First Report of Allergic Contact Dermatitis to Loteprednol Etabonate Gel

Estefanía Cruzval-O'Reilly, BA[1,2]; Aída Lugo-Somolinos, MD[3]

1. School of Medicine, Universidad Central del Caribe 2. Research Fellow, University of North Carolina at Chapel Hill
3. Department of Dermatology, University of North Carolina at Chapel Hill

INTRODUCTION

Loteprednol etabonate 0.5% gel (Lotemax®) is a corticosteroid (CS) used for the treatment of post-operative pain and inflammation following ocular surgery. It is structurally similar to other corticosteroids. However, it has a labile ester in lieu of a ketone group at carbon 20.

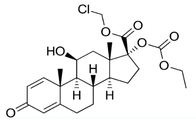

Figure 1. Loteprednol etabonate Chemical Structure

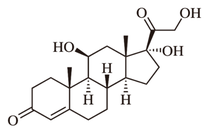

Figure 2. Cortisone Chemical Structure

To the best of our knowledge, true contact dermatitis to loteprednol etabonate gel has not been reported in the literature. We report the first case of allergic contact dermatitis (ACD) to loteprednol etabonate gel confirmed by patch testing.

CASE HISTORY

A 59- year-old woman presented to dermatology for evaluation of periorbital erythema, edema, induration and scaling of the right eye following pterygium surgery (Figure 3). Symptom onset was gradual and began one week after applying a series of eye drops. The post- operative medications used included moxifloxacin drops, ciprofloxacin drops, latanoprost drops , timolol drops, fluorometholone drops, preservative- free (PF) Refresh® gel drops, PF Refresh Plus® lubricating eye drops, and PF loteprednol etabonate ointment. Past medical history was significant for a similar reaction 18 years prior following pterygium surgery of the left eye. The patient used the same eye drops during the post-operative period of this prior surgery. However, the loteprednol etabonate eye gel used at the time did contain preservatives. Following the initial reaction, ophthalmologists suspected ACD to benzalkonium chloride preservative and recommended avoidance for the following surgery. Recently, she developed a rash on the arm that worsened with the use of Cortizone 10® cream.

METHODS

A thorough review of the ophthalmology post- surgical notes was conducted to identify the ophthalmic solutions used following both pterygium surgeries. Using the information gathered, a custom patch tray was created based on the overlapping ophthalmic medications and personal care products the patient used after both procedures (Figure 4). A total of 17 patches were applied on the back and she was asked to return 48 and 96 hours later for reading.

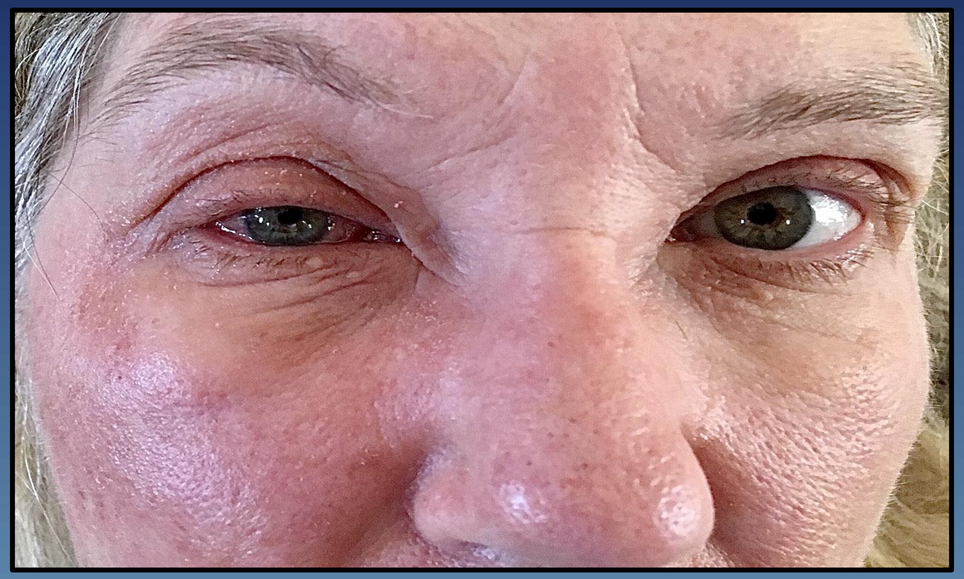

Figure 3. Well demarcated erythematous plaque with edema, induration and scaling of the right peri-orbital region extending down to the mid-check and nasal sidewall.

RESULTS

At the 96-hour reading, the patient developed a 1+ reaction to loteprednol etabonate 0.5% gel, a product she had used in various formulations (drops, gel, and preservative - free ointment) during the post-operative course of both surgeries. She also had a positive reaction to Cortizone 10® cream and tixocortol-21-pivalate 1% petroleum at the 48-hour reading. No reaction was noted for the preservative benzalkonium chloride, an excipient frequently used in ophthalmic medications. Based on the patient's history and the patch test results, she was diagnosed with ACD to loteprednol etabonate.

DISCUSSION

Loteprednol etabonate is one of the first-generation soft CSs approved by the FDA for inflammatory and allergy – related ophthalmic disorders. Its molecular configuration corresponds most closely to the D2 CS group. Intra-group and inter- group cross reactions between CSs in groups A and D2 are known to occur. This patient's patch test results are significant for an inter- group reaction between group D2 loteprednol etabonate and group A tixocortol-21-pivalate 1% petroleum. Furthermore, the positive reaction to Cortizone 10® cream represents an intra-group reaction with group A tixocortol- 21- pivalate 1% petroleum. This explains the recent worsening skin rash she experienced while using Cortizone 10® cream.

References

1. Baeck M, Marot L, Nicolas JF, Pilette C, Tennstedt D, Goossens A. Allergic hypersensitivity to topical and systemic corticosteroids: a review. *Allergy*. 2009;64(7):978–994.
2. Bodor N, Buchwald P. Ophthalmic drug design based on the metabolic activity of the eye: soft drugs and chemical delivery systems. *AAPS J*. 2005;7(4):E820–E833.

#	TEST SUBSTANCE	48 HOURS	96 HOURS
1	Benzocaine 5% pet.	-	-
2	Lidocaine – HCl 15% pet.	-	-
3	Benzalkonium Chloride 0.1% pet.	-	-
4	Olay® Eye Lifting Serum	-	-
5	Olay® Miracle Boost Serum	-	-
6	Olay® Micro- Sculpting Serum	-	-
7	Clinique® Lid Smoothie cream eye shadow	-	-
8	Cortizone 10® Cream	1+	1+
9	Benadryl® Cream	-	-
10	Refresh® PF Gel Drops	-	-
11	Moxifloxacin HCl Ophthalmic Solution	-	-
12	Timolol Ophthalmic Solution	-	-
13	Loteprednol Etabonate Gel (Lotemax®)	-	1+
14	Refresh Plus® Eye Drops (preservative-free)	-	-
15	Timolol Ophthalmic Solution (preservative-free)	-	-
16	Povidone-Iodine 10% water	-	-
17	Olay Regenerist Micro- Exfoliating Wet Cleansing Cloths	-	-
18	Paraben Mix [B] 12% pet.	-	Not read*
19	Tixocortol-21-Pivalate 1% pet.	1+	Not read*
20	Propolis 10% pet.	-	Not read*
21	Cetylstearylalcohol 20% pet.	-	Not read*

Figure 4 . Patch Test results at the 48- and 96-hour reading. Substances 18-21 were applied following the 48-hour reading. Delayed reading of these substances was not performed.

CONCLUSION

Physicians should consider the diagnosis of allergic contact dermatitis to loteprednol etabonate ophthalmic solutions in patients presenting with periorbital dermatitis following their use. Finally, the frequent cross- reactions that can occur between the group A and group D2 corticosteroids should be taken into consideration when prescribing corticosteroids for patients with previous allergic reactions. This will help reduce drug intolerance and adverse reactions.