



Title: Silver: an underdiagnosed allergen?

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CASE:

We present a case of a 90-year-old man who developed eczematous and bullous lesions around ulcers on the left leg with itching sensation shortly after Silvederma cream® (Aldo Union Lab, Barcelona, Spain) was applied. The patient had varicose ulcers difficult to manage. Hence, a variety of topical treatments were used, some of which included silver in their composition such as wound dressings like Actisorb Plus 25® Ag (Systagenix Lab, Madrid, Spain), Urgotul Ag® (Urgo Lab, Chenove, France) and Mepilex® Ag/silver (Molnlycke Health Care Lab, Madrid, Spain), and also cauterizing rods Argenpal® (B. Braun Medical Lab, Jaén, Spain). Additionally, other treatments with different composition were used such as Aquaphor® ointment (Eucerin, Beiersdorf, Hamburg, Germany) or Tulgrasum® (S.I.T Srl Lab, Mede, Italy)

Patch tests were performed with the Spanish Contact Dermatitis Research Group (GEIDAC) baselines series, Silvederma cream® as is (whose composition includes the following ingredients: Silver sulphadiazine, cetylstearyl alcohol, isopropyl myristate, white petrolatum, polyoxyethylene stearate, sorbitan oleate, propylene glycol, methyl paraben and purified water) and the Leg Ulcers series (Chemotechnique Diagnostics®, Vellinge, Sweden), expanded with additional allergens from Marti Tor® Lab (Barcelona, Spain) (Table 1). The remaining ingredients of the cream that were not included in these series, were also tested using allergens from Chemotechnique Diagnostics® (Cosmetics series).

We read patch tests at D2 and D4 according to ICDRG guidelines. We found positive patch test to Silvederma cream® as is (+ D2 and ++ D4) (Fig 1A) The standard battery shows a positive patch test to lanolin alcohol 30% pet. (++) D4), present in Aquaphor® ointment, Myroxylon pereirae 25% pet. (+++ D4) present in Tulgrasum®. Also epoxy resin 1% pet. (++) D4) and p-phenyldiamine 1% pet. (++) D4) were positive but they did not show clinical relevance in this case. A positive patch test was also found in the Leg Ulcers series to propylene glycol 5% pet. (++) D4) present in Silvederma cream® and Menaderm® (Grupo Menarini Lab, Barcelona, Spain) and silver nitrate 1% pet. (++) D4) (Fig 1B). The rest of its ingredients were negative. Therefore, a diagnosis of allergic contact dermatitis (ACD) to Silvederma cream® was confirmed due to silver and propylene glycol included in its composition.

After silver-containing treatments were discontinued, corticosteroids and antihistamines were administered as a result of which symptoms remitted in two weeks.

DISCUSSION:

It is known that patients with chronic ulcers can develop ACD more easily, probably due to the fact, that they present an altered skin barrier and the prolonged use of multiple topical treatments.^{1,2} Our patient had sensitization to several of the previously used treatments, such as Aquaphor®, Tulgrasum® or Menaderm®. On the other hand, he had also used various products that contained silver among their components as mentioned above, so a prior sensitization to silver could be suspected before the use of Silvederma cream®.

Silver is a natural mineral widely used topically due to its antimicrobial properties. Silvederma cream® (containing silver sulphadiazine) is a topical antibacterial agent prescribed for the treatment and prevention of infections in second and third degree burns, as well as in chronic ulcers. Reported cutaneous side effects by silver or silver sulphadiazine include hypersensitivity reactions¹, ACD³⁻¹¹, erythema multiforme¹² and cutaneous and systemic argyria.¹³

Despite the widespread use of silver-containing products in wound care, ACD to silver has been described scarcely in the literature. Some cases seem to be related to occupation such as in jewelry^{3,4}, explosive manipulation due to silver fulminate⁵, or the use of silver reinforced footwear, of which the first case was described in 1948.⁶ On the other hand, some cases have been found related to the application of silver sulphadiazine under different trade names such as Silvederma cream®, Silverdin® cream 1% (Deva Lab, Istanbul, Turkey) or Flamazine® cream 1% (Solvay Lab, Benburg, Germany), with different composition of ingredients.⁷⁻⁹ The patient who used Silverdin® developed a subsequent allergic reaction to Chemotechnique® skin markers that contained silver in their composition. We found a case in which a positive “edge effect” at the periphery of the patch test site could be shown but relevant allergic contact dermatitis could not be confirmed by patch testing but if through the clinical dates and the biopsy.¹⁰ We have found three cases of ADC due to silver sulphadiazine, described in an article of Gilissen L. and Goossens A., all of which confirmed by patch test only by silver sulphadiazine but not with silver nitrate.¹¹

There are few published cases of ACD confirmed by patch test with silver nitrate^{2-4,6-9} or silver fulminate⁵. To our knowledge, our case would become the seven one of ACD due to silver sulphadiazine cream^{7-9,11} and it would be the fourth case confirmed by silver patch testing likely due to its presence in silver sulphadiazine.

Some case displayed a concomitant sensitization to colophonium³ or to cetyl alcohol⁹, also a concomitant sensitization to propylene glycol was found in our patient.

To conclude, we believe that it would be advisable to include other contact allergens (such as silver nitrate) as an extension of the study of dermatitis in patients with skin ulcers, since it is not present in some of the commercial series. In this way, a greater number of cases of ACD to silver could probably be diagnosed earlier.

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Figure legend

Fig 1. A) Positive patch test to Silvederma® cream as is D4(++).

B) Positive patch test to silver nitrate 1 % pet D4 (++).

- Amerchol L-101 50% pet
- Fusidic acid sodium salt 2% pet
- Chlorhexidine Digluconate 0.5% aq
- Benzalkonium Chloride 0.1 aq
- Nitrofurazone 1% pet
- Bacitracin 5% pet
- Cetearyl Alcohol 20% pet
- Butyl hydroxy toluene 2% pet
- Chloramphenicol 5% pet
- Benzoyl peroxide 1% pet
- Propylene Glycol 5% pet
- Propolis 10% pet
- Thimerosal 0.1% pet
- Sorbic Acid 2% pet
- Eosin 5% pet
- p-Chloro-m-Cresol 1% pet
- Budesonide 0.01% pet
- Triethanolamine 2% pet
- Framycetin Sulphate 20% pet
- Sorbitan Sesquioleate 20% pet
- Tixocortol-21-pivalate 0.1% pet
- Sorbitan Oleate 5% pet
- Phenyl Mercure Acetate 0.01% aq
- Chloroacetamide 0.2% pet
- Diazolidinyl Urea 2% pet
- Imidazolidinyl urea 2% pet
- Wood tar mix 12% pet
- *Silver Nitrate 1% pet
- *Triamcinolone 0.1% pet
- *Gentamicin Sulfate 20% pet
- *Hydrocortisone-17-butyrate 0.1% pet
- *Betamethasone-17-valerate 1% pet
- *Pindolol 2% pet

Table 1. Leg Ulcers Series (Chemotechnique Diagnosis®) with additional allergens*.

A)

SILVEDONA

D4

B)

PLATA

D4