



Berloque dermatitis

Berloque dermatitis obtains its name from the German word *berlock* or the French *berloque*, meaning trinket or charm. Rosenthal

¹

coined the term in 1925 to describe pendantlike streaks of pigmentation on the neck, face, arms, or trunk. He suspected they were due to fluid droplets, unaware that Freund

²

in 1916 had described hyperpigmented macules due to sun exposure after the application of eau de cologne. The phototoxic ingredient causing the pigmentation proved to be bergapten, a component of oil of bergamot, derived from the rind of

Citrus bergamia

, the bergamot lime. Several cases were reported in the 1950s and 1960s following increased use of perfumes containing oil of bergamot and the passion for sunbathing. Since the introduction of artificial oil of bergamot and the reduced use of the natural product in perfumes, berloque dermatitis has become rare. Note the image below.

Pathophysiology

Phototoxicity or photoirritation is a chemically induced nonimmunologic acute skin irritation requiring light (usually within the UVA spectrum, ie, 320-400 nm). The skin response resembles exaggerated sunburn and does not require prior sensitization; it can be caused by a single simultaneous exposure to the chemical and light source. The photoactive chemical may enter the skin via topical administration, or via ingestion, inhalation, or parenteral administration. The reaction can be evoked in all subjects as long as the concentration of the chemical and the dose of light are sufficient.

In the case of berloque dermatitis, the phototoxic reaction is induced by the effect of long-wave ultraviolet (UVA) radiation on bergapten, or 5-methoxypsoralens, a furocoumarin now known to be the only photoactive component of bergamot oil (see the image below). The bergapten-UVA radiation combination induces an intensification of melanogenesis and a corresponding increase in the number of functional melanocytes, which are more dendritic and dopa-positive. The distribution of melanosomes in keratinocyte changes from the aggregate to nonaggregate form

History

The clinical presentation of berloque dermatitis may be classically divided into 2 phases. The initial acute inflammatory phase consists of erythema, edema, pain, pruritus, and increase in skin temperature around the area of contact with the phototoxic agent. The second stage is hyperpigmentation of the lesion. Patients usually present with small areas of redness or pigmentation of the skin, usually on sun-exposed areas, such as the neck. Pain and, sometimes, pruritus may be felt during the acute erythematous phase before the lesions become hyperpigmented. However, hyperpigmentation is the chief complaint; sometimes patients may not even recall the inflammatory phase. A careful history may reveal use of a perfume or fragrance-containing product on the skin prior to a period of sun exposure, such as sunbathing or a picnic. If untreated, the natural history of the disease also is biphasic; the inflammatory lesions resolve in days to weeks, but the pigmentation may last months or even years.

Physical

Erythema, edema, vesiculation, hyperpigmentation, and desquamation are typical phototoxic skin effects. In classic berloque dermatitis, brown hyperpigmentation with or without preceding erythema is seen in a droplike or pendantlike configuration. It usually is distributed over the sides of the neck in adult females, although it may be seen in any part of the body where perfume was applied followed by sun-exposure.

Some less typical presentations of berloque dermatitis are, for example, symmetrical facial pigmentation on a man, caused by aftershave lotion containing bergapten, and an infant who developed pigmentation on her body and arms where her mother applied eau de toilette prior to taking her to the beach.

Causes

Bergapten, or 5-methoxypsoralen, is the photoactive component of bergamot oil from the bergamot lime (*C bergamia*), which is a popular ingredient in perfumes and fragrances. Apart from their obvious existence in cosmetics and toiletries (such as toilet water, aftershave lotions, colognes, sunscreen lotions, moisturizers), perfumes also are found in soap, household cleaners, detergents, air fresheners, and a myriad of other everyday items.

Besides the bergamot lime, bergapten is a naturally occurring component of various other fruits and plants (see the image below). Examples of these are figs (*Ficus carica*), celery (*Apium graveolens*), lemon oil, Tromso palm (*H laciniatum*), Queen Anne's lace (*Ammi majus*), and giant Russian hogweed (*H mantegazzianum*). All these are capable of inducing bergapten phototoxicity, although they are not perfume-related and, therefore, classified as phytophotodermatitis rather than berloque dermatitis

Laboratory Studies

Phototoxicity testing is not carried out diagnostically, but rather for predictive purposes. It routinely is included in the safety evaluation of raw materials by the Research Institute for Fragrance Materials and several methods for identifying phototoxic compounds have been reported. Both in vitro and in vivo methods are used currently. Generally, for in vivo testing, measured amounts of fragrance material are tested, either in laboratory animals (eg, mouse, rabbit, guinea pig models),⁶ or ultimately in humans, with an artificial light source. This identifies potential phototoxic substances before they are marketed.

In an attempt to decrease animal use in predictive dermatology, the European Union, in cooperation with the European Centre for the Validation of Alternative Methods (ECVAM) and the Interagency Coordinating Committee for the Validation of Alternative Methods (ICVAM), has supported the development of in vitro alternatives.^{7,8,9,10} Initial trials revealed reasonable sensitivity and specificity^{11,12,13,14}; false-positive results and false-negative results have already been documented.^{15,16,17}

Thus far, several cosmetic products have been examined in vitro for phototoxicity.

Other Tests

Clinical identification of phototoxicity largely resides in morphology and a high index of clinical suspicion. Photopatch testing may be performed if photoallergy is strongly suspected. This consists of occlusive application of the test chemical(s) to the back, followed by irradiation with an UV light source. The results are evaluated at several time intervals, according to an established score based on the skin reaction pattern. Adequate controls are imperative to differentiate phototoxicity from photoallergy. In phototoxicity, all controls will have a positive response, whereas in photoallergy, controls should be negative.

Histologic Findings

The histopathological findings in berloque dermatitis are identical to other phototoxic reactions, an irritant cutaneous response. The epidermal changes consist of keratinocyte necrosis, intercellular and intracellular edema, and intraepidermal blisters. In severe cases, these blisters may rupture, resulting in subepidermal bullae. Neutrophils enter the epidermis at an early stage. In contrast to the extensive epidermal damage, only a mild perivascular infiltrate is present. Changes associated with berloque pigmentation are an increased number and size of melanosomes, melanocyte hypertrophy with increased arborization of dendrites, increased transfer of melanosomes to keratinocytes, and increased tyrosinase activity within the proliferating melanocytes.

Medical Care

The primary aim of the therapeutic regime is discontinuation of the offending substance. If berloque dermatitis is the putative diagnosis, all bergamot oil-containing perfumes should be avoided. Any perfumes that are worn should be worn on covered-up areas, not on areas of sun exposure.

If the patient presents in the acute phase and is in considerable discomfort, wet compresses may be helpful in relieving the discomfort. Simple analgesia may be given if the patient is in pain.

For secondary hyperpigmentation, the natural course of the dermatitis is spontaneous resolution

after several months, but some lesions may persist much longer. The most important step is to minimize exposure to the sun. This may be done by avoiding strong sunlight whenever possible, avoiding the use of sunbeds and using a strong sunscreen (SPF 30 or higher) with activity in both the UVA and UVB spectra. Camouflage also may be used on exposed hyperpigmented areas, for cosmetic reasons. Dermablend and Covermark are preparations combining a water-resistant opaque base with a broad-spectrum sunscreen.

If the pigmentation is persistent, hydroquinone constitutes the mainstay of medical therapy. It usually is given twice a day, at a concentration of about 2%, for several months. At higher concentrations, the patient would be at risk of irritation. Hydroquinone sometimes is administered in conjunction with topical tretinoin (Retin-A). Kligman and Willis¹⁹ devised a concoction known as Kligman's formula, consisting of hydroquinone, tretinoin, dexamethasone, ethanol, and propylene glycol, which they found effective in treating hyperpigmentation.

Medication

Medical therapy is largely unnecessary for the treatment of berloque dermatitis, except in cases with persistent hyperpigmentation. In these cases, skin-bleaching agents (eg, hydroquinone) are the mainstays of therapy.

Depigmenting agents

Skin bleaching agents are indicated for the gradual depigmentation of hyperpigmented skin conditions.

Hydroquinone (Claripel cream with sunscreens)

Produces reversible depigmentation of skin by inhibiting enzymatic oxidation of tyrosine to 3-(3,4-dihydroxyphenyl)-alanine (dopa)) and suppression of other melanocyte metabolic processes. Exposure to sunlight or ultraviolet light will cause repigmentation, which may be prevented by the broad-spectrum sunscreen agents contained in this product.

- Dosing
- Interactions
- Contraindications
- Precautions

Adult

Apply to affected areas bid

Pediatric

<12 years: Not established

>12 years: Administer as in adults

- Dosing
- Interactions
- Contraindications
- Precautions

None reported

- Dosing
- Interactions
- Contraindications
- Precautions

Documented hypersensitivity to drug or related products

- Dosing
- Interactions
- Contraindications
- Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

May produce unwanted cosmetic effects if not used as directed; physician should be familiar

with contents of prescribing insert before prescribing or dispensing medication; test for skin sensitivity before using product by applying to small area of unbroken skin (minor redness is not a contraindication, but discontinue use if there is itching, vesicle formation, or excessive inflammatory response); avoid contact with eyes; do not use for prevention of sunburn; discontinue use if no lightening effect is noted after two mo of treatment; on rare occasions, a gradual blue-black darkening of the skin may occur (discontinue use if it occurs)

Hydroquinone (Eldopaque-Forte, Solaquin Forte, Lustra)

Indicated for the gradual bleaching of hyperpigmented skin conditions such as chloasma, melasma, freckles, senile lentigines, and other unwanted areas of melanin hyperpigmentation. Also is used to reduce hyperpigmentation caused by photosensitization associated with inflammation or with the use of certain perfumes (berloque dermatitis).

Topical application of hydroquinone produces a reversible depigmentation of the skin by inhibition of the enzymatic oxidation of tyrosine to 3, 4-dihydroxyphenylalanine (dopa) and suppression of other melanocyte metabolic processes. Depigmentation may take 1-4 mo to occur while existing melanin is sloughed off and excretion of new melanin is increased by hydroquinone. Exposure to sunlight or ultraviolet light will cause repigmentation, which may be prevented by broad-spectrum sunscreen agents.

Available topically, in strengths of 2-4%, in the form of a cream, lotion, solution, powder, or gel.

- Dosing
- Interactions
- Contraindications
- Precautions

Adult

Apply uniformly to affected areas and rub-in bid; use until desired degree of pigmentation obtained; frequency can be tapered down to a maintenance regime

Pediatric

<12 years: Not established

>12 years: Administer as in adults

.