



Excited skin syndrome (“angry back” syndrome) induced by proximity of carbamazepine to another drug with strong positive allergic reaction in patch test: A first of its kind

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Excited skin syndrome (ESS) or angry back syndrome (ABS) was first described with nickel¹; later, ESS was described with multiple contact allergens as well²; however, only few studies are available on cases triggered by drugs.

CASE REPORT

A 77-year-old male with trigeminal neuralgia was initially treated with carbamazepine (CBZ). Three weeks later pregabalin (PG) was added to his

treatment regimen as the pain persisted. However, 1 week after initiating the combination therapy (CBZ + PG), the patient developed a generalized maculopapular rash, facial edema, and fever. On physical examination a skin rash was observed and hepatomegaly and lymphadenopathy detected. Laboratory tests revealed the following measurements: leukocytes 13 100/mm³, lymphocytes 3800/mm³, eosinophils 2900/mm³, aspartate aminotransferase 62 IU/L, alanine aminotransferase 101 IU/L, urea 80 mg/dL, and creatinine 1.5 mg/dL. A skin biopsy was performed which showed moderate spongiosis with few eosinophils and signs of vasculitis.

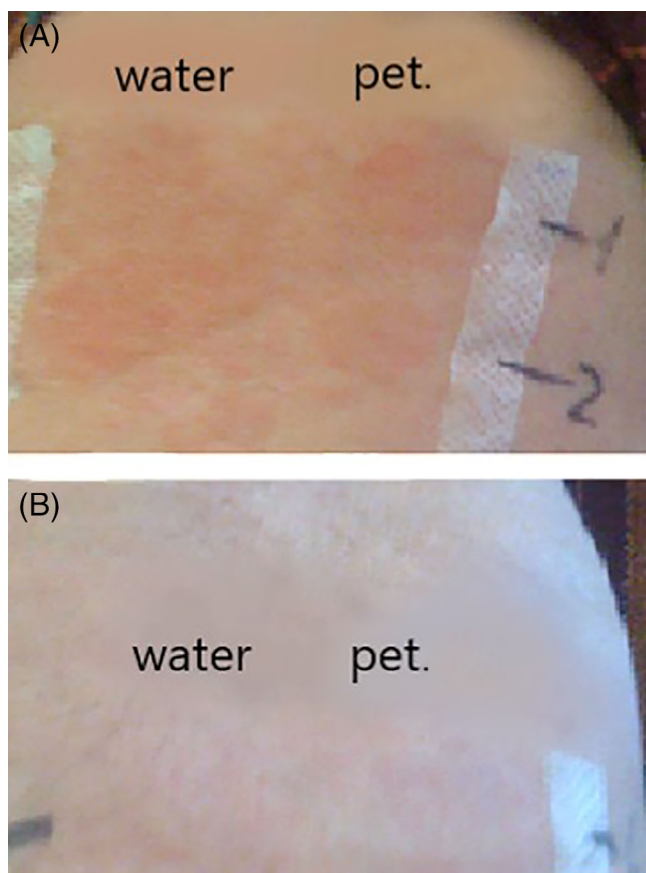


FIGURE 1 Patch tests with (A) carbamazepine (marked 1) and pregabalin (marked 2) and (B) pregabalin alone

The patient was eventually diagnosed with drug rash with eosinophilia and systemic symptoms (DRESS) syndrome and therapy with CBZ and PG was stopped. The patient recovered within 1 month, following treatment with only levocetirizine. Allergy tests were performed 1 month after his recovery. Patch tests were performed with PG (Lyrica) 5% and CBZ (Tegretol) 5% in both water and pet., with both drugs initially placed at the dorsal region of the left arm, and readings obtained on day (D) 2 and D4 (Figure 1). Test results were positive with both drugs in aq. and pet. for readings obtained on D2 and D4 (Figure 1A).

The same tests were then repeated with these two drugs but on different arms and after a 2-week interval: PG 5% (Lyrica) at the dorsal region of the right arm and, 2 weeks later, CBZ 5% (Tegretol) at the dorsal region of the left arm. These patch tests were negative with PG (Figure 1B) but positive with CBZ. The patient then underwent an oral challenge with PG (75 mg/d/4 d) which did not trigger a reaction.

DISCUSSION

Mitchell emphasized that skin hyperirritability is a serious problem in patch testing and demonstrated that, in the presence of a strong positive patch test reaction, other concomitant weak positive reactions may be false positive.^{1,2} Skin hyperirritability affects the entire skin; for this reason, Bruynzeel and Maibach proposed the name EES instead of ABS.² Our patient has had a rash 1-2 months earlier, so he

could still have some degree of skin hyperirritability. In the initial patch test, both drugs were placed very close to each other and the positive response of PG was not reproducible when re-examined separately^{3,4}; therefore, the proximity of the patch tests has likely caused this syndrome.^{1,2}

However, it was important to identify the drug that had triggered DRESS syndrome in our patient because PG could have been effective in treating pain; therefore, we decided to repeat the patch test with PG alone and on the contralateral arm, and demonstrated that the previous result had indeed been false-positive due to EES.^{1,4} Most allergens that give false-positive results are "marginal irritants," such as nickel (1) but are usually not drugs.

EES may have many causes depending on both the contact allergen and the characteristics of the patient. Patch test with more than one positive result may be due to EES, especially if reactions are not related to the symptoms of the patient. This problem can be solved by repeating the study with each suspected allergen placed at various sites on the skin, far from one another, and at different times.^{5,6}

In conclusion, we present the first case of ABS/EES in a patient with DRESS syndrome and possible subsequent skin hypersensitivity who had a false-positive patch test result with PG only when this drug was tested together with and in proximity to CBZ.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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