

Allergic Contact Dermatitis (ACD) by Anti-allergic Agents

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Abstract

Background: Allergic contact dermatitis (ACD) by anti-allergic agents is not so common. We have experienced 3 cases of Ketotifen induced ACD.

Methods: We present 3 case studies visited in our Department of Ophthalmology of Tsurumi University between February 2012 and March 2013.

Results: 3 patients were diagnosed ACD and treated with the other anti-allergic eye drops, 0.1% fluoromethorone eye drops and prednisolone ointment for blepharitis. Inflammations of these lesions are healed within two weeks.

Conclusions: ACD might be care even anti-allergic eye drops.

Keywords: Allergic conjunctivitis; Allergic contact dermatitis; Ketotifen

Introduction

Allergic contact dermatitis (ACD) is a form of contact dermatitis that is the manifestation of an allergic response caused by contact with a substance; the other type being irritant contact dermatitis (ICD) [1]. The most common cause of ACD of the lids and periorbital area is cosmetics applied to the hair, face, or fingernails rather than to the eye area itself. We present 3 cases of ocular allergic contact blepharitis induced by anti-allergic eye drops (Ketotifen fumarate). They have no atopic disposition. Ketotifen is a second-generation noncompetitive H₁-antihistamine and mast cell stabilizer. It is most commonly sold as a salt of fumaric acid, ketotifen fumarate, and is available in two forms of eye drop; vial or unit dose (UD).

Case Reports

First case

A 51 years old women was consulted our clinic with itching and epiphora on March 3 2013 that was happened yesterday, when Japanese Cedar Pollen season. She did not have history of contact dermatitis or atopic diseases. She was prescribed Zaziten UD (Alcon Japan) 4 times a day. The conjunctivitis, discharge, eyelid swelling, and eye pain occurred 1 day after first application without another application (Figure 1a). Dermatological examination revealed irregular bordered, erythematous, edematous plaque extending from eye lid to the face region of inner surface. Mild desquamation was also observed on the skin lesion. She was diagnosed as ACD to Ketotifen fumarate. Ketotifen fumarate was stopped and topical steroid therapy including 0.1% fluorometholone eye drop (Santen Japan), Sodium cromoglicate eye drop (Intal UD; Sanofi Japan), and 0.1% Prednisolone Mylan ointment (Prednisolone ointment, Shionogi Japan) for the lid and face were started. Skin tests were not performed. Conjunctivitis and blepharitis was healed around a week (Figure 1-b; one week, c; two weeks).

Second case

80 years an old woman was consulted our clinic with itching and foreign body sensation on March 14 2013 that was happened 3 days ago. She had been treated with dry eye using 0.1% sodium hyaluronate eye drop. She was prescribed Zaziten UD (Alcon Japan) 4 times a day.

The conjunctivitis, discharge, eyelid swelling, and eye pain occurred

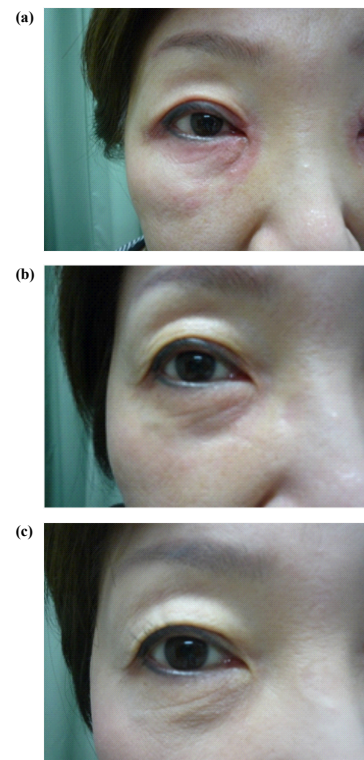


Figure 1: a: The conjunctivitis, discharge, eyelid swelling, and eye pain occurred 1 day after first application without another application. b-c: Conjunctivitis and blepharitis was healed around a week (Figure 1-b; one week, Figure 1c; two weeks).

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soon after first application without another application. Conjunctival and lid skin injections (Figure 2; next day) were disappeared and symptoms were relieved for 1 week treatment as case 1.

Third case

31 years an old man was consulted our clinic with itching and foreign body sensation on February 14 2012 that was happened 1 day ago. He was prescribed Zaziten UD (Alcon Japan) 4 times a day. Soon after use of eye drop, conjunctivitis, discharge, eyelid swelling, and eye pain occurred after first application without another application. (Figure 3; next day) Symptoms and these injections were disappeared for 5 days treatment of 0.1% fluorometholone eye drop and 1.5% Levofloxacin hydrate eye drop (Cravit; Santen Japa).

Discussion

Delayed hypersensitivity reactions involving the conjunctiva and eyelids frequently cause an individual to seek medical attention whereas cutaneous reactions elsewhere on the skin are less of concern. Contact dermatitis is the most common eruption of the eyelid. Stinging and burning of the eyes and lids on application of an eye-area cosmetic are the most common complications. Although less common than ICD, ACD is accepted to be the most prevalent form of immunotoxicity found in humans [2]. By its allergic nature, this form of contact dermatitis is a hypersensitive reaction that is atypical within the population.

The mechanisms by which these reactions occur are complex, with many levels of fine control. ACD arises as a result of two essential stages: an *induction phase*, which primes and sensitizes the immune system for an allergic response, and an *elicitation phase*, in which this response is triggered [2]. As such, ACD is termed a Type IV delayed hypersensitivity reaction involving a cell-mediated allergic response. Contact allergens are essentially soluble haptens and, as such, have

the physico-chemical properties that allow them to cross the stratum corneum of the skin. They can only cause their response as part of a complete antigen, involving their association with epidermal proteins forming hapten-protein conjugates. The conjugate formed is then recognized as a foreign body by the Langerhans cells (LCs) (and in some cases other Dendritic cells (DCs)), which then internalize the protein; transport it via the lymphatic system to the regional lymph nodes; and present the antigen to T-lymphocytes. As the LC's are transported to the lymph nodes, they become differentiated and transform into DCs, which are immunostimulatory in nature.

Once within the lymph glands, the differentiated DCs present the allergenic epitope associated with the allergen to T lymphocytes. These T cells then divide and differentiate, clonally multiplying so that if the allergen is experienced again by the individual, these T cells will respond more quickly and more aggressively. Common allergens implicated include the following: Nickel sulfate hexahydrate, Gold sodium thiosulfate, Fragrance used in perfumes and skin lotions, Chromium, Neomycin, Formaldehyde, Cobalt chloride, Bacitracin, Topical anesthetics, Other preservative in cosmetic products and in industrial products and topical ointment [3].

The symptoms of ACD are very similar to the ones caused by ICD, which makes the first even harder to diagnose. The first sign of ACD is the presence of the rash or skin lesion at the site of exposure. Characteristic of the ACD rash is that it usually appears after a day or two after exposure to the allergen, unlike ICD that appears immediately after the contact with the trigger.

Other symptoms may include itching, skin redness or inflammation, localized swelling and the area may become more tender or warmer. The symptoms of allergic contact may persist for as long as one month before resolving completely. Once an individual has developed a skin reaction to a certain substance it is most likely that they will have it for the rest of their life, and the symptoms will reappear when in contact with the allergen.

Persons who develop the rash and the other symptoms from a certain trigger are most likely to have it for the rest of their lives and detecting and avoiding the allergen is mandatory in treating the condition and resolving its symptoms. In mild to moderate cases, patients may use skin creams containing corticosteroids to reduce the inflammation. These creams should be used carefully and according to the instructions they come with because when overused over longer periods of time they can cause serious skin conditions. Usually, severe cases are treated with systemic corticosteroids which may be tapered gradually. Tacrolimus ointment and eye drop can also be used additionally to the corticosteroid or instead of these [4,5]. Oral steroid may also be used in more severe cases to relieve the intense itching.

Commonly, the symptoms may resolve without treatment in 1 to 2 weeks but specific medication may hasten the healing as long as the trigger is avoided.

Diagnosing ACD is primarily based on physical exam and medical history. In some cases doctors can establish an accurate diagnosis based on the symptoms that the patient experiences and on the rash's appearance. In the case of a single episode of ACD, this is all that is necessary. These 3 cases are diagnosed on this base. Chronic and/or intermittent rashes which are not readily explained by history and physical exam often will benefit from further testing. A patch test is a commonly used examination to determine the exact cause of an ACD. According to the American Academy of Allergy, Asthma, and Immunology, "patch testing is the gold standard for contact allergen



Figure 2: Conjunctival and lid skin injections (Next day).

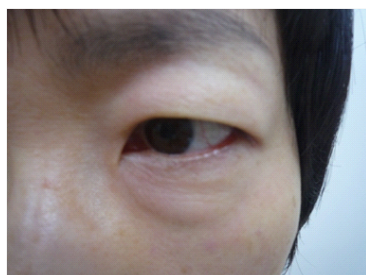


Figure 3: Soon after use of eye drop, conjunctivitis, discharge, eyelid swelling, and eye pain occurred after first application without another application (Next day).

identification”, but we could not perform it due to the poor potentials of ophthalmologist.

Ketotifen relieves and prevents eye itchiness and/or irritation associated with most seasonal allergies. It starts working within minutes after administering the drops. Possible side effects of ketotifen ophthalmic reactions are; get emergency medical help of difficulty breathing to eye and eye lid and to mild burning. Preservatives is shown to cause conjunctivitis and eyelid dermatitis as ACD. Benzalkonium chloride and thimerosal are some of the most widely used ophthalmic preservatives. UD is preservative-free lubricants and is used in single-use disposable units. All of patients of three cases are used UD and preservative effects have not been affected.

Consequently, the present cases are the rare cases of ACD induced anti-allergic eye drop. For dermatologist, allergic hypersensitivity to corticosteroids is a common finding in a dermatological practice. The skin may be the main sensitization route, and delayed-type allergic reactions are much more frequently encountered than immediate-type reactions. As a result of the anti-inflammatory properties of corticosteroids, however, the clinical signs of ant-allergic drug may be masked. Hence, ant-allergic drug allergy still remains unfamiliar to

many clinicians who often prescribe these drugs. Ketotifen may be a potent sensitizer in susceptible people and may trigger ACD after the first conjunctiva or skin contact. Moreover, it may cause immediate contact skin reaction in the lid or face. The clinicians who want to use anti-allergic eye drops for allergic conjunctivitis must know and be careful in terms of ACD.

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