LETTERS TO THE EDITOR

Photoaggravated Eczema Due to Promethazine Cream

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To the Editor:

Promethazine, a member of the phenothiazine group, is the active ingredient of Phenergan cream, a topical antihistamine.

We describe the case of a 24-year-old man with no relevant history who developed pruriginous lesions in the antecubital crease of the left forearm. Following application of emollients (Nivea cream, Lactovit body milk, and Johnson oil), lesions also appeared on the contralateral forearm. One week later, the patient used Phenergan cream and the lesions then spread to both arms. After 5 days, he discontinued the product and resumed treatment with emollients, with new lesions appearing on the face, abdomen, and legs. After starting treatment with topical corticosteroids (diflucortolone valerate) and oral corticosteroids (prednisone) at a dose of 0.5 mg/kg, the lesions disappeared within 10 days.

Because photosensitive eczema due to Phenergan cream was suspected, patch tests were performed using the standard series of the Spanish Research Group for Contact Dermatitis and Skin Allergies (Grupo Español de Investigación en Dermatitis de Contacto y Alergia Cutánea) and photopatch tests were done using the photoallergens of the Spanish Photobiology Group (Grupo Español de Fotobiología) and the products used by the patient (Figure 1). The standard allergen series was from the True Test (Alk Abelló, Hillerod, Denmark), supplemented with others from Chemotechnique (Malmo, Sweden). The photoallergen series was from Martí Tor (Barcelona, Spain). The photopatch test was done twice on the back and read at 48 and 96 hours, with 1 of the 2 series irradiated with UV-A at 10 J/cm². Positive results were obtained to Phenergan cream and promethazine at 96 hours on the irradiated area, but only to Phenergan cream in the nonirradiated area (Figure 2). Positive results were also obtained with wool alcohols, gum rosin, quaternium 15, and formaldehyde in the standard series at 96 hours. The result obtained with Phenergan cream and promethazine in the photopatch was relevant in this case, as were the wool alcohols, because these were also excipients in Phenergan cream and Nivea cream. We found no relevance for gum rosin, quaternium 15, or formaldehyde. The diagnosis was photosensitive eczema due to promethazine and allergic contact eczema caused by the excipient ingredients of Phenergan cream.

Previously, the topical use of antihistamines was extremely common. This is the apparent cause of many cases of sensitization to these products. Sidi et al⁵ and Suurmond² found 68 cases of positive reactions to Phenergan cream in patch tests. Only 17 of these reacted to promethazine. However, these studies are old, the methodology is unclear, and we have no information about the relevance.

At present, not many cases of allergic contact eczema due to promethazine are found. Between 1980 and 1987, de la Cuadra Oyanguren et al³ performed patch tests in 95 patients, obtaining 1 positive case for promethazine.

In a study done in Belgium by Goossens et al⁴ in 1998, 14 cases were positive for promethazine among 12 460 patch tests carried out.

There is little information in the literature on the development of photosensitive eczema because of this topical antihistamine. Articles from the 1950s and 1960s mentioned that promethazine was capable of photosensitization, with eczematous lesions in areas exposed to light; however, the studies were not rigorous and no photopatch tests were done. In Scandinavia, a multicenter study was conducted between 1980 and 1981, collecting the results from 745 photopatch tests.⁵ Of these, 24 were positive for promethazine, most of them due to phototoxicity. In the study by Goossens et al,⁴ in 2 of the 14 patients with a positive reaction to promethazine photosensitization to this drug was also observed. The Spanish Photobiology Group recently published the results of photopatch tests at 7 Spanish hospitals.
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In addition to photosensitization to promethazine, our patient developed allergic contact eczema to wool alcohols, an excipient ingredient in Phenergan cream. We found only 1 article on sensitization to an excipient of Phenergan cream, specifically to triethanolamine.7 Among 22 patients with positive patch test results for Phenergan cream, 4 reacted to triethanolamine. However, we found no cases of photosensitive eczema due to an excipient of Phenergan cream reported in the literature.

In summary, in terms of delayed reactions to Phenergan cream, cases of photosensitive eczema due to promethazine considered to have current relevance are uncommon, and no cases have been found in which this diagnosis was associated with allergic contact eczema caused by the excipient ingredients of Phenergan cream.

References

Unilateral Contact Dermatitis Caused by Footwear

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To the Editor:
Contact dermatitis caused by footwear is usually bilateral. It generally starts on the dorsum of the fifth toe and gradually extends to the dorsum of the foot, sparing the interdigital folds. Potassium dichromate is the most frequent allergen. We report the case of a patient diagnosed with dermatitis caused by contact with shoe dye on 1 foot who was initially wrongly diagnosed with dermatitis artefacta.

The patient was a 64-year-old woman who consulted with an outbreak of blisters that had begun 1 month earlier and that was evenly distributed along the lateral aspects of her right foot (Figure 1). Examination revealed 2 flaccid blisters on the side of the foot resting on an erythematous base and a linear erythema on the dorsum of the foot. Residual lesions were also present. The other foot was not affected and the rest of the skin was spared. A first possible diagnosis was thought to be contact eczema, although it was strange that this did not affect both feet. The patient was taking cinitapride, domperidone, and diazepam; her basic medication was suspended but the blisters remained. Dermatitis artefacta was also considered in the differential diagnosis. The patient had been receiving psychiatric treatment for anxiety-depression syndrome for many years. We insisted that it was strange that the lesions only affected the right foot and, during the following visit, she presented with erythema and vesiculation on the left foot that had begun a few hours earlier, and with distant lesions on her chest; furthermore, the right foot was now free of lesions for the first time. A biopsy was performed and histopathology revealed characteristics typical of acute eczema.

The patient eventually noticed that the lesions were related to the use of shoes that had been dyed 2 months previously. The dye had stained the internal sides of the right shoe (Figure 2), exactly where the blisters had

![Figure 1. Blisters on the lateral aspects of the right foot with linear erythema on the dorsum of the foot. Residual lesions were also observed. No lesions were apparent on the other foot.](image-url)

"Letters to the Editor"
Two Cases of Hypertrichosis Cubiti

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To the editor:
Hypertrichosis cubiti, also known as hairy elbows syndrome, is an uncommon form of localized congenital hypertrichosis in which an excessive amount of long, fine, lanugo-type hair is found on skin of normal texture and morphology. The hair growth follows a bilateral symmetrical distribution and affects the extensor surface of the distal third of the upper arms and the proximal region of the forearms. The condition usually appears

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in early infancy (1-3 years). With time, the hair becomes thicker, reaching maximum thickness at age 5. It usually regresses in adolescence, but in some cases persists throughout life. The syndrome may present in sporadic or familial forms and its mode of inheritance is unclear. It is associated with short stature in about 50% of patients; such patients may present other malformations, the most common of which is facial asymmetry.

Two girls, aged 6 and 10 years, with the sporadic form of the syndrome were recently referred to our department by the pediatrics department. The girls were unrelated and had no relevant personal or family history. Both had suffered from the condition since the age of 2-3 years. A large amount of fine long hair was observed in both patients, dark in 1 case (Figure 1) and blond in the other (Figure 2). The hair was distributed over the distal region of the upper arms and the proximal region of the forearms. There was no excessive hair growth in any other area. The patients’ height, weight, and intellectual development were normal. Blood tests (complete blood count; biochemical analysis; liver profile; thyroid function profile; and plasma cortisol, testosterone, and dehydroepiandrosterone sulfate levels) showed no abnormalities. The patients were advised to lighten or shave the area until the condition subsided in adolescence.

Hypertrichosis cubiti was first described by Beighton in 1970 in twin brothers belonging to an Amish family. Of the few cases reported, approximately 50% have been associated with short stature or with intrauterine growth retardation. It is in such children that other abnormalities such as facial dysmorphism, abnormalities of the extremities, delays in language development, attention deficit, mental retardation, and mobility difficulties may be found. Our 2 patients presented none of these abnormalities, and the syndrome was considered a purely esthetic problem. As was observed in our patients, additional tests do not provide information of interest, and consequently, exhaustive studies are unnecessary.

Skin biopsy has been performed on only 2 occasions, together with a trichogram in 1 case. The trichogram showed 90% of the hair follicles to be in anagen, 9% in telogen, and 1% in catagen. This would explain the greater length of the hair, as occurs in the scalp. Some authors suggest that the syndrome may be explained by mosaicism, based on the distribution of excess hair, which is confined to very localized areas and resembles that of cutaneous lesions with mosaicism; others consider it a nevoid condition of the hair follicles.

Hypertrichosis cubiti may therefore be part of a complex syndrome with varying manifestations. It is probably more common than it would appear from dermatology practice, but in cases with no associated malformations the only reason for consultation is its psychological and esthetic repercussions at a certain age. When associated with other abnormalities, these are usually identified first. In our opinion, if the condition is observed at a young age, the patient should be followed by a pediatrician, who can monitor growth and check for possible associated malformations; at later ages, as in our patients, it is advisable to reassure parents with respect to the course of the condition.

References


Management of a Patient With Calciphylaxis and Requiring Anticoagulant Therapy

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To the Editor:
The different disorders associated with calciphylaxis include the possible relationship with oral anticoagulants, nadroparin calcium, and hypercoagulable states linked to lower concentrations of proteins S or C. The disorder most commonly associated with calciphylaxis, however, is chronic renal failure, with between 1% and 4% of these patients suffering from calciphylaxis. Calciphylaxis has also been observed in association with neoplasia, hyperthyroidism, proteinuria, rheumatoid arthritis, and alcoholic cirrhosis.

The pathogenesis remains obscure, although abnormal calcium and phosphorus metabolism (elevated calcium-phosphate product and high phosphorus metabolism) are observed and may lead to vascular and extravascular calcification.

The foregoing leads us to ask several questions: what attitude should be adopted in the case of a patient with calciphylaxis who requires anticoagulation therapy? What are the available antithrombotic alternatives? Which is the most recommendable option?

We present the case of a 58-year-old man with calciphylaxis who was receiving anticoagulant treatment with acenocoumarol due to ischemic heart disease that had been treated with a double coronary artery bypass graft and who had severe pulmonary hypertension, tricuspid insufficiency, and right ventricular dilation and hypokinesis. The patient visited the dermatology outpatient clinic with painful skin lesions on the legs that had appeared 10 days previously. The lesions were between 3 and 4 cm in diameter with a necrotic base and erythematous borders, and the patient was undergoing hemodialysis due to chronic renal failure. The patient presented secondary hyperthyroidism with high levels of aluminium (as a phosphorous chelating agent) but normal levels of calcium, phosphorous, and alkaline phosphates, along with anemia, high blood pressure, and dyslipidemia. The diagnosis of calciphylaxis was confirmed following a pathological study of the lesion biopsy.

In patients diagnosed with calciphylaxis, it is reasonable for both oral anticoagulant therapy and therapy with both unfractionated heparin and low-molecular-weight heparin calcium (nadroparin calcium) to be omitted as they may give rise to calcium deposits. The following are proposed as recommendable alternative anticoagulant therapies: fondaparinux sodium and low-molecular-weight heparin sodium (preferably tinzaparin in patients who also present renal failure), with the clear aim of avoiding exacerbation of the calciphylaxis and the instability inherent in oral anticoagulant therapy in patients with a poor clinical prognosis.

References


Melanotic Macules of the Penis
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To the Editor:
After reading the article by Laguna et al., published in this journal, we wished to contribute a new example, and to propose a series of considerations for improved management of these patients.

We present the case of a 29-year-old patient, with no relevant personal history, who consulted for multifocal pigmented macules of varying coloration on the penis; these were symptom free and had been present since the patient was 14 years old. The patient described the ongoing appearance of pigmented lesions with varying dark coloration (Figure 1). Histology revealed hyperpigmentation of the basal layer, with no increase in the number of melanocytes or the frequency of atypical cells (Figure 2).

Melanotic macules on the penis—wrongly termed lentigines—are idiopathic and benign lesions, occasionally multifocal, of varying color, and irregular, which require differential diagnosis from mucosal melanoma.1 Unlike melanoma, melanotic macules tend to appear in adulthood, not amongst the elderly, and they tend to remain stable for decades.

Histology confirms that the macules are benign. They are characterized by acanthosis with no elongation of the papillary ridges, hyperpigmentation of the basal layer with no increase in the number of melanocytes (hence they should not be termed lentigines), pigmentary incontinence, and the occasional presence of melanophages, all this with an absence of atypical melanocytes.2 When the lesions are irregular with varied coloration, or the patient reports changes or an increase in number of the same, ideally the entire macule would be surgically removed for a complete histological examination. In multifocal lesions, which are those that tend to necessitate differential diagnosis with melanoma, complete excision of the lesion is not usually feasible, and consequently several biopsies should be performed, choosing the sites carefully, in order to confirm if the case is benign. Dermatoscopy may be a useful tool to identify the most suitable biopsy site.3

In spite of the fact that melanotic macules are not considered precursors of melanoma, a small number of publications describe the possibility of their becoming malignant.4,5 Kahn et al4 reported the case of a pigmented lesion on the palate that developed into mucosal melanoma. However, a significant clinical abnormality was observed in the initial lesion, and histology revealed melanocytic hyperplasia, and it can therefore be assumed that this was not a true melanotic macule. Taylor et al5 do appear to have documented the development of a melanotic macule into an invasive melanoma. In this case, in the first biopsy—which included the entire lesion—increased pigmentation only occurred in the basal layer with neither hyperplasia nor atypical melanocytes, yet in biopsies performed 5 years later, nests of malignant melanocytes could be seen migrating through the mucosa.

Figure 1. Multifocal macules of varying coloration.

Figure 2. Hyperpigmentation of the basal layer, with no increase in number or atypical features of melanocytes (Hematoxylin-eosin, ×40).
While no definitive decision can be made on the potential for malignancy, we believe periodic follow-up is advisable. In most cases, given the stability of the lesions, further biopsies would not be necessary, although these would be proposed in cases presenting suspicious clinical changes. Once again, dermatoscopy, and monitoring with digital dermatoscopy, can be used to detect early changes and to choose the timing and location of the biopsy.3

References