Case Report

Fixed drug eruption by etoricoxib confirmed by patch test*

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Abstract: Non-steroidal, anti-inflammatory drugs, followed by antibiotics, are the main causes of fixed drug eruption. They provoke one or several round erythematous or bullous lesions that recur in the same place after taking the causative medication. A positive patch test on residual, lesional skin can replace satisfactorily oral reintroduction. We describe the case of a 74-year- old woman with numerous, rounded, erythematous lesions on the trunk and recurrent blistering on the fifth right-hand finger, which developed a few hours after taking etoricoxib. Lesional patch testing with etoricoxib was positive and reproduced the typical pattern of a fixed drug eruption upon histopathology. We emphasize the specific reactivity of the etoricoxib patch test, and the capacity to reproduce the histologic pattern of the reaction.
Keywords: Drug eruptions; Histology; Patch tests

INTRODUCTION

Fixed drug eruption (FDE) is a cutaneous adverse drug reaction characterized by one or multiple skin lesions that begin one to two weeks after the first exposure to the drug. These lesions present as erythematous and edematous round plaques, sometimes with a central blister. They can be found anywhere on the body but favor the oral mucosa, lips and genitalia. With subsequent exposures, lesions reactivate within 24 hours and then fade several days, often leaving a residual, post-inflammatory, grey-brown pigmentation. After a further administration of the culprit drug, lesions appear at the same locations but may also emerge at new locations. In the presence of numerous lesions, it is termed generalized FDE and may be difficult to differentiate from erythema multiforme major, Stevens-Johnson Syndrome and toxic epidermal necrolysis, with which it shares histopathological findings.[1]

The drugs most frequently associated with FDE are non-steroid, anti-inflammatory drugs (NSAIDs), followed by antibiotics.[2]

Oral drug rechallenge is considered the gold standard diagnostic test, but even with low doses, the culprit drug may cause simultaneous reactivation of all lesions and create new ones, which is impracticable in patients with numerous bullous lesions.

Alternatively, patch testing on a previously involved site may be the preferred test[3], especially in cases induced by NSAIDs.[3] Patch testing should be performed six weeks after the acute eruption, with lesions in remission. The culprit drug and related drugs (if possible) are applied under occlusion for 24 hours in test chambers or in open tests, in both non-lesional skin on the back and in previously involved areas. Readings should be performed 24 and 48 hours thereafter. The test is considered positive if there is erythema and pruritus, infiltration or more intense reactions.[3,4,5] In highly suspicious cases entailing negative patch tests, it is advisable to repeat the patch test on the affected area with the suspected allergen at the same or higher concentrations (up to 20%), under occlusion. If tests remain negative, oral rechallenge under strict surveillance is an option. Rechallenge tests are considered positive if recurrence of inflammatory signs in residual lesions occurs within the following 24hours.[4,5,6]

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CASE REPORT

We report the case of a 74-year-old female patient who regularly consumed multiple drugs, with no previous adverse reactions. She was observed in the emergency room for a violaceous plaque of 5cm in diameter with central blistering on the medial side of the fifth right-hand finger, as well as multiple, smaller, round erythematous lesions on the upper back and lateral side of the arms.

These skin lesions appeared less than 12 hours after taking etoricoxib (Exxiv®) for joint pain. The patient described a similar episode two months beforehand, involving only the right-hand finger. She was treated with betamethasone cream and fusidic acid, leading to clinical improvement.

Six weeks later, with the cutaneous reaction in remission and some residual macular pigmented lesions, patch testing was performed, applying the allergens from the European baseline series and a series of 12 NSAIDs on non-lesional skin, involving occlusion for 48 hours in Finn Chambers. Additionally, in ill-defined residual hyperpigmented areas (two on the upper back, and one on the right-hand finger), we applied etoricoxib 10% in vaseline using Finn chambers with occlusion periods of 24 hours. As we did not have pure etoricoxib, an Exxiv® 90mg pill was grinded into fine powder and manipulated in vaseline to obtain a 10% concentration of the active drug. Readings performed after 24 hours revealed a positive reaction to etoricoxib only in previously involved areas (Figures 1 and 2). No positive reaction to celecoxib (Celebrex®) 10% was observed in lesional or normal skin.

A cutaneous biopsy in a positive test area located on the upper back at 24 hours revealed spongiosis, lymphocyte exocytosis and marked vacuolization of the basal cell layer, with some apoptotic keratinocytes, associated with a lymphocytic dermal infiltrate, with some intravascular neutrophils, consistent with the diagnosis of FDE (Figure 3).

DISCUSSION

We present the case of a polymedicated, elderly patient with etoricoxib-induced FDE. Diagnosis was based on the typical clinical presentation and confirmed by a positive lesional patch test that reproduced the typical histopathology of FDE. Etoricoxib is a newly developed NSAID, a cyclo-oxygenase 2 selective inhibitor, rarely described as the culprit drug in FDE, which makes this a peculiar case.[7]

In agreement with previous studies, patch testing on lesional skin was useful to confirm etoricoxib as the culprit drug in this FDE case.[7,2] It should be highlighted that patch testing must be performed on residual lesional areas, where epidermal CD8+ memory T lymphocytes are retained for many years[6]. This explains the exclusive reactivity of these locations facing oral rechallenge and probably facilitates reactivation after cutaneous exposure due to patch testing.[2,5,7]

Figure 2: Highlight of reactivation of the skin lesion in the fifth right-hand finger after contact test

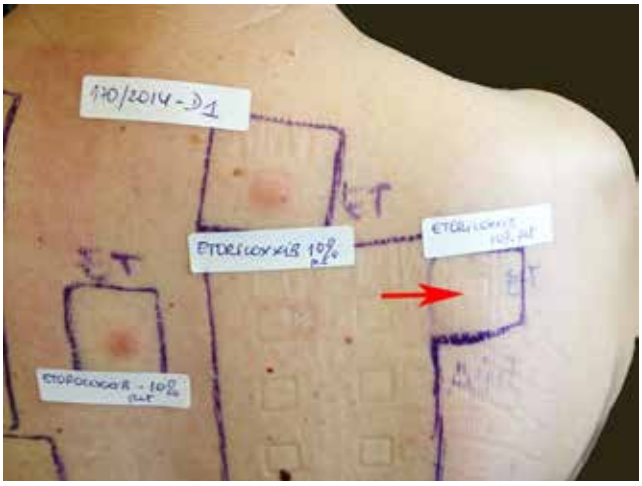

Figure 1: Positive patch test at 24 hours with erythema and infiltration of the patch test area on residual lesions, and negative patch test when performed on non-involved skin (red arrow)

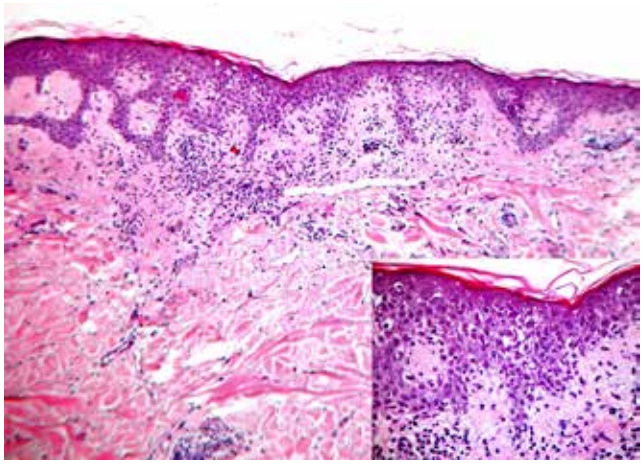

Figure 3: : Dermal infiltrate, with some intravascular neutrophils at a lower magnification. Spongiosis and lymphocytic exocytosis with vacuolization of the basal cell layer as well as apoptotic keratinocytes, at a higher magnification

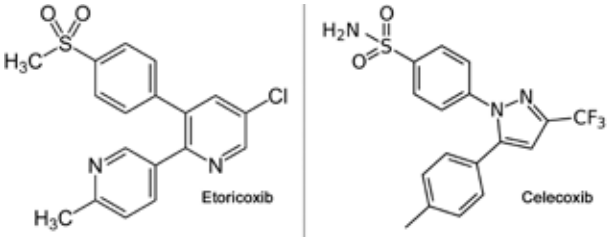

Figure 4: : Etoricoxib and Celecoxib chemical structure

Histologically, after oral reactivation, there is a lichenoid reaction with pigment incontinence; in more exuberant lesions, there is a significant hydropic degeneration of basal cells with dyskeratotic cells in the epidermis, a dermal lymphocytic infiltrate and dermal melanophages.[7,5,4] Similar features were observed in our patient's positive lesional patch test, demonstrating that in cutaneous adverse drug reactions, the histology of patch tests can reproduce many aspects of the acute reaction.[8]

Since the presence or absence of cross-reactions can also be evaluated by lesional patch testing, these data can be important in recommending alternative safe drugs. In FDE induced by etoricoxib, patients can safely use the other coxib with a different chemical **structure. The** absence of cross-reactivity with celecoxib has also been confirmed by lesional patch testing, as in our case (Figure 4).[2,7,9]

With an aging population, the growing consumption of medication and the commercialization of new drugs by the pharmaceutical industry, there is an increased incidence in adverse cutaneous drug reactions. Etiologic confirmation of FDE is sometimes hard, particularly in polymedicated patients. After identification of the culprit drug, patients should be given a list of drugs to avoid, to prevent new and more severe episodes of cutaneous adverse drug reactions.[10] ❑

REFERENCES

1. Revuz J, Allonore LV. Drug Reactions. In: Bolognia JL, Jorizzo JL, Schaffer JV, editors. Dermatology. 3rd ed. St Louis: Elsevier; 2012.p.345-347.
2. Andrade P, Brinca A, Gonçalo M. Patch testing in fixed drug eruptions - a 20 year review. Contact Dermatitis. 2011;65:195-201.
3. Gonçalo M, Oliveira H, Fernandes B, Robalo-Cordeiro M, Figueiredo A. Topical provocation in fixed drug eruption from nonsteroidal anti-inflammatory drugs. Exogenous Dermatology. 2002;1:81-6.
4. Barbaud A, Gonçalo M, Bruynzeel D, Bircher A; European Society of Contact Dermatitis. Guidelines for performing skin tests with drugs in the investigation of cutaneous adverse drug reactions. Contact Dermatitis. 2001;45:321-8.
5. Gonçalo M, Bruynzeel, D. Patch testing in drug eruptions. In: Johansen JD, Frosch PJ, Lepoittevin JP. Contact Dermatitis. 5th ed. Berlin-Heidelberg: Springer-Verlag; 2011. p.475-92. .
6. UpToDateR.com [Internet]. Shiohara T, Mockenhaupt M, Corona R. Fixed drug eruption. UpToDateR [cited 2014 Jan 09]. Available from: http://www.uptodate.com
7. Andrade P, Gonçalo M. Fixed drug eruption caused by etoricoxib - 2 cases confirmed by patch testing. Contact Dermatitis. 2011;64:118-20.
8. Gonçalo M, Cardoso JC, Coutinho I, Garneiro AR, Tellechea O. Histopathology of patch tests depends on the pattern of CADR, not on the culprit drug. Contact Dermatitis 2014: 70:36-7
9. Oliveira HS, Gonçalo M, Reis JP and Figueiredo A. Fixed drug eruption to piroxicam.Positive patch tests with cross-sensitivity to tenoxicam. J Dermatolog Treat. 1999;10:209-12.
10. Varalda DB, Motta AA. Adverse reactions to nonsteroidal anti-inflammatory. Rev. bras. alerg. imunopatol. 2009;32:27-34.

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