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Challenge-based pregabalin induced urticaria and angioedema. A case report

To the Editor,

Pregabalin is an antiepileptic drug, which is analogous of the gamma aminobutyric acid (GABA) and exhibits a structure similar to gabapentin. It is an $\alpha 2$–δ ligand that has analgesic, anticonvulsant, anxiolytic, and sleep-modulating activities. Pregabalin has also been used successfully in the treatment of itch – for instance in haemodialysis and brachioradial pruritus. Pregabalin binds to the $\alpha 2$–δ subunit of calcium channels, resulting in a reduction in the release of several neurotransmitters, including glutamate, noradrenaline, serotonin, dopamine, and substance P.[1–3] In the last years, there has been an increase in its use and it has shown to be effective in neuropathic pain, fibromyalgia, incisional, inflammatory, and formalin-induced injury. It is also effective in the treatment of anxiety as well as sleep-modulating drug.[4,5]

Phase 3 clinical studies with pregabalin indicate the rare occurrence of skin reaction, ranging from purpuric to vesiculobullar and desquamating Stevens–Johnson syndrome. Although a hypersensitivity reaction due to pregabalin has been reported before,[6] the involvement of pregabalin as causative agent was not definitely tested with an appropriate challenge. We describe a case report of a patient who developed urticaria and angio-oedema after beginning pregabalin therapy for managing chronic pain.

The patient was a 65-year-old woman with personal history of obesity, glaucoma and chronic pain due to a degenerative joint disease. Pain was treated with etoricoxib, pregabalin, tramadol and acetaminophen. Two months later, she presented eyelid and lip angio-oedema and a diffuse pruritic erythematous maculopapular exanthema on trunk and face, which yielded once treatment was discontinued. She tolerated later acetaminophen, ibuprofen, metamizol, diclofenac and tramadol.

Risk and benefits of a rechallenge with etoricoxib and/or pregabalin, which had not been reintroduced after the adverse reaction, were discussed with the patient in order to elucidate a definite causal relationship of the cutaneous reaction. A single-blind, placebo-controlled (SBPC) oral challenge with etoricoxib was carried out in a supervised hospital setting with good tolerance. Skin prick test (2) (dilutions 0.01 mg/ml, 0.1 mg/ml, 1 mg/ml), intradermal test (0.01 mg/ml, 0.1 mg/ml, 1 mg/ml), and patch test (1 mg/ml) with pregabalin were negative. The patient underwent a single-blind, placebo-controlled oral challenge with pregabalin (10 mg, 25 mg and 50 mg at 1-h interval). A pruritic maculopapular exanthema developed 30 min after 25 mg dose. Symptoms resolved 1 h after treatment with prednisone 50 mg and dexclorpheniramine 5 mg. Tryptase levels, total and specific IgE were not obtained. No skin tissue pregabalin levels were measured.

We present the first case report of immediate extensive cutaneous reaction induced by pregabalin confirmed with a SBPC oral challenge. Skin tests were not useful in our patient. Further cases will be needed to assess their value.

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