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Delayed hypersensitivity to α -lipoic acid: look at dietary supplements

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α -Lipoic acid (LA; INCI: thioctic acid, CAS no. 1077-28-7 as racemate) is an eight-carbon disulfide containing a single chiral nucleus, and is reduced *in vivo* to its dithiol form, dihydrolipoic acid (1). It is an essential cofactor in metabolic reactions through mitochondrial-specific pathways, and it is synthesized in small amounts in humans. LA shows antioxidant and metal-chelating activity (2). Hence, it is widely used in a variety of conditions, including diabetes, insulin resistance, atherosclerosis, neuropathy, neurodegenerative diseases, ischaemia–reperfusion, and eye-related disorders. Memory loss, chronic fatigue syndrome, human immunodeficiency virus infection/acquired immunodeficiency syndrome, cancer, liver diseases and Lyme disease are also among the wide variety of conditions in which LA is supposedly of benefit. Finally, LA is used in anti-ageing products, such as ‘anti-wrinkle’ cream (3). Three cases of contact dermatitis caused by LA in an anti-ageing product have been published so far; however, no truly allergic reactions to nutritional supplements containing LA have yet been described (4).

Case Report

We report the case of a 34-year-old woman suffering from shoulder pain resulting from cervical disc herniation, who developed a pruritic maculopapular rash on the face and scalp after 10 days of treatment with Dianural[®] [dietary supplement of prolonged-release LA 600 mg, L-carnosine 1650 mg, zinc 7.5 mg and B group vitamins (PP 9 mg, B5 3 mg, B6 1 mg, B2 0.8 mg, B1 0.7 mg,

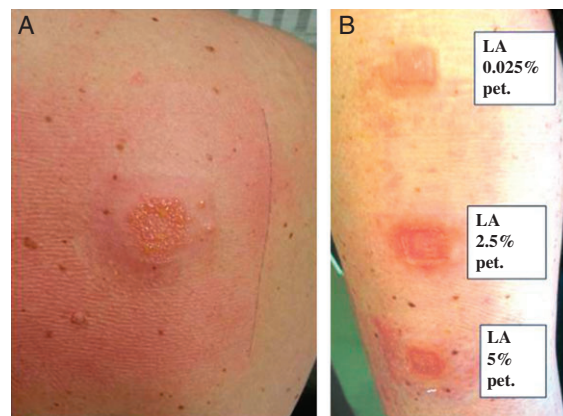


Fig. 1. (a) Positive patch test reaction to Dianural[®] 10% pet. at D3. (b) α -Lipoic acid (LA) dilution series with intense positive reactions even to 0.025% pet.

B12 0.5 μ g, folic acid 100 μ g)], oral etoricoxib (Tauxib[®]) 60 mg, intramuscular diclofenac (Voltaren[®]) 75 mg, and oral naproxen (Synflex[®]) 550 mg. The patient stopped taking all drugs and was treated with oral corticosteroids for 2 days; the symptoms promptly receded. Diagnostic work-up was performed 4 months later. Prick tests were performed with Dianural[®], etoricoxib, diclofenac and naproxen in the form of powdered tablets dissolved in saline, according to the recommendations of the European Network for Drug Allergy (ENDA) (5). Readings were performed after 20 min. Histamine was used as a positive control and saline as a negative control. Immediate reactions with a diameter at least 3 mm larger than in negative controls were considered to be positive. Patch tests, applied to the interscapular region, were performed with the same drugs as used for prick tests, dissolved in pet. at a concentration of 10%, according to ENDA recommendations (5). The prick tests all gave negative results after 20 min, whereas an extreme positive patch test reaction to Dianural[®] was seen at D2 and D3 (+++, infiltrated and vesicular reaction) (Fig. 1a).

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Patch tests with the constituents of the dietary supplement (LA powder, L-carnosine powder, zinc citrate powder, B group vitamins powder, micronized silica powder, calcium pantothenate powder, magnesium stearate powder, synthetic iron oxide E172 powder, hydroxypropyl-methylcellulose powder, polyvinylpyrrolidone powder, and croscarmellose sodium powder) were supplied by the manufacturer, and patch tested at a concentration of 5% in pet. as previously described. LA gave a strong positive reaction (++) at D3), and also gave positive reactions at 2.5% and 0.025% (Fig. 1b). Patch tests with LA were also performed in 12 healthy subjects with no history of contact dermatitis and/or drug hypersensitivity, with negative results. These results

are consistent with a cell-mediated, type IV allergic reaction to LA.

Discussion

To the best of our knowledge, this is the first case of delayed hypersensitivity induced by LA confirmed by a positive patch test result. Our observation emphasizes that not only well-known drugs, but also apparently harmless products can be responsible for serious allergic reactions. Therefore, we think that attending physicians and pharmacists should be aware of the possibility of allergic reactions to dietary supplements. Patients with LA hypersensitivity should carefully read the information leaflets of drugs to avoid further allergic reactions.

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