

losartan and treatment with oral prednisolone 50 mg/day, the angioedema cleared within 3 days. The symptoms of the transient ischemic attack cleared within 1 day, leaving only a residual minimal mimic paresis of the facial nerve (slight hanging of the right mouth angle) for about a week. As antihypertensive treatment, a calcium antagonist was given instead of losartan. No relapse of the angioedema had occurred within 4 months of follow-up. Because of the risk, no attempt of re-exposure to losartan was made.

There was no hint of an atopic disposition. No nonsteroidal antiphlogistic drugs had been taken. C1-esterase inhibitor (amount and function), C3, and C4 were normal. As no other cause could be identified, losartan was probably the cause of the angioedema.

Angioedema has been found to be due both to conventional angiotensin-converting enzyme inhibitors (1) and, in some cases, to angiotensin II receptor antagonists (2, 3). Recently, increased plasma bradykinin concentrations have been measured during episodes of angioedema caused by an angiotensin-converting enzyme inhibitor, supporting the hypothesis that the well-known interference with the bradykinin system is part of the underlying pathogenetic mechanism in these adverse drug reactions (4). However, angiotensin II receptor antagonists do not interfere with the kallikrein-kinin system (5); therefore, these findings cannot be applied to losartan. Until now, the pathogenetic mechanism of angioedema due to losartan has remained unclear.

Cerebral manifestations and transient ischemic attacks have been reported in association with angioedema of unknown cause (6) or angioedema caused by C1-esterase inhibitor deficiency (7). To our knowledge, this case is the first described case of angioedema due to an angiotensin II receptor antagonist associated with a transient ischemic attack.

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Allergic contact dermatitis to propylene glycol

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Key words: allergic contact dermatitis; electrode gel; irritation; patch tests; propylene glycol; ultrasonic gel.

● PROPYLENE glycol (PG) (propane-1,2-diol) is widely used in pharmaceutical manufacturing as a solvent and vehicle, especially for drugs unstable or insoluble in water. It may also be employed as a preservative, and is extensively used in foods and cosmetics (1). PG may cause contact dermatitis and local irritation of the skin and mucous membranes. We report a case of allergic contact dermatitis due to PG included in contact gels.

A 66-year-old man was referred to our department because of an eczematous eruption at the sites where a gel used for echocardiography had been applied (Geleco[®], Lab. Carreras, Barcelona, Spain). The eruption

appeared 3-4 h after application, peaked after 48 h, and resolved in a period of 7-9 days without treatment. The patient had suffered similar reactions previously (4-5 times) related to the application of gels for ECG, abdominal echography, or cardioversion. He had a history of atopic eczema as a child and occasional eczema related to cosmetics and adhesive tape.

The patient was patch tested with the European standard series, the gel (as is), and its preservatives 2 months after the last reaction.

According to the information provided by the manufacturer, the concentration of PG in the gel was 20%, so we tested with serial dilutions in water from 2% to 20%. Patch tests were performed on the back with Leukotest[®] (Beiersdorf AG, Hamburg, Germany) covered by Mefix[®] (Mölnlycke AB, Sweden). Readings

Contact dermatitis to propylene glycol in contact gels confirmed by a combination of test methods.

Table 1. Patch test results

		48 h	96 h
Standard series			
Wool alcohols		+++	+++
Fragrance mix		+++	+++
Colophony		+	++
Balsam of Peru		++	++
Black rubber		+++	+++
mix			
Geleco [®] (as is)		+++	+++
Preservatives of Geleco			
Nypagin A ^{®1}	3% pet	-	-
Nypasol M ^{®2}	3% pet	-	-
Propylene glycol	2% aq.	+++	+++
	5% aq.	+++	+++
	10% aq.	+++	+++
	20% aq.	+++	+++

¹ethyl-p-hydroxybenzoate. Concentration and vehicle recommended by ICDRG.

²propyl-p-hydroxybenzoate. Concentration and vehicle recommended by ICDRG.

were made at 48 and 96 h according to the ICDRG (International Contact Dermatitis Research Group) guidelines. The results are shown in Table 1. The positive reactions to wool alcohols, fragrance mix, colophony, and balsam of Peru had past relevance, but the positive reaction to black rubber mix did not. Six weeks later, we retested the patient with PG (0.5%, 1% and 2% aq.) showing positive results at D2 with PG 1% and 2% aq. We also performed a ROAT (repeated open application test) with PG 2% aq. (two applications per day) in the antecubital fossa. After 2 days, an eczematous reaction appeared on the treated area.

Funk & Maibach classify skin reactions to PG into four mechanisms: irritant contact dermatitis, allergic contact dermatitis, nonimmunologic contact urticaria, and subjective or sensory irritation (2). The distinction between irritant and allergic reactions associated with PG application remains unclear. Furthermore, the irritation threshold of PG and the optimal standard concentration in patch tests are not well established. Usually a PG concentration of 1–10% aq. is recommended for patch tests in order to avoid irritation (2, 3). However, some authors recommend raising the standard PG concentration in patch tests to 20% and in doubtful cases even higher (50%) (4, 5). True allergic sensitization to PG should be confirmed by repeated patch testing, serial dilutions, usage tests/ROAT, or oral challenge tests (in certain cases). Data on the incidence of allergic sensitization to PG are problematic, as different groups of subjects have been tested with varying PG concentrations (ranging between 100% and 2% aq.), and inconsistent criteria for the interpretation of positive results have been used; furthermore, additional tests have been rarely applied. Irritative reactions have been seen in up to 40% of subjects, and allergic reactions in up to 4.1% of subjects (2, 3). Some authors think that true allergic contact reactions to PG are uncommon and that the clinical significance has probably been overestimated (2). In contrast, other recommend the addition of PG to the current

standard patch tests in view of the increasing number of preparations containing PG (3).

In relation to contact dermatitis associated with PG included in contact gels, we have found only two reports in the literature (5, 6). Ayadi et al. observed a similar case with a carotidian Doppler gel and demonstrated a positive patch test with PG 2.5% aq. (6). In contrast, Uter & Schwanitz could not demonstrate positive patch tests to PG 1%, 5%, and 10% aq.; the sensitization was proved by patch tests and ROAT with PG 20% aq. (5). In our patient, a concentration of 1% aq. has been suitable for the diagnosis, and additional tests have confirmed the diagnosis.

In summary:

- 1) one must be aware that formulations for contact gels can include PG
- 2) our results confirm allergic contact dermatitis to PG
- 3) in some cases, only a combination of test methods can provide reliable data to allow objective interpretation of PG patch tests.

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Phenytoin hypersensitivity syndrome with fatal evolution

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Key words: anticonvulsant; hepatic; involvement; hypersensitivity syndrome; phenytoin

● PHENYTOIN (DFH) is an anticonvulsant in common use. In allergic reactions to phenytoin, only very rarely has the multisystemic syndrome called hypersensitivity syndrome to phenytoin been described. This syndrome of low incidence usually appears between weeks 2 and 5 of treatment with phenytoin. Among its more common signs are desquamative skin rash, fever, lymphadenopathies, and eosinophilia. Less frequently, hepatic alterations and aplastic marrow appear.

We present a patient with hypersensitivity syndrome to phenytoin who developed hepatic failure with fatal evolution. We would like to pay special attention to this case and review the subject.

Phenytoin hypersensitivity often includes pyrexia, eosinophilia, skin reactions, and lymphadenopathies, while liver involvement is serious but rare.

A 62-year-old woman was the patient. Ten years before, she had had a depressive syndrome and had attempted suicide. She was not receiving any medical treatment. She went into the intensive care unit with a cranioencephalic traumatism in the parietal tract with loss of encephalic mass, secondary to attempted suicide with an axe.

She was operated on urgently by neurosurgeons, who carried out esquilectomy and suture. In the immediate, postoperative period, we began to administer a dose of phenytoin 100 mg/8 h IV (5 mg/kg per 24 h) to prevent epileptic crisis. The development was favorable, and during the following days, the phenytoin was given