

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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● 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

orally (100 mg/8 h), and she began to receive a tricyclic antidepressant.

In week 4 of the treatment with phenytoin, the patient developed in 24–48 h fever of 39°C combined with generalized erythematous skin rash. The other systemic and neurologic probes were normal. The blood cell count showed leukocytosis with eosinophilia (16 500 leukocytes/mm, 12% eosinophils), and the coagulation study, biochemical and hepatic profile, hemocultures, coprocultures, and urocultures then done, as well as the chest radiography, were normal. Computed tomography of the skull described the continuity to a parietal level without any other important alteration. With the clinical suspicion that there was an adverse reaction to medication, the phenytoin and the tricyclic antidepressant were stopped. During the following week, the patient continued to show fever and eosinophilia, and the skin rash became desquamative. The clinical situation worsened gradually and between days 8 and 10 after stopping the phenytoin, she showed acute hepatic failure with high cytolysis and cholestasis (glucose 57 mg/dl, SGOT 1535 U/l, SGPT 497 U/l, gamma GT 1055 U/l, alkaline phosphatase 662 U/l, cholesterol 110 mg/dl, total bilirubin 17.5 mg/dl, LDH 2862 U/l, albumin 1.7 g/dl), linked to severe coagulopathy (prothrombin Ac. 21%, APTT 53/29).

The analysis then done did not reveal any indication of a possible cause, and the abdominal echography showed only a spleen slightly increased in size. In the following days, the patient developed acute renal failure and pancytopenia with severe neutropenia (2400 leukocytes/mm with 190 neutrophils, 10 000 blood platelets/mm, hemoglobin 8.9 g/dl).

The patient died 15 days after stopping the phenytoin. The autopsy showed submassive hepatic necrosis linked to splenomegaly, and moderate inflammatory infiltrated vascular congestion of the skin. The anatomopathologic diagnosis was phenytoin hypersensitivity syndrome.

Phenytoin is an anticonvulsant affecting hepatic metabolism. Among its more frequent side-effects are gastric intolerance, skin rash, and gingival hyperplasia. Less frequently, cases of hypersensitivity syndrome to DFH have been described.

This syndrome with anticonvulsants was first described in 1950 by Chaiken et al. (1); they called it dilantin hypersensitivity syndrome. Later, cases involving carbamacepine, primidone, and phenobarbital were described.

The hypersensitivity syndrome to phenytoin is of low incidence (1/1000–10 000 treated with DFH), and it usually appears between weeks 1 and 4 of treatment. Risk factors have not been clearly identified when they appeared and their origin is not dose dependent.

Skin signs were the most common in the syndrome in the study by Silverman (2).

Fever, lymphadenopathies, and megalies are common, as well as leukocytosis and eosinophilia. Aplastic marrow and hepatic affection are less common. Those rare signs appear late during the development of the syndrome, and most of the patients who develop them have previous skin alterations. The pathogenic mechanism of this syndrome has not been established. Most of the facts suggest a hypersensitivity phenomenon, although idiosyncratic and toxic mechanisms with enzymatic induction of Cp 450 and the production of intermediary metabolites have also been involved. These metabolites are potentially cytotoxic, and they can alter the lymphocytic function, increasing the hepatocellular necrosis and lymphadenopathies, as described by Haword et al. (3). The diagnosis of this syndrome is clinical and analytic. Studies of lymphocytic stimulation and the patch test can indicate the therapeutic option of withdrawal of DFH, although the patient's condition can alter.

This emphasizes the danger of a premature diagnosis. Steroids are usually used during the treatment, although their indexing is not well established and does not alter the mortality rate. However, they are effective in

the skin symptoms and can shorten their course. Excessive medication taken with DFH can worsen the prognosis. Dreifuss et al. (4) have shown cross-reactivity with other anticonvulsants and interaction with antidepressants.

The mortality rate in this syndrome rises to 30–40% if hepatic damage occurs. Mullick (5), in a clinical pathologic study, has reported 20 cases of hepatic injury associated with diphenylhydantoin; the mortality rate without hepatic affection was 10%. Our patient showed hypersensitivity syndrome to DFH after 4 weeks of treatment. She developed fever, desquamative erythema, and eosinophilia linked to aplastic marrow and severe hepatic failure, which caused her death.

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Pattern of food-induced anaphylaxis in children of an Asian community

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Key words: anaphylaxis; children; food allergy.