CASE REPORT

Unilateral Conjunctival Chemosis as a Unique Symptom of Nonsteroidal Anti-Inflammatory Drug Intolerance

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Abstract

Patients with nonsteroidal anti-inflammatory drug (NSAID) intolerance usually have cutanous-mucosal or/and respiratory symptoms. We report the case of a patient who developed several episodes of left-eye conjunctivitis, manifested as conjunctival chemosis, with no other symptoms, after taking metamizole and other unidentified NSAIDs. We performed both a single blind placebo-controlled oral challenge test and conjunctival challenge test with different NSAIDs. The single blind placebo-controlled oral challenge was positive to ketoprofen and diclofenac. The conjunctival challenge with diclofenac and flurbiprofen was negative. The patient tolerated celecoxib and nabumetone.
We believe this to be an exceptional case of NSAID intolerance as conjunctival chemosis has not hitherto been included in any of the classic types of pseudoallergic reactions.

Key words: NSAID intolerance. Conjunctival chemosis.

Resumen

Los pacientes con intolerancia a antiinflamatorios no esteroideos (AINES) presentan, generalmente, síntomas cutaneo-mucosos o respiratorios. Presentamos un paciente que sufrió varios episodios de conjuntivitis en ojo izquierdo, manifestado únicamente como quemosis conjuntival, sin otros síntomas, después de tomar metamizol y otros AINES cuyos nombres no recordaba. Realizamos el estudio alergológico mediante pruebas de provocación simple ciego oral y conjuntival con diferentes AINES. La provocación oral fue positiva con ketoprofeno y diclofenaco. La provocación conjuntival con diclofenaco y flurbiprofeno fue negativa. Toleró celecoxib y nabumetona.
Presentamos un caso excepcional de intolerancia a AINES, manifestado exclusivamente como quemosis conjuntival, no incluido en ninguno de los tipos clásicos de reacciones pseudoalérgicas.

Palabras clave: Intolerancia a AINES. Quemosis conjuntival.

Introduction

Nonsteroidal anti-inflammatory agents (NSAIDs) are the drugs of choice in the treatment of chronic arthropathies and other connective-tissue diseases and are widely used to treat febrile and acute inflammatory processes. The adverse reactions caused by these drugs are well known and include gastrointestinal symptoms (pyrosis, vomiting, gastralgia), neurological reactions (tinnitus, deafness, vertigo), blood dyscrasias and nephrotoxic and hepatotoxic reactions. From the point of view of allergies, there are two main adverse reactions to NSAIDs: true allergic and anaphylactoid reactions. Patients with intolerance may have cutaneous-mucosal (urticaria, angioedema) and/or respiratory (asthma, rhino-conjunctivitis) symptoms.

We report an exceptional case of a patient who suffered NSAID intolerance manifested exclusively as unilateral conjunctival chemosis.

Case Description

A nonatopic 56-year-old man reported over the last 20 years 15-20 episodes of edema ("bag-like") at the external angle of the left-eye conjunctiva, without palpebral angioedema, lacrimation, cutaneous-mucosal or respiratory symptoms. These episodes appeared one or two hours after oral administration of metamizole, acetyl salicylic acid (ASA) and other unrecalled NSAIDs. These episodes lasted several hours and disappeared without any treatment. Subsequently, he tolerated paracetamol.

After written informed consent had been obtained, a single blind placebo-controlled oral challenge test with ketoprofen was performed. Two hours after the oral administration of 6 mg of the drug, the patient developed ocular itching, followed by mild erythema and conjunctival edema at the external angle of the left-eye (figure). No other symptoms were observed. Oral antihistamines and corticosteroids were administered and the reaction was controlled in a few hours.

Three weeks later, a single blind placebo-controlled oral challenge with an accumulated total dose of 50 mg of diclofenac was performed and the patient developed a similar reaction (conjunctival chemosis at the external angle of the left-eye) in three hours.

Fifteen days later, diclofenac (0.1%, 1 drop) and flurbiprofen (0.03%, 2 drops) eye-drops were applied on different days to both eyes without any reaction.

Two weeks later, the patient tolerated therapeutic doses of oral celecoxib and nabumetone.

Conjunctival Chemosis After Oral Challenge Test With Ketoprofen.

Discussion

As NSAIDs are widely used, different clinical manifestations of intolerance have been reported. Basically these include: urticaria, angioedema, rhinoconjunctivitis [1], asthma and, in some selected cases, anaphylactoid reactions or isolated seizures [2]. Recently a classification of pseudoallergic and allergic reactions to ASA/NSAID has been proposed [3]: type 1, NSAID-induced asthma and rhinitis in asthmatic patients; type 2, NSAID-induced urticaria/angioedema in patients with chronic urticaria; type 3, ASA/NSAID-induced cross-reacting urticaria in otherwise normal individuals; type 4, blended reactions in otherwise normal individuals; type 5, single-NSAID-induced urticaria/angioedema in otherwise normal subjects; type 6, single-NSAID-induced anaphylaxis and anaphylactoid syndromes; type 7, aseptic meningitis caused by a specific NSAID and type 8, hypersensitivity pneumonitis caused by a specific NSAID.

Periorbital angioedema is known to constitute the most frequent manifestation of NSAID cutaneous-mucosal intolerance [4], sometimes affecting exclusively a single eyelid. However, local eye reactions such as conjunctivitis [5] or conjunctival chemosis, as a sole manifestation of NSAID intolerance are exceptional To our knowledge only one other case similar to that of our patient has been reported. In that particular instance, the topical eye challenge with NSAID reproduced the left-eye conjunctivitis [6]. In contrast, our patient did not suffer any reaction to diclofenac and flurbiprofen eye-drops. This may be because only one dose was applied and this mechanism is dose-dependent or because of a limited systemic absorption of the drug. Results from bioavailability studies have established that plasma levels following ocular instillations of two diclofenac ophthalmic drops to each eye are below the limit of quantification (5 ng/mL) over a 4 hour period [7].

The pathogenesis of this peculiar form of intolerance is unknown. It has been suggested that an idiosyncratic specific local inhibition of the cyclo-oxigenase pathways may be present [5]. However, we highlight the good tolerance to topical NSAID observed in our patient, in spite of the adequate penetration of diclophenac into ocular tissues [7].

As in other NSAID intolerance reactions [8], new COX-2 inhibitors such as nabumetone were found to be good alternatives in this case.

In conclusion, we present a new case of conjunctivitis resulting from NSAID intolerance which has not been included in any of the pseudoallergic reactions listed in the new classification of intolerance syndromes.

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