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# Letters to the editor

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## ASPIRIN-INDUCED ISOLATED PERIORBITAL ANGIOEDEMA

*To the Editor:*

We have several considerations about the recent case-report by Price and Thomson.<sup>1</sup> First, there is another previous report documenting fifty-two patients with isolated (or localized) periorbital angioedema. In 1996 we evaluated the clinical characteristics of single-blind, placebo-controlled oral challenge with several non-steroidal antiinflammatory drugs (NSAIDs) in 98 patients with NSAID sensitivity.<sup>2</sup> Isolated periorbital angioedema accounted for 53% of the patients in our population. Until this date, a few patients with this specific clinical pattern had been reported.<sup>3</sup>

Second, the crossreactivity pattern among NSAIDs in this patient group has been also previously reported.<sup>2</sup> We have carried out 255 challenges with several NSAIDs in 52 patients with isolated periorbital angioedema. Most patients reacted to NSAIDs not involved in a previous reaction. As other authors described,<sup>4</sup> it is possible that the activity inhibition of at least one of the different prostaglandin-synthase isoforms play a key role of this type of manifestation; however, only the NSAID involved in previous reaction determined a positive challenge response in two patients. The lack of crossreactivity could suggest that other mechanisms (such as IgE-mediated) may be operative in some patients with isolated periorbital angioedema.<sup>5</sup>

Possibly, the patient with unilateral periorbital angioedema had an underlying atopic disease; he showed positive prick-test to several aeroallergens and foods. We have clinically characterized this previously considered unusual manifestation of NSAID sensitivity. In our population, isolated

periorbital angioedema constituted the most frequent subset involving atopic subjects.<sup>2</sup> In fact, a significant increase ( $P < .001$ , chi square test) in prevalence of atopy was found among patients with isolated periorbital angioedema (100%) in comparison to other NSAID reactors (45%). All patients had respiratory allergy to mites, mainly rhinoconjunctivitis. Perhaps the presence of a specific atopic disease may predispose patients to certain clinical syndromes of NSAID sensitivity. Unfortunately, we have not understood the reasons for the association of this form of NSAID sensitivity and atopy. We agree with Price and Thomson that further studies involving several likely candidates for containing an atopy gene(s), such as the cluster of cytokines on chromosome 5q31, certain regions of the T cell receptor locus on chromosome 14q, the high-affinity receptor for IgE on chromosome 11q13, or the major histocompatibility complex on chromosome 6p will be needed in this patient group.

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## REFERENCES

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## Response:

We are pleased that a single-blind, placebo-controlled NSAID oral challenge study has been published. Unfortunately, the paper by Dr. Quiralte et al was not yet in press when we performed the literature search for our paper. Otherwise, it would have been an important reference for our case. Our report, however, remains unique in that to our knowledge it is the only case of unilateral periorbital edema induced by aspirin. In particular, our patient's history of unilateral ocular trauma and surgery 20 years before manifesting his unique aspirin intolerance in that same eye suggests an important role for environmental conditioning and or triggering. As does the association between atopy and aspirin sensitivity described by Quiralte et al, and also seen in our case. Finally, the mechanism(s) of aspirin and NSAID sensitivity will only come through the study of patient groups such as reported by Quiralte et al. Understanding the molecular and genetic basis for aspirin and NSAID sensitivity and how these are influenced by environmental conditions or insults is essential and will hopefully lead to advances in allergy, pharmacology, and therapeutics.

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