Allergic Contact Dermatitis and Systemic Contact Dermatitis in a Patient With Polysensitization to Topical Corticosteroids

E. Gómez-de la Fuente, A. Rosado, M. Gutiérrez-Pascual, F.J. Vicente, and J.L. López-Esteban

To the Editor:

Although allergic contact dermatitis (ACD) due to corticosteroids is a well-known and relatively common phenomenon, the systemic administration of corticosteroids only rarely produces skin reactions (systemic contact dermatitis [SCD]). We present the case of a patient with ACD to various corticosteroids, and who subsequently developed SCD to multiple systemic corticosteroids.

A 47-year-old man was seen in our outpatient clinic for a plaque of alopecia areata on the scalp. A 0.1% methylprednisolone aceponate emulsion was prescribed. Four days later, pruritic, macular, desquamative, erythematous lesions developed on the eyelids, neck, and around the plaque of alopecia. With a suspected diagnosis of corticosteroid-related ACD, 1% pimecrolimus cream was prescribed and skin patch testing was performed with True Test, using a series of corticosteroids and steroid-containing products (Lexxema emulsion). Readings were made on days 2, 5, and 7, obtaining positive reactions to multiple corticosteroids (Table 1, Figure). Skin prick and intradermal reaction tests were performed with hydrocortisone, prednisone, methylprednisolone, prednisolone, dexamethasone, and deflazacort, giving negative results, and oral therapeutic doses were then administered. Pruriginous, erythematous lesions affecting the neck, axillas, groin, and perineum (baboon-like) developed in all cases after a period of 6 to 24 hours. The lesions did not recur on placebo challenge. The skin biopsy of one of the lesions showed spongiotic dermatitis with a superficial perivascular inflammatory infiltrate and dermal edema. A diagnosis was made of ACD and SCD due to corticosteroids, with polysensitization. A use test was performed with 0.1% mometasone furoate cream, which did not produce lesions after 10 days, and this was therefore indicated for treatment if topical corticosteroids were required.

Corticosteroid-related ACD must be suspected when there is a deterioration or prolongation of a previous dermatitis or when the expected improvement does not occur. Using patch tests, Gonul and Gul demonstrated sensitization in 22% of patients diagnosed with ACD who did not respond to topical corticosteroids. The rates of positivity to corticosteroids in patch tests vary between 0.52% and 6%, which has led to these allergens being included in a number of standard series. In Spain, the Spanish Contact Dermatitis Research Group (GEIDC) initially introduced 1% tixocortol pivalate in petroleum jelly, subsequently adding 0.1% budesonide in petroleum jelly. In 2007, hydrocortisone-17-butyrate was also added to the True Test. In the epidemiologic study of ACD in Spain published by the GEIDC in 2001, positivity to corticosteroids was only detected in 1.01%. We do not know the present levels with the new corticosteroids used for screening.

In a retrospective study of 1188 patients undergoing patch tests with a specific corticosteroid series, it was shown that if tixocortol pivalate alone had been used, less than 50% of the sensitizations would have been detected.

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Figure. Various positive patch tests after application of a corticosteroid series (48 hours).
With the 3 corticosteroids currently used for screening in the True Test, 71% would be detected; however, a significant number would remain undiagnosed. For this reason, the North American Contact Dermatitis Group has added 2 further corticosteroids to their standard series: 1% triamcinolone acetonide in petroleum jelly and 1% clobetasol-17-propionate in petroleum jelly. If positive results are obtained or there is a suspicion of sensitization, skin patch testing must be performed using a corticosteroid series to detect possible cross reactions. These series must include the substances most commonly used in that country. However, corticosteroids as widely used as mometasone furoate, prednicarbate, or methylprednisolone aceponate, among others, are not included in the commercially available specific series. Because of this, it is important to patch test the specific products used by the patient in order to minimize the loss of cases.

A late reading should be performed on day 6 or 7. Some studies have shown losses of 30% if this late reading is not performed, whereas in others it is less than 1%.6,7

Multiple sensitization (coreactions or cross-reactions) is relatively common. In 1989, Coopman et al8 classified the corticosteroids into 4 groups according to their chemical structure and to the skin reactions that were observed with patch tests (Table 2). But this is of limited value as cross reactions have been reported between all the groups. It is much less common to find sensitization to a large number of corticosteroids from all groups, as occurred in our case.9 The mechanism for this is not clear, as it may be due to sensitization to the basic corticosteroid structure or to a common metabolite.

Given the sensitization to multiple corticosteroids and the possibility of a reaction after their systemic administration, it was decided to perform a controlled
challenge test. A baboon-like pruriginous skin reaction, which is a recognized clinical pattern of SCD, occurred with all the corticosteroids tested. Although the patient can use pimecrolimus/tacrolimus or mometasone furoate topically, we have not been able to find a safe systemic corticosteroid in case the patient needs it in the future, and the risk-benefit relationship will have to be carefully evaluated. This is an exceptional situation, and although cases of ACD to multiple corticosteroids have been reported, we have only found one case in the literature similar to the patient presented in this article.10

We would like to draw attention to the importance of suspecting an ACD in those cases that do not respond adequately to corticosteroid treatment, and they should be studied in specific contact units, both to confirm the diagnosis and to offer safe therapeutic alternatives.

Correspondence: Enrique Gómez de la Fuente Unidad de Dermatología Hospital Universitario Fundación Alcorcón C/ Budapest, 1 28922 Alcorcón, Madrid, Spain egomezf@fhalcorcon.es

Conflicts of Interest
The authors declare no conflicts of interest.

<table>
<thead>
<tr>
<th>Group</th>
<th>Structure</th>
<th>Component</th>
<th>Typical Cross-reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Without methyl substitution at C16, no side chain at C17, possible short side chain at C21</td>
<td>Tixocortol pivalate</td>
<td>With D2 Hydrocortisone Prednisolone Methylprednisolone Prednisone</td>
</tr>
<tr>
<td>B</td>
<td>cis-ketal or cis-diol structure at C16 and C17; possible side chain at C21</td>
<td>Budesonide</td>
<td>Budesonide with D2 Triamcinolone Triamcinolone acetonide Fluocinolone acetonide Fluocinonide Halcinonide</td>
</tr>
<tr>
<td>C</td>
<td>Methyl substitution at C16, no side chain at C17, possible side chain at C21</td>
<td>Betamethasone</td>
<td>Dexamethasone Desoximetasone Fluocortolone</td>
</tr>
<tr>
<td>D1</td>
<td>Methyl substitution at C16, side chain ester at C17/C21</td>
<td>Clobetasol propionate</td>
<td>Betamethasone dipropionate Betametasone-17 valerate Mometasone furoate Diflucortolone valerate</td>
</tr>
<tr>
<td>D2</td>
<td>No methyl or halogen substitution at C16, side chain ester at C17, possible side chain at C21</td>
<td>Hydrocortisone 17-butyrate</td>
<td>With A and with budesonide Hydrocortisone 17-aceponate Methylprednisolone aceponate Prednicarbate</td>
</tr>
</tbody>
</table>

The molecule used for screening is in bold text.
To the Editor:

Neurofibromatosis type 1 (NF-1) or von Recklinghausen disease is the most common neurocutaneous syndrome. It is characterized by the appearance of various cutaneous stigmata, neurological manifestations, and an increased susceptibility to develop tumors. Although it is frequently associated with a wide variety of central nervous system (CNS) dysplasias, the association with Arnold-Chiari malformation type I is unusual.

A 60-year-old woman with a past history of systemic hypertension, hiatus hernia, and iron-deficiency anemia, was seen in our outpatient clinic for lesions on her neck that had been present for years and that caused discomfort due to friction. On physical examination of the skin, multiple soft fibromas were observed in the cervical region; however, a large number of hyperpigmented macules with a homogeneous, light brown color and well-defined borders were also observed, mainly on the trunk, though also at the root of the limbs, and 9 of them were over 15 mm in diameter, and there were also groups of hyperchromic macules between 2 and 10 mm in diameter in both axillae, clinically consistent with lentigo simplex (Crowe sign). The patient stated that those lesions had been present since birth, and that her father had similar spots. Based on these findings, the patient was diagnosed with NF-1 and was referred to the neurology and ophthalmology departments to exclude CNS and optic nerve involvement. Ophthalmologic examination was normal, with no evidence of Lisch nodules. The patient had no neurological symptoms and neurological examination revealed generalized, symmetrical muscle hyperreflexia but no other alterations. Cerebral magnetic resonance imaging (MRI) showed herniation of the cerebellar tonsils into the upper cervical canal, below the level of the occipital foramen, consistent with Arnold-Chiari malformation type I.

![Figure 1. Sagittal cerebral magnetic resonance image: the T1-weighted image shows herniation of the cerebellar tonsils into the upper cervical canal, below the level of the occipital foramen, consistent with Arnold-Chiari malformation type I.](image-url)