Case-based review

Contact allergy to retapamulin: a case report and literature review

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Summary

We present the case of a 43-year-old non-atopic man affected by allergic contact dermatitis from retapamulin, a new semisynthetic pleuromutilin topical antimicrobial agent with efficacy against Staphylococcus aureus and Streptococcus pyogenes. Among topical antimicrobials, retapamulin is rarely reported as contact sensitizer. To date only four cases of allergic contact dermatitis from retapamulin are reported. Given the increasing occurrence of bacterial resistance, use of retapamulin ointment may increase over time and more cases of contact allergy to it are likely.

KEY WORDS: retapamulin; allergic contact dermatitis; patch test; topical medicament.

Retapamulin (CAS number 224452-66-8) is the first topical semisynthetic pleuromutilin antibiotic obtained from the fermentation of the edible mushroom Pleurotus passeckerianus. This antibacterial agent inhibits selectively bacterial protein synthesis by interacting with the 50S ribosomal subunit, blocking ribosomal P-site interactions and preventing peptidyl trasferase (1). In vitro it was shown to be predominantly bacteriostatic against Staphylococcus aureus, including the methicillin-resistant strains, and against Streptococcus pyogenes (2). It is also effective against the majority of the anaerobes, including Propionibacterium acnes.

In clinical trials topical retapamulin caused adverse events in less than 2% of treated patients, mainly irritation at the application site, nausea and diarrhoea (3). In a case study contact dermatitis prevalence was reported to be less than 1% (4). Retapamulin is available in Europe as Altargo® ointment (retapamulin 1% w/w, butylated hydroxytoluene and white petrolatum) from 2009 and in USA as Altabax® (retapamulin 1%, white petrolatum) from 2007. To date only 4 cases of allergic contact dermatitis from retapamulin have been reported (5, 6).

Case report

A 43-year-old non-atopic man was referred to us for erysipelas of right leg. During hospitalization he was successfully treated with piperacillin-tazobactam (4.5 g/8h iv for 7 days). Ten days after he started therapy with Altargo® ointment once daily for residual moderate inflammation. The patient had never previously used this topical antibacterial agent. Two weeks after he noticed itching eczematous dermatitis on the site to which he was applying Altargo® (Figure 1); no lymphadenitis and lymphangitis were present. The symptoms resolved in 10 days after withdrawal of the suspected offending agent and administration of steroid topical treatment (betamethasone ointment). ROAT (Repeated Open Application Test) was performed on the volar aspect of forearm with Altargo®: a positive reaction appeared within 3 days. Two months after the resolution of the skin lesions patch testing with Italian So-
ciety of Allergological, Occupational and Environmental Dermatology baseline series, topical antimicrobials series, excipients and preservatives series, Altargo® ointment as is and butylated hydroxytoluene (3,5-di-tert-butyl-4-hydroxytoluene) (BHT) (2% pet.) was performed. The allergens (FIRMA Diagent, Florence, Italy) were tested on the upper back with Haye’s Test Chambers® (Haye’s Service B.V., Alphen aan den Rijn, the Netherlands) on Soffix® tape (Artsana, Grandate, Italy) and removed after 2 days. The readings (D2 and D4) were performed according to International Contact Dermatitis Research Group criteria. Positive reaction was observed to Altargo® as is (D2 ++, D4 +++). Despite our repeated requests to the Altargo® producer (GSK, Verona, Italy) it was not possible to obtain retapamulin to carry out a patch test with it.

**Discussion**

To date 4 cases in 2 articles of contact allergy to retapamulin were reported (5, 6). Comparing the data of these 4 patients, only in 1 of these there was isolated sensitivity to retapamulin, being associated to neomycin in 3 (case 1, 3 and 4 in Table 1) and to bacitracin in 2 (case 1 and 4 in Table 1). All patients with multiple positive patch tests had reported previous use of antimicrobials in the past. In particular, case 1 had applied various antimicrobial ointments during the course of chronic vesicular hand dermatitis; case 3 had had previous earlobe dermatitis after ear piercing and some episodes of impetigo treated with topical antimicrobials; case 4 was given a prescription with bacitracin on a scrape 4 years prior. The chemical structure of retapamulin differs significantly from that of neomycin and bacitracin, the latter 2 bearing no structural similarities to each other (Figure 2). Therefore it seems likely to exclude in these subjects cross-reactivity with retapamulin and to assume that reported multiple positive patch test reactions are co-sensitivities. Our patient as well as the case 2 was sensitized only to retapamulin ointment. He referred that he had never used topical antimicrobials in the past.

As shown by literature data and our reported case, retapamulin was never tested alone, but always as Altabax® (5, 6) or Altargo® (our case) as is. Therefore, we can’t perform a comparison on possible differences in patch testing results related to the positivity of marketed ointment as is or retapamulin alone.

<table>
<thead>
<tr>
<th>Case no./age (years)</th>
<th>Gender</th>
<th>Indication to retapamulin therapy</th>
<th>Patch test results</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1/40</td>
<td>M</td>
<td>Pruritic and vesicular hand dermatitis</td>
<td>Retapamulin*</td>
<td>+++</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bacitracin (15% vas)</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Neomycin (5% vas)</td>
<td>++</td>
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<tr>
<td>Case 2/16</td>
<td>F</td>
<td>Folliculitis with secondary impetigo</td>
<td>Retapamulin*</td>
<td>++</td>
</tr>
<tr>
<td>Case 3/3</td>
<td>F</td>
<td>Impetigo of earlobe after ear piercing</td>
<td>Retapamulin*</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Neomycin (5% vas)</td>
<td>+</td>
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<tr>
<td>Case 4/79</td>
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<td>Cryosurgery for actinic keratoses</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Bacitracin (15% vas)</td>
<td>++</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Neomycin (5% vas)</td>
<td>++</td>
</tr>
</tbody>
</table>

Table 1 - Clinical data and patch test investigations in 4 reported patients with contact allergy to retapamulin (5, 6).
Given the permanent increasing occurrence of bacterial resistance, the use of retapamulin ointment may also increase over time. Therefore dermatologists should not underestimate the possibility that retapamulin could become a new antimicrobial allergen.

References