

# An Unusual Local Reaction after Microsclerotherapy with Chromated Glycerin

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**A case of papular itching lesions after microsclerotherapy with chromated glycerin (CG) at a 72% concentration for telangiectases of the thighs is reported. Patch-test results were strongly positive for nickel sulfate (+++/++) and thimerosal (++) whereas results were negative for the sclerosing agent CG 72% and glycerol (control). Intradermal injection of CG 72% in the thigh and intravascular injection of CG 72% into telangiectases of the knee produced erythematous papular itching lesions in about 5 to 6 hours. As a negative control, glycerol and sodium chloride 0.9% injected intradermically on the thigh did not cause any reaction. CG can elicit allergic reactions in patients who are sensitive to chromium and can cause new sensitizations to chromium. In our case, no positivity to potassium dichromate was observed.**

**S**CLEROTHERAPY consists of the intravenous introduction of a corroding agent into the lumen of a vessel causing thrombosis, endothelial damage (endosclerosis), and subsequent endofibrosis.<sup>1,2</sup> Microsclerotherapy is considered the therapy of choice for telangiectases.<sup>3</sup> Sclerosing agents can be classified in three groups based on their action: (1) detergents (sodium tetradecyl sulfate, polidocanol, ethanolamine oleate, and sodium morrhuate), (2) osmotic solutions (hypertonic saline or glucose), and (3) chemical irritants (chromated glycerin).<sup>4</sup> Chromated glycerin (CG) is not approved by the Food and Drug Administration but is widely used, especially in Europe. Chromium alum is added to glycerin to enhance its sclerosing properties; chromium alum is also a potent coagulating factor.<sup>5</sup>

We report an unusual case of hypersensitivity in a patient after microsclerotherapy with CG.

## Case Report

A 49-year-old woman presented with primary telangiectases and reticular leg veins on her thighs. After informed consent was obtained, microsclerotherapy with CG at a 72% concentration subsequently diluted 3:1 in a 0.9% sodium chloride solution (Scleremo, Laboratoires Bailleul, Paris, France) was administered to her thighs. Three days

after the first treatment with the sclerosing agent, she developed erythematous and edematous pruritic papules at every injection site. The lesions spontaneously disappeared in 1 to 2 days. After 2 weeks, the injections were repeated, and erythematous and edematous itching papules appeared again at the sites of injection after 5 to 6 hours, remaining for approximately 4 days.

Our patient, who was sensitized to *Dermatophagoides* and plants of the family Graminaceae, had a personal history of atopy with allergic rhinitis.

Patch tests with the Società Italiana di Dermatologia Allergologica Professionale ed Ambientale (SIDAPA) standard series yielded allergic reactions to nickel sulfate 5% (+++ at day (D) 2; +++ at D3) and to thimerosal 0.1% (++) at D2; ++ at D3). No positive reaction to potassium dichromate was observed. We also carried out patch tests with the sclerosing agent CG 72% and with glycerol as is; the results were negative at 48 and 72 hours.

As a confirmatory test, an intradermal injection in the left thigh and an intravascular injection into the telangiectases of the medial face of the knee were administered with CG 72% diluted 3:1 in a 0.9% sodium chloride solution. In both cases, the sclerosing agent produced erythematous pruritic papules in 5 to 6 hours (Fig 1). The patient refused further intradermal injections with serial dilutions.

As a negative control, a 0.9% sodium chloride solution and glycerol (diluted in a 0.9% sodium chloride solution at a 70% concentration) were injected intradermically in the right thigh; these solutions caused no reaction.

Because our patient was sensitized to nickel sulfate and we suspected the presence of this allergen in the solution,

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**Figure 1.** Erythematous edematous reaction after intravascular injection of chromated glycerin 72% into telangiectases on the medial face of the patient's knee.

chemical analyses were performed to detect its presence in the Scleremo solution, in the control glycerol (at 70% concentration), and in the needle. Atomic absorption spectroscopy of three standard metal needles used for microsclerotherapy revealed a composition of 6.5% nickel, 17.7% chromium, and 0.9% manganese.

Graphite furnace atomic absorption spectroscopy revealed nickel sulfate at a quantity of 1.10  $\mu\text{g/L}$  ( $\approx 0.0011$  ppm) in the Scleremo solution (as is). The amount of nickel sulfate in the control solutions was also measured. The quantity of nickel was 1.0  $\mu\text{g/L}$  ( $\approx 0.0010$  ppm) in glycerol 70%; in the 0.9% sodium chloride solution, the quantity of nickel was under the limit of detection of the atomic spectrophotometer. (The limit of detection of the atomic spectrophotometer was 0.05  $\mu\text{g/L}$  [ $\approx 0.00005$  ppm]).

After two passages through the needle (aspiration and ejection) and after six passages (to better simulate the prolonged contact of Scleremo solution with the needle during microsclerotherapy), the quantities of nickel in the Scleremo solution were respectively 1.25  $\mu\text{g/L}$  ( $\approx 0.00125$  ppm) and 3.22  $\mu\text{g/L}$  ( $\approx 0.00322$  ppm). After two and six passages through the needle, the values of nickel detected in glycerol 70% were 1.04  $\mu\text{g/L}$  ( $\approx 0.00104$  ppm) and 1.27  $\mu\text{g/L}$  ( $\approx 0.00127$  ppm). The higher percentage (3.22  $\mu\text{g/L}$ ) detected in Scleremo solution after six passages may be explained by possible corrosive reactions or ionic exchanges due to the presence of chromium alum in the Scleremo solution.

To detect thimerosal in the Scleremo solution, analysis was performed by means of both thin-layer

chromatography and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry; both analyses ruled out the presence of thimerosal.

## Discussion

CG, considered a weak sclerosing agent, is used at a concentration of 25 to 100%.<sup>4</sup>

Ecchymosis and pigmentary changes due to extravasation of red blood cells through damaged vessels and hemosiderin deposition are common complications of microsclerotherapy.<sup>3</sup> Local pain, itching, and mild erythematous and edematous reactions (localized urticaria) at the sites of injection are commonly observed local effects occurring after microsclerotherapy with any sclerosing agent but especially microsclerotherapy with polidocanol and sodium tetradecyl sulfate.

Contact urticaria lasting a few hours may be explained by the release of histamine, endothelial, or platelet-derived factors and other inflammatory mediators that increase endothelial permeability.<sup>4</sup>

Allergic reaction to the chromic component of CG has been reported. Chromium is a common sensitizer. Some authors have reported that CG can induce allergic reactions in patients who are sensitive to chromium and that it can also induce new sensitizations to chromium in other patients.<sup>4,6,7</sup>

In our case, patch-test sensitivity to chromium was not observed whereas strong reactions to nickel sulfate and thimerosal were noted. The delayed onset of the local reactions, the progressive reduction of the latency period, and the persistence of the lesions suggest a delayed-type reaction.

Chemical analysis ruled out the presence of thimerosal and detected a very low quantity of nickel in the solution. Even after numerous passages of the solution through the needle (two and six passages), small amounts of nickel were found but at lower than the least concentration that can elicit a positive allergic reaction.

A wide variety of threshold values for reactivity to nickel in sensitized individuals are reported in the literature. The minimal eliciting concentration (MEC) of aqueous nickel sulfate that can produce an allergic reaction by patch testing on normal back skin in highly sensitized subjects is 1 to 10 ppm whereas the minimum level in nickel-sensitive subjects with irritated or inflamed skin is 0.5 ppm.<sup>8,9</sup> We found no data in the literature on the MEC of aqueous nickel sulfate when intradermally injected.

Allergic contact dermatitis due to nickel released by needles of infusion pumps, acupuncture needles, and electromyography has been reported.<sup>10,11</sup> In these cases, the permanence of the devices or the electric flow have been considered favoring factors for nickel release and for the development of local delayed reaction.

In our case, three hypotheses can be formulated, as follows:

1. The sclerosing solution, nickel enriched by the needle (even though in a total small amount), may be responsible for the dermatitis. In fact, microsclerotherapy leads to a deep intradermal penetration of nickel; furthermore, the therapeutic sclerosing effect could contribute to the persistence of the allergen in the dermis.
2. The patient, who had a negative reaction to the chromium patch test, could be sensitized to chromium to a very high threshold of sensitization. The high concentration of this element in the intradermically injected Scleremo solution could cause allergic lesions.
3. Although the clinical course of dermatitis supported a delayed-type reaction, a local nonallergic inflammatory reaction developed. Unfortunately, the patient would not consent to a biopsy.

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