Phytophotodermatitis: Bulla Formation and Hyperpigmentation During Spring Break

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ABSTRACT Phytophotodermatitis is a phototoxic dermatologic reaction that occurs with exposure to ultraviolet light after contact with certain plant chemicals. Recognition is vital to proper management and avoidance of unnecessary distress for patients. Sun-sensitizing compounds, known as furocoumarins, are found in many plants (limes, celery, and natural grasses) and are excited by ultraviolet A (UVA) irradiation. UVA irradiation induces covalent linkages of nuclear DNA resulting in cutaneous photosensitivity and vesicular skin damage while increasing melanin production. Delayed erythema, hyperpigmentation, and vesicle or bullae formation are hallmarks. Literature review reveals most cases occur during or after vacation in a sunny destination with exposure to citrus fruit or in children playing outdoors in the summer when furocoumarins are abundant. Hyperpigmented lesions typically appear on the hands or around the mouth. Overall incidence is unknown and there appears to be no predilection for race, although typically more easily recognized in the fair skinned. Of concern are the many cases where misdiagnosis of child abuse has occurred with unnecessary legal action taken and emotional distress for innocent families. Phytophotodermatitis is relatively common and easily diagnosed with awareness and a careful history. Accurate diagnosis avoids unnecessary concern by patients and potential misdiagnosis of abuse. Consider phytophotodermatitis when hyperpigmentation in bizarre streaks on sun-exposed areas with vesicles in a nondermatomal distribution is present. Presented is an illustrative case.

INTRODUCTION Phytophotodermatitis is a phototoxic dermatologic reaction that occurs with exposure to ultraviolet light after contact with certain plant chemicals.1 Delayed erythema, hyperpigmentation, and vesicle or bullae formation are clinical hallmarks of this condition.2 Sun-sensitizing compounds (furocoumarins) found in many plants are the chemical offenders behind the clinical presentation.3

In terms of military medicine, a brief overview shows that dermatologic diseases have always been present. In World War I, 126,365 soldiers were admitted to hospitals because of cutaneous disorders between April 1917 and December 1919 and more than 2 million man-days lost because of dermatology-related conditions were noted.4 In World War II, about 15–25% of all outpatient visits were because of a dermatological conditions; this percentage increased to about 75% in tropical climates.4 The Korean War also saw skin diseases as a major source of disease nonbattle injuries and man-days lost. In the warm wet climate of Vietnam, cutaneous disease was the most common presenting outpatient complaint at U.S. Army medical facilities, exceeding the combined totals of diarrheal and respiratory disease. Cutaneous diseases led to 70% of the combat man-days lost.5 In Operation Desert Shield, one forward deployed U.S. unit saw cutaneous disease represent 7.1% of all disease nonbattle injuries.4 In Operation Desert Storm, 13.9% of all admissions were because of dermatologic symptoms.5 In an overview of 12 periodic deployments conducted by Army dermatologists in Bosnia from June 2001 to July 2002, a total of 429 patient visits were recorded, which included 40 surgical procedures. It was noted that referring these patients back to Germany for evaluation would have accrued $117,546 for military air transport alone and 1,287 man-days lost.4

Although rarely fatal, skin diseases can severely impact the combat effectiveness of any unit. Therefore, the correct diagnosis and treatment would be more cost effective in terms of money and man-days lost and thus preserve the fighting force. We present a case of phytophotodermatitis to illustrate the importance of prompt and accurate diagnosis of an increasingly common skin condition.

CASE PRESENTATION A 28-year-old male active duty sailor developed several hyperpigmented macules on the dorsa of both hands and right forearm (Figs. 1–3). The macules were uniformly brown, well demarcated with minimal erythema. Lesions were located near the knuckles and between the thumb and forefinger, with guttate macules scattered along the radial right forearm. He also developed a large (3 × 5 cm) bullous lesion on the dorsum of his left hand. The palms were spared and there were no other related cutaneous or mucosal lesions. The patient stated that the reaction started during the previous week, while on vacation in the Bahamas during mid-March of 2007. The patient denied constitutional symptoms, pruritis, injury, or trauma. There was no history of a similar rash in the past or any form of drug or medication use.

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While in the Bahamas, he sunbathed, swam, and snorkeled. He used sun block regularly and denied any stings, bites, or coral scrapes. After being specifically asked about contact with limes or lime juice, he recalled making fresh lime salsa several days before the lesions appeared. His medical history was otherwise unremarkable. On the basis of the physical examination and most importantly, the patient history, his condition was diagnosed as phytophotodermatitis.

**DISCUSSION**

Psoralen is an example of a furcoumarin that is released from the stem, leaves, or juice of citrus fruits. After the chemicals contact the skin and are excited by ultraviolet A (UVA) irradiation, a cutaneous photosensitivity occurs. UVA irradiation causes covalent linkages of nuclear DNA resulting in vesicular skin damage. Concomitant increases in melanin production lead to hyperpigmentation.

Erythema typically develops within 24 hours and vesicles or bullae typically develop within 72 hours. Hyperpigmentation occurs over 1 to 2 weeks and can persist for 6 to 12 months. Hyperpigmentation can appear in bizarre streaks or drop-like patterns where the furocoumarins contact sun-exposed skin. Phototoxic reactions range from minor linear hyperpigmentation to large painful bullae and may include a burning sensation. Resolution of the pain and bullae usually occurs within a few days to a week. Most cases occur after cutaneous exposure to citrus juices during or after vacation in a sunny destination. Hyperpigmented lesions subsequently appear on the hands or around the mouth. Our patient, in particular, had made salsa with freshly squeezed lime juice before participating in outdoor beach activities. Limes have a high concentration of psoralens and are often the culprit of phytophotodermatitis. The patient’s pattern of hyperpigmentation conforms to the lime-squeezing motion (Fig. 4).

Phytophotodermatitis is most common in mid-to-late summer when psoralen concentrations are highest in plants. The timing coincides with people being outdoors more often and less covered, thus increasing their surface exposure to the chemicals as well as UVA. The plant families Umbelliferae, Rutaceae, and Moraceae have the highest concentrations of furocoumarins (Table I). Brushing against rue plants or application of rue to the skin as an insect repellent are probably the most common cause of phytophototoxic reactions. Wearing leis of *Pelea anisata* (Rutaceae family) in Hawaii also has been noted to cause a reaction on the neck area. Use of “weed whackers” or “strimmers” to cut grass and weeds may deliver small shots of phototoxic plant products to the skin resulting in strimmer dermatitis.

The phototoxic reactions can range from minor linear hyperpigmentation of the skin to large painful bullae. Resolution of the pain and bullae usually occurs within a few days to a week. The reactions are not dependent on an antigen–antibody relationship nor are they cell-mediated. The reaction can occur in any individual since neither a hypersensitivity reaction nor an allergic mechanism is involved. There is no predilection for race, gender, or age, but it is most easily recognized in fair-skinned people. The severity of the reaction depends on the extent of exposure to UVA irradiation and the concentration of furcoumarins. Wet skin, sweating, and heat enhance this type of phototoxic response and had played a part in the patient’s spring break trip to the Bahamas.

Not all furcoumarins are phototoxic; the phototoxicity depends upon the linearity of the compound. Linear furcou-
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marins (psoralens) are more phototoxic than the angular furcoumarins (angelicin), except for the angular furcoumarin pimpinellin, found in the Umbelliferae family and genus Heracleum (Fig. 5).

Phototoxicity also depends upon the substituents and substituent pattern of the molecule. The severe acute reactions of phytophotodermatitis are associated with psoralens, or one of its major derivatives, 8-methoxypsoralen or 5-methoxypsoralen (Fig. 6).

The major pathway for psoralen photosensitization in biological systems is a UVA-induced covalent binding of the psoralen molecule into nuclear DNA. Monoadducts are formed by a [2+2]-photocycloaddition at the 3,4 double bond or the 4′,5′ bond to the 5,6 double bond of thymidine (Fig. 7). The skin reactions obtained by psoralen monoadduct formation alone are very mild. Although monoadducts may produce mutations and cell death, it is the cross-link formation that has the greatest effect. Upon UVA exposure of the 4′,5′ monoadduct product, cross-links of DNA, mainly in the epidermis, result in the severe skin damage of phytophotodermatitis. Monoadducts of a pyrimidine and the 3,4 coumarin double bond do not go on to form bifunctional adducts.

After cross-linked photoadducts are formed in keratinocyte and melanocyte DNA, increased mitosis of basal layer keratinocytes and melanocytes is observed. Melanocyte population can double or triple within 3 to 7 days and melanocyte hypertrophy is also seen. Tyrosinase activity is increased to make more melanin which results in hyperpigmentation. It may also cause the development of radicals, which damage cell membranes and intracellular contents, resulting in edema, erythema, and the formation of vesicles or bullae.

Harvesters of parsnips, parsley, dill, fennel, and celery have occupational-related contact with furcoumarin-containing plants. Individuals exposed to the oil of Persian limes and canny workers who pack carrots, celery, figs, and limes are also at risk. Phytophotodermatitis can also be observed in gardeners, florists, and bartenders. The overall incidence of phytophotodermatitis is unknown because of the wide range of possible sources of exposure, the variety of patient groups that can be exposed, and the correct diagnosis being made.

Common differential diagnoses for phytophotodermatitis include allergic contact dermatitis, porphyria cutanea tarda, polymorphous light eruption, sea bather’s eruption, and chemical or thermal burn. Chemical or thermal burn and abuse are suspected with the appropriate history; the remainder of the diagnoses have defining characteristics, which allow for proper identification and are listed in Table II.

Knowledge and awareness of phytophotodermatitis is important since it is especially common in children playing outdoors in the summer when psoralens are most abundant in wild and garden plants. The distribution pattern may be bizarre and can cause clinical confusion. It is not uncommon for the hyperpigmentation to take on a handprint pattern from lime juice contact from parent to child. The resultant linear streaks have led to misdiagnosis of herpes simplex virus infection and child abuse and battering. In San Diego County, 10 cases of phytophotodermatitis in children were misdiagnosed. Six of the 10 cases had the appearance of hand marks and fingerprints on the children’s skin where the parents had picked up the children after coming in contact with a phototoxic substance. The parents in 2 of the above cases were wrongfully accused of child abuse.

In 2 separate cases, 2 children were seen with hyperpigmented lesions that had begun within days after the children had been around adults preparing drinks made with limes.
Consequently, misdiagnosis of phytophotodermatitis in children could and has led to inappropriate accusations of child abuse. Thus, knowledge of phytophotodermatitis, an awareness of its occurrence, and a detailed history are important in determining the correct diagnosis. In some cases, it may be more important to ruling out common misdiagnoses, such as child abuse.

Management of phytophotodermatitis is typically limited to supportive or symptomatic care. If contact with relevant plants or known photosensitizing compounds is suspected before the appearance of the skin changes, soap and water should be used to wash off the exposed skin. Application of sunscreen and avoidance of sun exposure is recommended for the following 48 hours. If skin changes have occurred, treatment involves use of mild topical steroids and cool compresses for comfort. Corticosteroids, such as hydrocortisone valerate 0.2% cream, clobetasol, and betamethasone have been used to reduce local inflammation. Nonsteroidal anti-inflammatory drugs (NSAIDS), such as indomethacin, have been used for the relief of mild-to-moderate pain. Patients should use sunscreen to prevent further hyperpigmentation. A topical bleaching agent can help reduce hyperpigmentation, although most lesions fade with time. Our patient was relieved to know what the condition was, the cause, and the clinical course. He did not seek any treatment and his lesions have almost faded after 8 months (Fig. 8).

**TABLE II.** Selected Differential Diagnosis for Phytophotodermatitis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergic contact dermatitis</td>
<td>Pruritic papules or vesicles on an erythematous base. Exposure to <em>Rhus</em> species or other allergens does not cause rapid hyperpigmentation.</td>
</tr>
<tr>
<td>Porphyria cutanea tarda</td>
<td>Inborn enzyme deficiency in the heme biosynthetic pathway that results in mechanical fragility, subepidermal bullae, hypertrichosis, and pigmentation. Patients present with erythema and blistering of sun-exposed skin.</td>
</tr>
<tr>
<td>Polymorphous light eruption</td>
<td>Pruritic, erythematous lesions appear following the first intense sun exposure of the year (spring or early summer). Lesions are often most prominent on the arms and thighs.</td>
</tr>
<tr>
<td>Sea bather’s eruption</td>
<td>Hypersensitivity rash caused by nematocysts of stinging marine species (larval form of sea anemones). Erythematous papular rash appears in areas covered bathing suit.</td>
</tr>
<tr>
<td>Phytophotodermatitis</td>
<td>Delayed erythema, hyperpigmentation, and vesicle or bullae formation following plant contact with sun exposure.</td>
</tr>
</tbody>
</table>

**CONCLUSION**

Phytophotodermatitis is relatively common. The diagnosis is based on a careful history and inquiry regarding exposure to psoralen-containing plants, such as limes, celery, or fennel. Accurate diagnosis is important to avoid unnecessary concern by patients and to exclude potential misdiagnosis of abuse, as has been reported. Skin diseases in military personnel may produce significant morbidity, particularly because of extreme environmental conditions such as new and different areas of deployments. In these cases, many infectious and parasitic diseases, from insect bites and ticks to filariasis and leishmaniasis, can present as skin infections. A correct diagnosis of phytophotodermatitis can also save a service member the stigma of a misdiagnosis of dermatitis artefacta, an intentionally produced skin lesion to achieve sick leave from military duties. Dermatitis artefacta may be confused with phytophotodermatitis since they both can present with a bizarre cutaneous pattern with linear morphological features mimicking acute contact dermatitis. In terms of military medicine, the correct diagnosis and treatment can also save money and man-days lost. Consider phytophotodermatitis when patients present...
with hyperpigmentation in bizarre streaks on sun-exposed areas or with vesicles in a nondermatomal distribution.\textsuperscript{2,11}

**REFERENCES**


**FIGURE 8.** The dorsum of the patient’s left hand after 8 months with no treatment.