

Maculopapular eruption to rivastigmine's transdermal patch application and successful oral desensitization

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Rivastigmine is a reversible and non-competitive acetylcholinesterase and butyrylcholinesterase inhibitor used for the treatment of mild to moderate dementia of the Alzheimer's type and dementia because of Parkinson's disease (1). Rivastigmine has been available in capsule and liquid formulations since 1997, and in 2007 became available also in transdermal patch (2). Common adverse reactions to rivastigmine such as nausea, vomiting, diarrhea are transient and typically mild (3).

Although transdermal patches are widely used, for their advantages over the conventional delivery methods (3), this is the first well-documented case of a delayed type hypersensitivity reaction to rivastigmine patch application in the form of an erythematous maculopapular eruption.

An 85-year-old woman, with a medical history of dementia of the Alzheimer type referred to us reporting that almost 8 weeks ago she had started daily

Transdermal rivastigmine's application can produce delayed hypersensitivity reaction; oral desensitization can be effective in that case.

application of rivastigmine transdermal patch (Exelon® 4.6 mg/24 h; Novartis, International AG, Basel, Switzerland) and from the fifth day of treatment a maculopapular itchy rash that lasted 3–4 days, appeared at the application sites. Fifteen days later, the neurologist increased the dose to 9.5 mg/24 h and the site reaction was more severe with small pin-head vesicles and unbearable pruritus. The patch application because of the aforementioned reaction was replaced with rivastigmine solution (Exelon®, oral sol. 2 mg/ml; Novartis, International AG) at an initial dose of 6 mg/day. The second day of oral treatment, the patient developed, a highly pruritic maculopapular eruption on the upper trunk, chest, arms and back that progressively expanded on her abdomen and buttocks and thus she was admitted to Allergy Unit. On admission, she had normal temperature, blood pressure of 130/70 mmHg and routine hematological and biochemical tests yielded normal results. The rivastigmine solution was immediately discontinued, she received a course of antihistamines (levocetirizine 10 mg/day) and corticosteroids (methylprednisolone 0.5 mg/kg with gradual tapering) and the rash completely resolved after 2 weeks.

A complete allergologic investigation was carried out to evaluate the hypersensitivity reaction. A cutaneous biopsy performed upon admitting the patient revealed an edema of the papillary dermis, a massive perivascular infiltrate of lymphocytes, monocytes and eosinophils in the dermis and some T cells into the epidermis. Skin prick and intradermal tests with certain dilutions of Exelon® oral solution were carried out 4 weeks after full remission with negative results on the immediate and delayed readings. Patch testing with Exelon® 4.6 mg/24 h produced a strong positive result with vesiculation after 48 and 72 h (Fig. 1). A cutaneous biopsy of patch-tested skin confirmed the findings of the first biopsy.



Figure 1. The reaction of patch testing at 72 hours.

Because her neurologist decided that the offending drug was irreplaceable, we generated a 18-step oral desensitization protocol using four solutions of ten-fold diluted oral commercial solution (0.002, 0.002, 0.02, 0.2 mg/ml) and doubling of dose every 15 min from an initial dose of 1 : 1 000 000 to the target therapeutical dose of 3 mg (4). The patient completed the desensitization procedure successfully and gradually increased the dose every 3 weeks up to 9 mg/day (oral sol. Exelon® 3 mg/ml) that receives until now without any adverse reaction.

The allergological investigation of drug hypersensitivity presented as maculopapular eruption is difficult and especially when sufficient data for the suspected drug is lacking. Although our patient had a delayed probably cell-mediated hypersensitivity reaction according to her personal history combined with the histopathologic findings and the positive patch testing, we managed to deliver the offending drug through a desensitization protocol.

To our knowledge, this is the first case of a delayed hypersensitivity reaction after the transdermal application of

rivastigmine. Unlike other cases of eruptions because of acetylcholinesterase inhibitor in which the offended drug was withdrawn (5, 6) in our case, the patient was able to continue receiving the rivastigmine thanks to the desensitization protocol.

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