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Case Series

Security in Anti-CGRP Switch after Hypersensitivity Reactions

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Abstract

Introduction: Migraine is globally the second cause of disability. Recently, there have been developed new treatments against calcitonin gene-related peptide (CGRP).

Cases: We present two patients who have developed allergic reactions to anti-CGRP, causing its suspension.

Discussion: Erenumab in the majority of cases is well tolerated, although there are some reports of severe hypersensitivity reactions.

Nowadays, in clinical practice there is an anti-CGRP switch due to lack of response.

Conclusion: We propose, anti-CGRP switch after hypersensibility reaction, with assessment by the Allergology service.

Keywords: *Anti-Cgrp Switch; Hypersensitivity Reactions; DALYs (Disability Adjusted Life Years); Calcitonin Gene-Related Peptide (CGRP)*

Introduction

Migraine is a highly prevalent neurological disease that affects 14% of population, and is thesecond cause of disability measured in DALYs (Disability Adjusted Life Years) globally, and thefirst in Western Europe, particularly under 50 years old [1].

In recent years, more specific migraine treatments have been developed directed against calcitonin gene-related peptide (CGRP), which plays an important role in the genesis of painduring headache [3].

Anti-CGRP monoclonal antibodies act by blocking circulating CGRP (fremanezumab, galcanezumab and eptinezumab) or its receptor (erenumab). Erenumab is a human antibodywhile the other antibodies are humanized. They are effective in the treatment of episodic and chronic migraine [4].

There is currently little published evidence on what to do in situations of allergy to thesedrugs, so we present these two cases from our hospital as an option to assess.

Cases Series

Case 1

A 68-year-old woman with previous history of Wolf-Parkinson-White syndrome and asthma,followed up in neurology for more than 10 years for chronic migraine. She had not responded to nine oral preventive drugs or botulinum toxin, so we started treatment with erenumab 70. She presented a very significant clinical improvement, going from 13 days of migraine per month to none, but a few hours after receiving the third dose of the drug, shedeveloped a severe itchy rash and asthmatic decompensation that lasted for several days.

Treatment with erenumab was suspended, causing a new increase in the frequency of migraine attacks without response to other prophylactics, including botulinum toxin, which was tried again. For this reason we contacted the allergology service of our center to test tolerance to another anti-CGRP antibody. Allergy tests were performed with negative resultsfor fremanezumab, thus we decided to start treatment with this drug.

Currently, 20 doses of fremanezumab have been administered with significant clinicalimprovement and no side effects.

Case 2

47-year-old woman with previous history of anorexia, anxiety and depression, was being followed up in our neurology clinic for chronic migraine with onset in her childhood. She hadnot responded to five oral treatments or botulinum toxin, so we started fremanezumab 225mg. After three doses without clear amelioration, we switched to erenumab 140mg, with improvement from every day migraine to 13 migraine days a month. Unfortunately, shedeveloped a rash and generalized pruritus on the fifth dose a few hours after administration, causing its suspension. After evaluation by the allergy department of galcanezumab's safety, it was considered safe and we started with 120 mg. After 6 months of treatment there have not been remarkable incidents and the migraine has significantly improved.

Discussion

Lately, the use of monoclonal antibodies is increasing for inflammatory diseases treatment and anticancer therapies, with the resulting increase in hypersensitivity reactions associatedwith these drugs.

These reactions can be infusion reactions, cytokine release syndrome, or allergic reactionstype I (IgE or non-IgE), type III and type IV.

Regarding the time of appearance of the adverse reaction and the symptoms referred to incases 1 and 2, these reactions would be a type I hypersensitivity reaction, mediated by IgEand mast cells [5].

Erenumab is a well tolerated drug in the vast majority of cases, whose most frequent adverse effects are local skin reactions and pruritus at the injection site, constipation, andmuscle spasms; although some cases of severe hypersensitivity reactions have been reported after its commercialization: skin rash, angioedema and anaphylactic reactions.

These reactions can occur within minutes up to a week after treatment [6].

After the results of various series, it seems that the change of an anti-CGRP with lack of response to treatment for another one would be indicated because it could improve pain,but there are no reported cases in the literature of a change after an adverse reaction [7].

In other pathologies in which monoclonal antibodies are also used, such as cancer or rheumatologic diseases; after a hypersensitivity reaction, premedication with corticosteroidsand/or antihistamines is administered prior to the infusion of the treatment; and the infusion rate is decreased; since the change of treatment sometimes usually involves a second line [8].

Conclusion

Currently, no antiCGRP antibody has been positioned as more effective than others, therefore we propose that substituting one anti-CGRP antibody for another after an allergicreaction is a possible option, with prior safety assessment by the Allergology service.

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