.c). The lesions fully cleared with oral steroids. yet intermittently flared-up for 6 years.

In 2014, more intense and spreading lesions developed associated with arthralgias, positive antinuclear antibodies (1:320), and a mild leucopenia. An autoimmune collagen vascular disease was suspected; however, no improvement was obtained with oral hydroxychloroquine and a new biopsy showed eczematous features (Online supplemental Fig. 1.d). Further extended

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patch tests including a cosmetic and a fragrance series (Chemotechnique Diagnostics, Vellinge, Sweden), as well as the patient´s hygiene products were performed with negative results. These products were replaced and skin lesions fully cleared. Three months later, new lesions developed (Fig. 2) following the re-application of Diadermine gentle cleansing milk and gentle facial tonic (Henkel, Düsseldorf, Germany), products which previously had been patch tested with negative results. A repetitive open application test (ROAT) was negative, however, dilutions of their individual ingredients provided by the manufacturer were patch tested with positive results to calcium panthotenate 5% pet., present in both products, yielding a ?+ reaction on day 3 (D3). The following week, the patient agreed to be patch tested again and stronger results were noted, interpreted as a booster effect (+ on D5) (Fig. 2). Twenty controls were negative. Panthenol 5% pet., also contained in both products, was negative. After exposure avoidance, no further lesions were observed in a 5-year follow-up period.

DISCUSSION

To our knowledge, no previous cases of contact sensitization from calcium panthothenate have been reported. However, a case of systemic dermatitis (flare up of hand eczema) after the ingestion of a nutritional supplement with it in a patient previously sensitized to dexpanthenol in a baby cream has been published (3). On the other hand, contact dermatitis from D-panthenol, a vitamin

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B5 alcohol analogue stereoisomer, has recently been the focus of several publications (5-8) and its inclusion in cosmetic and topical drug patch tests series has been encouraged (6,7). Immediate hypersensitivity to D-panthenol has also been described involving one patient with contact urticaria (from a hair conditioner) and another patient with an anaphylactic reaction (from oral multi-vitamin tablets) as well as prior contact urticaria (from a sunscreen) (9,10). Additionally, two reports of contact dermatitis to a related compound, panthenyl ethyl ether (CAS no. 667-83-4), following use of a hair lotion and an emollient stick, respectively, have also been published (11,12). Interestingly, in one of them panthenol was patch tested with negative results as in our case, showing that cross-reactions among these related compounds do not necessarily occur. In 2015, we screened the labels of 609 cosmetics from 8 brands (those most often prescribed by us) for the presence of calcium panthothenate. This was found in 4 cosmetics (0.65%) from 3 brands (two shampoos, one lotion against hair-loss, and one leave-on “facial cell regeneration treatment”) and further in 8 hair cosmetics (1.3%) from 3 brands.

In our patient, both the negative patch tests with the culprit products and the atypical clinical picture mimicking an autoimmune disease were misleading and significantly delayed the correct diagnosis. This case points out the importance of patch testing with the individual ingredients of cosmetic products when usage tests trigger reactions even when a patch test with the entire products is negative.

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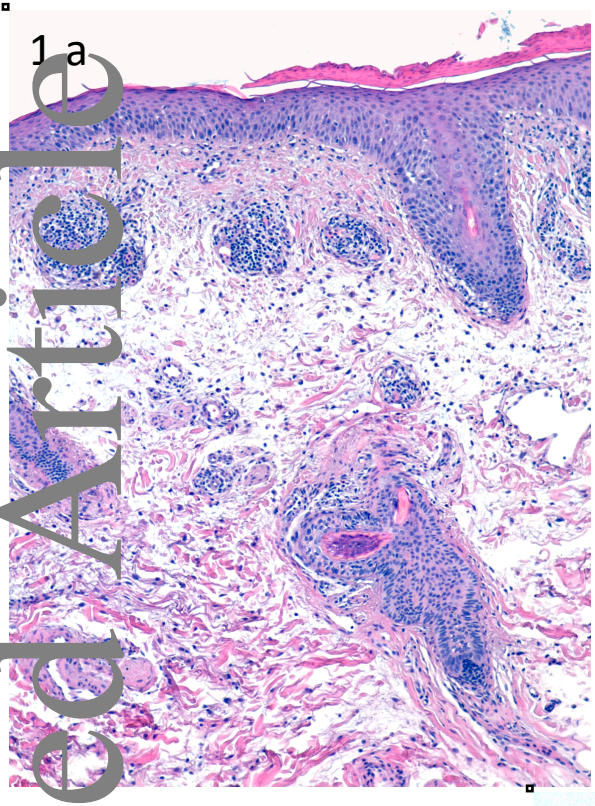
FIGURES

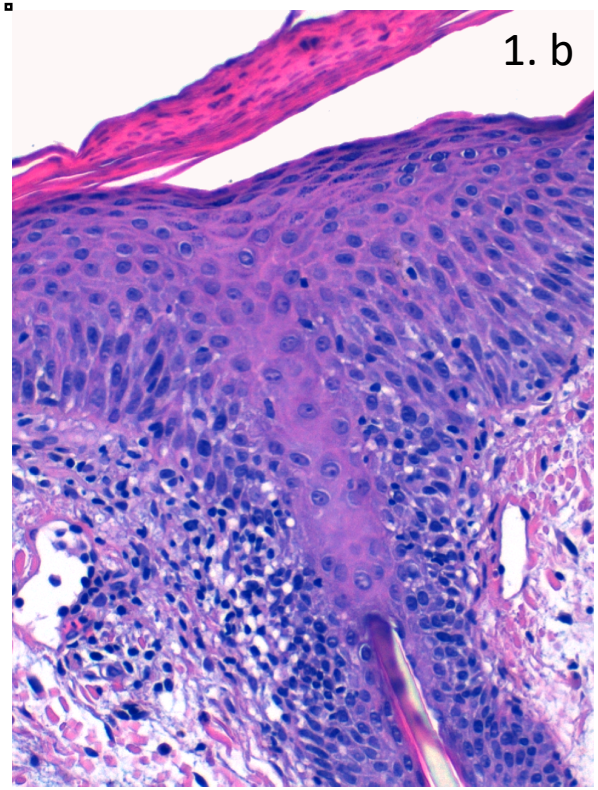
Online supplemental FIGURE 1. First biopsy: 1.a. Superficial perivascular dermatitis, dermal edema, slight spongiosis and exoserosis in the horny layer; 1.b. focal images of interphase dermatitis and parakeratosis with exoserosis; 1.c. dense lymphocytic perivascular cuffs and interstitial lympho-histiocytic dermal infiltrates with eosinophils. Second biopsy: 1.d. Intense spongiosis, exoserosis and dermal edema (eczematous features).

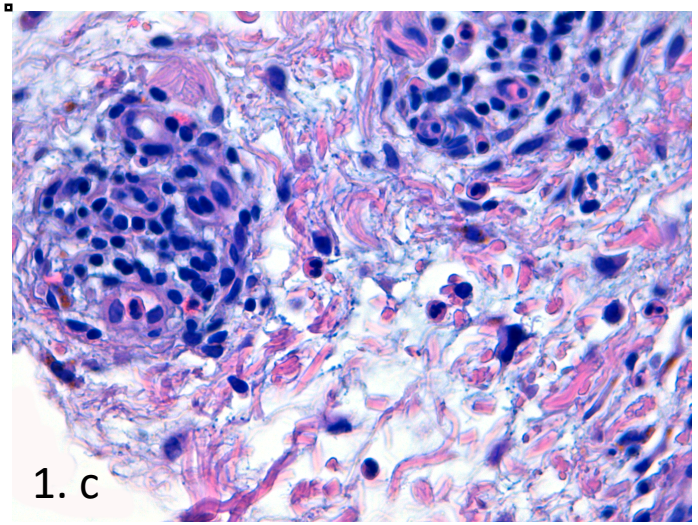
FIGURE 2. Erythematous and intensely edematous plaques involving the eyelids, cheeks and perioral areas. The lesions were diffuse and bilateral, however not strictly symmetrical and margins were artifact and angulated. Worsening after applying two products that had been negative in previous patch tests was noted by the patient. Further patch tests with one of their ingredients (namely, calcium panthothenate) was clearly positive, with the reaction spreading beyond the exposed area.

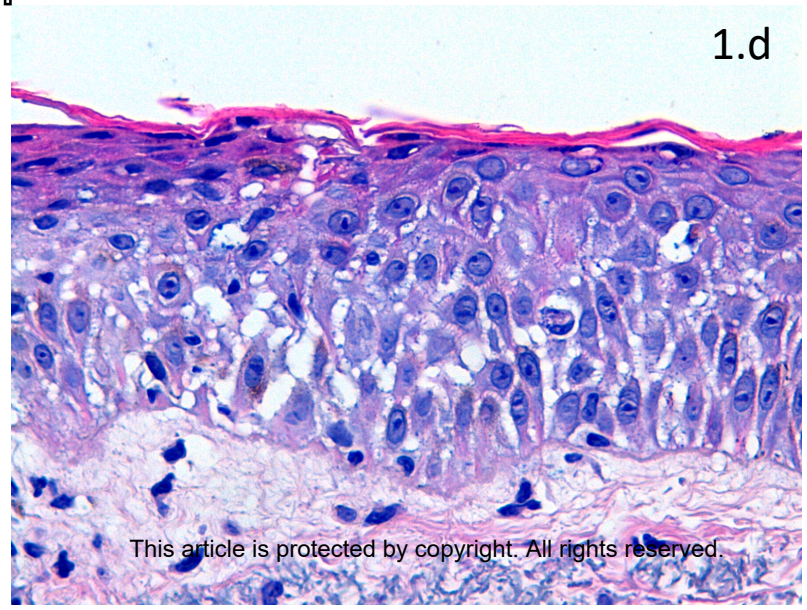
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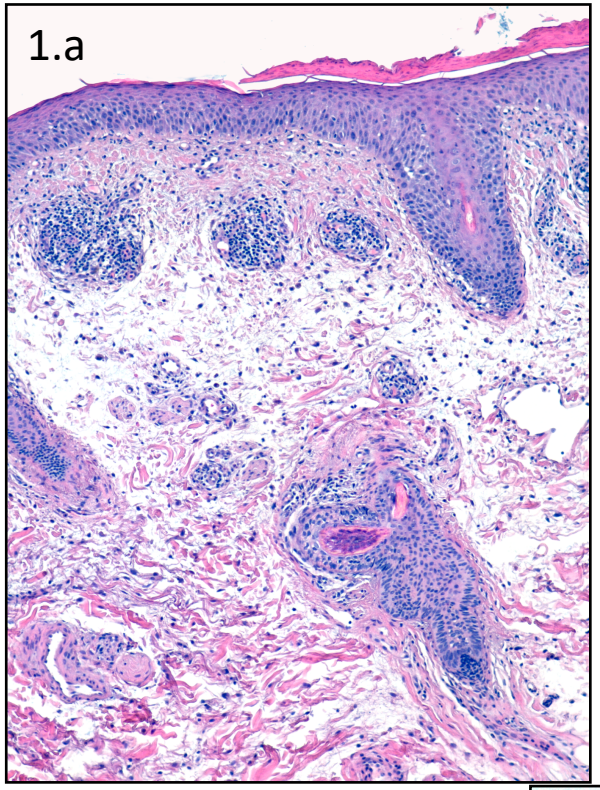


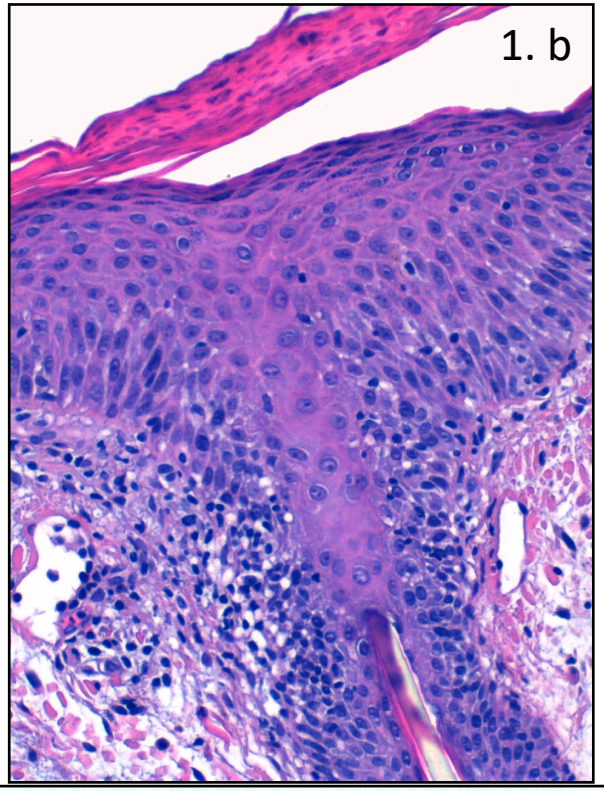


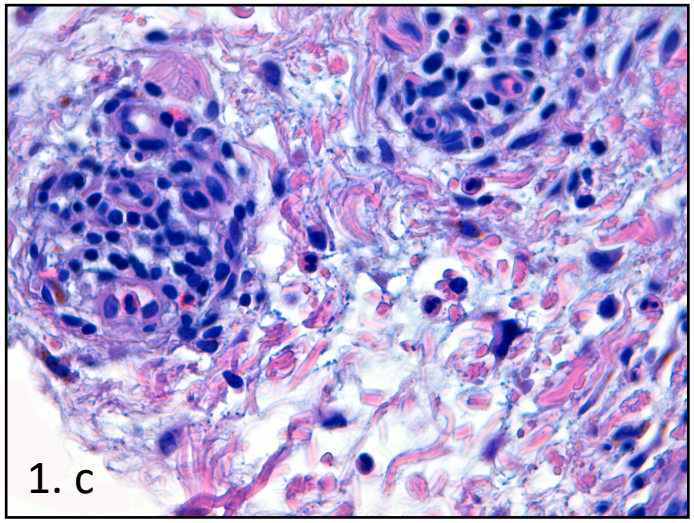


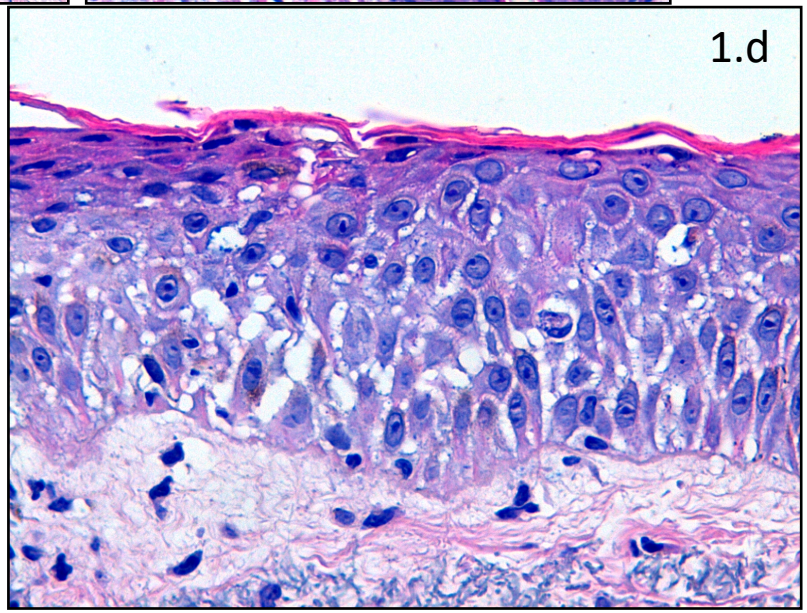


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1.a


1. b


1. c


1.d