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Review

Allergic Hypersensitivity Skin Reactions Following Sun Exposure

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A B S T R A C T

Photoallergic dermatoses are skin lesions following sun exposure, characterized by activation of immunological mechanisms, involving photosensitizers and photoallergens that can cause photosensibilization in some individuals. In this group of disorders, photoallergic contact dermatitis should be accentuated. It manifests as contact allergic dermatitis on sun-exposed skin areas, following direct contact with photoallergens during UV exposure (predominantly UVA). Under influence of light, photosensitizers get activated, followed by fusion with cutaneous proteins which renders them to complete antigens, and consequential initiation of immunological mechanisms with resulting pathological skin lesions. The most common photoallergens are: sulfonamide antibiotics, phenothiazines, and halogenated salicylanilides. Photoallergic dermatoses are comprised of several disorders, although the causative photoallergen remains unknown (e.g. solar urticaria, polymorphous light eruption and hydroa vacciniforme). Solar urticaria is a rare, acute urticarial reaction on both sun-exposed and covered skin areas, which appears soon after exposure to sun or artificial lighting. Polymorphous light eruption is a relatively common polymorphous skin eruption, which usually appears in spring. Its pathogenesis is unknown, presumably photoallergic reaction. Hydroa vacciniforme is a rare photodermatosis of unknown etiology, which usually presents in summer-time. It is characterized by vesicobullous eruptions, with residual nonesthetic varioliform scarring.

Key words: *allergic reactions, sun allergy, photoallergic reactions, solar urticaria, polymorpheus light eruption, photodermatoses*

Introduction

Several skin reactions may follow sun exposure, mediated by activation of hypersensitivity allergic mechanisms[1,2]. We often hear of individuals »allergic to sun«, referring to the family of photodermatoses. This group of disorders comprises skin lesions following UV radiation doses that would normally not cause photosensibilization in healthy individuals. The most common are primary photodermatoses, characterized by skin photosensibilization with no evidence of any other underlying dermatosis, while secondary photodermatoses are associated with underlying conditions, such as porphyria, lupus erythematosus, or xeroderma pigmentosum. Primary photodermatoses are traditionally comprised of idiopathic photosensitivity forms, together with a group of reactions associated with known toxic or allergic triggers, while the third group of primary photodermatoses consists of persistent light reactions[1]. Idiopathic photodermatoses include solar urticaria, polymorphic light eruption, *hydroa vacciniformis* and actinic prurigo, characterized by activation of immunological mechanisms. Photodermatoses with known triggers are: photoallergic contact dermatitis, systemic photoallergic dermatitis, and phototoxic reaction; the former two represent delayed hypersensitivity allergic reactions, while the latter has non-immunological pathogenesis. The third group of primary photodermatoses, also known as chronic actinic dermatitis, encompasses persistent light reaction, actinic reticuloid, photosensitive eczema, chronic photosensitive dermatitis, and photoaggravated atopic dermatitis. The family of chronic actinic dermatitides is partially characterized by activation of allergic mechanisms, although their etiology mostly remains unknown (some of them are idiopathic, some have known triggers, but all of them have chronic course)[1,2].

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Solar Urticaria (Light Urticaria, Photoallergic Urticaria)

Solar urticaria is a rare, acute urticarial reaction, appearing within minutes following exposure to sun or artificial lighting, primarily affecting elderly[1,3]. A wide variety of wavelengths, including the most common UVA, UVB, UVC spectrum and visible light may provoke the condition. The radiation is absorbed by an endogenous chromophore, thus producing a new photoallergen, which elicits a primary IgE-mediated immune response to the mast cell-bound antigen. The subsequent exposure to the same radiation source may produce additional photoallergen quantities, which bind mast cells and cause urticaria. At present, solar urticaria is categorized as type I, with photoallergens unique to the patient, or type II, where the patient produces antibodies against normal components of the irradiated skin[1]. Solar urticaria appears within minutes following exposure to sun or artificial lighting, and is characterized by hives, pruritus and erythema on both sun-exposed and covered skin areas. The disease often follows a chronic course, persisting for several years, with minor tendency towards spontaneous regression. Clinical presentation of solar urticaria may resemble erythropoietic protoporphyria, and occasionally other forms of urticaria[1,3]. Phototesting can be performed for diagnostic purposes; hives develop within minutes of irradiation. The action spectrum (AS) (necessary for initiation of the clinical reaction) also has to be defined for the given patient (individuals report reactivity to UVA, UVB, UVC, and visible light), as well as the minimal urticarial dose (MUD). Long-acting antihistamines can be administered prior to sun exposure, although often without clear benefit. Phototherapy is the treatment of choice. Repeated UV radiation or visible light exposure results in temporary clinical improvement due to mast cell exhaustion and prolonged re-synthesis of their mediators. UV radiation and visible light of the appropriate AS are used to provide temporary clinical benefit, so PUVA therapy has become the treatment of choice. It is recommended, during this lull, to initiate PUVA therapy, sometimes in conjunction with systemic corticosteroid therapy, and to continue PUVA therapy throughout the summertime[1,3]. Severely affected patients can be treated with azathioprine and plasmapheresis.

Polymorphic Light Eruption (Polymorphous Light Eruption, Summer Prurigo, Summer Eruption, *Prurigo Aestivalis*, Eczema Solare)

Polymorphic light eruption (PMLE) is a common idiopathic photodermatosis, with mandatory monomorphous presentation for the given patient, but a wide range of clinical features among patients, as its name suggests[1,4]. It is the most common form of idiopathic photodermatosis, and the second most common skin reaction following sun exposure, resulting from sun burns. As estimated, at least 10–20% of individuals are affected, which is often described as toxic sun reaction or sun allergy. European population shows female predominance, with estimates ranging as high as 9:1, with similar ratio estimates for the US. The PMLE of Native Americans is described today as actinic prurigo, characterized by clinical features of both PMLE and atopic dermatitis. Patients with PMLE may often have stigmata of atopic dermatitis, and a positive family history of atopy. The etiology of PMLE is unknown; the reaction is probably type IV or delayed hypersensitivity reaction to an unknown allergen. The AS is usually in the UVA spectrum, but may fall into the UVB, although some patients react to both wavelengths. The majority of patients notice skin lesions during spring or early summer, which resolve spontaneously. Nowadays, with a massive tourist migration to sunny regions during the winter, PMLE has become a year-round problem[1,4]. Skin lesions appear hours to days following UV radiation and are presented on sun-exposed areas. Irregular erythema is seen initially, usually associated with pruritus. The most commonly affected sites are the face, lateral neck regions, the upper lateral aspects of arms, and dorsal sides of hands. The most common variant is a papular or a papulovesicular form, usually appearing on the décolletage, although other morphologic variants of PMLE may also appear, such as hemorrhagic lesions, plaques, erythema multiforme-like lesions, insect bite-like reactions, or vesiculobullous lesions. Individual lesions often coalesce. None of the lesions resemble dermatitis, although excoriations, weeping, crusting and scaring may be seen in patients with simultaneous atopic dermatitis. PMLE may resemble numerous dermatoses due to the various morphologic patterns. Papulovesicular form may mimic atopic dermatitis, photoallergic dermatitis, prurigo simplex and even hemorrhagic leukocytoclastic vasculitis. The plaque form can resemble solar urticaria, erythropoietic protoporphyria, erythema multiforme, or lupus erythematosus[1,4]. Juvenile spring eruption is a variant of PMLE affecting primarily boys or young men during early spring, with predilection for ear helices, hands, and nose. The lesions resolve spontaneously after discontinuation of sun exposure. However, the reaction is very likely to reoccur following re-exposure. This is a chronic disease; according to long-lasting studies that followed patients for over 30-year periods, about half of the patients showed improvement, 25% were cured, while 25% deteriorated during the course of disease. Lesions can be easily provoked by phototesting, irradiation of predilection areas with high doses of UVA, UVB, or both for 3 consecutive days. Most patients react to UVA or the combination irradiation; only several patients react only to UVB. Topical corticosteroids are usually administered. Sunscreens with good UVA coverage, appropriate protective clothing, and gradual sun exposure may serve as important prophylaxis.

Phototherapy is regarded the most effective prophylaxis; it has to be initiated 4–6 weeks prior to UVA or UVB radiation exposure, as required by the action spectrum[1,5,6]. PUVA causes even better improvement and probably represents the treatment of choice for severely

affected patients. Extremely sensitive patients may require simultaneous use of systemic corticosteroids and PUVA. A variety of systemic medications have been tested, including β-carotene, chloroquine, nicotinamide, antihistamines, and calcium supplements, unfortunately with disappointing results. Systemic corticosteroids can sometimes be used, with dose reduction over the course of disease.

Hydroa Vacciniformis

Hydroa vacciniformis is an extremely rare type of photosensitivity. Its etiology is largely unknown, although UVA appears to be responsible[1,7]. Its usual onset is during the first years of life; girls are more often affected than boys. Erythematous papules and plaques develop on photoexposed areas, such as nose, cheeks, tips of the ears, and dorsa of hands, usually in the spring. Skin lesions evolve into blisters that are often hemorrhagic, they acquire dark crusts, and tend to heal leaving residual depressed varioliform scars, as the name itself suggests. In addition, postinflammatory hypo- and hyperpigmentation may occur. In severe cases, it can result in mutilation of ears, nose and distal phalanges. Clinical presentation of *hydroa vacciniformis* may resemble erythropoietic protoporphyria or congenital erythropoietic porphyria, since both are characterized by early photosensitivity and scarring. In the most severe cases, corneal lesions may appear, thus leading to impaired vision. The attacks tend to reoccur each spring, but often diminish as the patient reaches adolescence. Repeated provocation of the back area with large doses of UVA may result in typical hemorrhagic lesions. There is no adequate therapy, except for sunlight avoidance. Broad spectrum UVB and UVA sunscreens ought to be used; patients should also wear sunglasses with a high degree of UVA protection. If lesions continue to progress, systemic corticosteroids should be administered. PUVA-induced amelioration can be tried, although patients are very sensitive and may not tolerate the induction[1,7].

Actinic Prurigo

Actinic prurigo is an extremely rare condition; most cases are sporadic. It usually appears before the age of 10 in the European population[1,8]. The condition is predominantly seen among Native Americans (the terms familial actinic prurigo or hereditary polymorphic light eruption are often used), and in Central and South America, especially in mestizos (mixed Spanish and Native American origin). Some authors believe the disease in Native Americans is not identical to the rare European entity, while others think they represent varying features in different racial groups of Americans. Actinic prurigo shows stigmata of atopic dermatitis. The mechanism of photosensitivity remains unclear. Different HLA predilections have been found. The AS for actinic prurigo is primarily UVA, although some patients are also responsive to the UVB spectrum[1,8]. Clinically, actinic prurigo represents an overlap between atopic dermatitis and PMLE. Characteristic prurigo lesions are uncommon; hence the name of the disease is rather inadequate. Its course is seasonal, with the onset in spring, and occasional regression in the late summer. The very characteristic feature is the presence of exudative cheilitis with predilection for the lower lip. Erythematous, edematous plaques tend to become excoriated and crusted. They affect cheeks, neck, ears, arms, and hands, and are associated with pruritus. Initially, lesions are limited to sun-exposed areas, with some signs of remission or involvement of non-exposed areas later on, in the off-season. Actinic prurigo may improve in adolescence, yet some individuals develop disease in adulthood. Considering low incidence in Europeans, clinical features of dermatitis with tendency for development of prurigo-like nodules, cheilitis, and overlap with light-sensitive atopic dermatitis and PMLE may suggest the diagnosis. The mainstay of therapy is topical, and in severe cases, systemic corticosteroid therapy. While β-carotene is not effective, thalidomide seems to be useful under appropriate control. Although experience in phototherapy application is limited, UVA or PUVA therapy seem to be beneficial[1,8].

Photodermatoses Caused By Exogenous Sensitizers

Such reactions can be divided into phototoxic and photoallergic reactions. According to the etiology, photoallergic reactions fulfill all criteria for allergic reactions, while phototoxic reactions have non-immunological etiology. Phototoxic reactions are more common than photoallergic reactions.

Photoallergic Dermatitis

Photoallergic dermatitis is a cutaneous reaction following photoallergen and UVA exposure, requiring prior exposure to the allergen[1,9,10]. The photosensitizing substance can be applied locally or entered systemically. The AS for photoallergic dermatitis is primarily UVA, although in rare cases, as with sulfonamides and diphenhydramine, it lies within the UVB spectrum. Photoallergic reactions are significantly less common than phototoxic reactions; their frequency is unknown. Men are more likely to have photoallergic reactions than women. Generally, drug-induced photosensitivity reactions can occur in individuals of any age[1,9,10]. Photoallergic reactions resemble allergic contact dermatitis and cell-mediated immune responses to a photo-activated compound and typically develop in sensitized individuals 24–48 hours post-exposure[10]. Previous exposure to the allergen is required and only small percentage of exposed individuals develops immune response and resulting clinical symptoms. Once the patient becomes sensitized, any method of exposure may subsequently lead to overt disease. The interaction between the potential allergen, the skin, and UV radiation produces a modified substance, usually a hapten that binds to protein carriers in the skin and thereby forms a complete antigen. Spe-

cifically, Langerhans cells (LCs) and other antigen-presenting cells take up the photoallergen and migrate to regional lymph nodes where they present it to T cells, which express antigen-specific receptors. Subsequent T cell activation, proliferation, and migration back to the site of photoallergen deposition, result in inflammatory skin response[10]. Many substances are capable of causing both phototoxic and photoallergic reactions. The most common photoallergic medications include neuroleptic drugs such as phenothiazines (chlorpromazine, fluphenazine, pherazine, perphenazine, thioridazine); antifungals (itraconazole); anti-inflammatory drugs (NSAIDs) such as ketoprofen; diuretics such as hydrochlorothiazide; hypoglycemics such as sulfonylureas (glipizide, glyburide); sunscreens, such as para-aminobenzoic acid (PABA), cinnamates, benzophenones, salicylates; fragrances, such as musk ambrette, 6-methylcoumarin and others, such as 5-FU, quinidine, dapsone etc[10]. Topical photoallergic substances are: halogenated salicylanilides (TCSA, TBSA), hexachlorophene, bithionol, musk ambrette, PABA and related compounds, benzophenones, methoxycinnamates, parsol 1789 (sunscreen cream), cyclohexanol etc. It has been noted that halogenated salicylanilides used in antibacterial soaps in the 1960s and early 1970s had caused an epidemic of photoallergic dermatitis and also led to many cases of persistent or chronic reactions to light. Since they have been revoked from the market, the most common topical photosensitizers nowadays are sunscreens[1,9,10]. Skin lesions in photoallergic contact dermatitis are pruritic and limited to sun-exposed areas, where photoallergen has been applied. Generally, eczema usually appears when a photoallergen is applied topically, but if a photoallergen is administered systemically, it results in skin drug reactions. The reaction usually manifests as a pruritic eczematous eruption with erythema and vesicles in the acute phase, while chronic exposure results in erythema, lichenification and scaling. Hyperpigmentation is not a feature of photoallergic reactions[10]. If the diagnosis is not made and exposure persists, it will result in chronic photoallergic dermatitis accompanied by lichenification, also lesions may progress to nonirradiated areas[1,9,10]. Occasionally, in case of more subtle exposure, for example, many photosensitizers are present in animal food products; farmers may develop reaction on photoexposed areas. In winter months or with minimal sun exposure, skin lesions may be trivial and the patient simply complains of pruritus or minor erythema. When photoallergic medication is taken, the reaction becomes systemic in its nature. The clinical reaction corresponds to photoallergic contact dermatitis, although it is usually more diffuse and uniform on sun-exposed areas, considering that topical application of medications often skips areas can be applied less abundantly. Photoallergic reactions are sometimes identical to phototoxic reactions, but systemic photoallergic reaction is more diffuse. Severe atopic dermatitis, especially if photoaggravated, may also be very similar. Photopatch testing is the proper way to identify photoallergic contact dermatitis, phototoxic dermatitis, and allergic contact dermatitis[11]. Avoidance of the allergen and application of UVA sunscreens and topical corticosteroids are the mainstays of therapy. Also avoidance of UV radiation is essential for protection of skin sun damages and developing skin malignant tumors[12,13].

REFERENCES

1. BRAUN-FALCO O, PLEWIG G, WOLFF HH, BURGDORF WHC, Dermatology (Springer, Heidelberg, 2000). — 2. KRUTMANN J, Photoimmunology (Blackwell, Oxford, 1995). — 3. ROELANDTS R, RYCKAERT S, Int J Dermatol, 38 (1999) 411. — 4. NORRIS PG, HAWK JLM, Photodermatology, 7 (1990) 186. — 5. MAN I, DAWE RS, FERGUSON J, Photodermatol Photoimmunol Photomed, 15 (1999) 96. — 6. NORRIS PG, BRITISH DERMATOLOGY GROUP, Br J Dermatol, 130 (1994) 246. — 7. KETTERER R, MORIER P, FRANK E, Dermatology, 189 (1994) 428. — 8. MAGANA M, J Am Acad Dermatol, 36 (1997) 504. — 9. GONZALES E, GONZALES S, J Am Acad Dermatol, 35 (1996) 871. — 10. LUGOVIĆ L, ŠITUM M, OŽANIĆ-BULIĆ S, SJEROBABSKI-MASNEC I, Coll Antropol, 31 (2007) 63. — 11. IBBOTSON SH, FARR PM, BECK MH, DIFFEY BL, FERGUSON J, GEORGE SA, GREEN C, MENAGÉ HDUP, MURHY GM, NORRIS PG, RHODES LE, WHITE IR, Br J Dermatol, 136 (1997) 371. — 12. SJEROBABSKI MASNEC I, VODA K, ŠITUM M, Coll Antropol, 31 (2007) 97. — 13. PEHARDA V, GRUBER F, KAŠTELAN M, PRPIĆ MASSARI L, SAFTIĆ M, ČABRIJAN L, ZAMOLO G, Coll Antropol, 31 (2007) 87.

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ALERGIJSKE REAKCIJE PREOSJETLJIVOSTI KOŽE PRI IZLAGANJU SUNCU

SAŽETAK

Fotoalergijske dermatoze obuhvaćaju promjene kože kod kojih se pri izlaganju suncu aktiviraju imunološki mehanizmi, koji uključuju senzibilizatore i fotoalergene koji uzrokuju fotosenzibilizaciju samo u nekih osoba. U toj skupini se

ističe *dermatitis e contactu photoallergica* koji se očituju slikom kontaktnoga alergijskog dermatitisa na svjetlu eksponiranim dijelovima kože, a nastaje nakon izravna kontakta s fotoalergenom pri obasjavanju UV svjetlom (obično UVA). Pod utjecajem svjetla fotosenzibilizator se aktivira, spaja se s proteinima kože i postaje potpuni antigen, nakon čega slijedi uključenje imunoloških mehanizama i pojava patoloških promjena na koži. Najčešći fotoalergeni su sulfonamidi, fenotiazin i halogenirani salicilanilidi. Neke bolesti ubrajaju se u fotoalergijske dermatoze, iako uzročni fotoalergen nije poznat (npr. urticaria solaris, polymorphous light eruption (prurigo aestivalis), *hydroa vacciniforme*). Urticaria solaris je rijetka akutna urtikarijska reakcija koja se pojavljuje ubrzo nakon izlaganja sunčevim zrakama ili umjetnom svjetlu, a smještena je na fotoeksponiranim i pokrivenim dijelovima kože. *Polymorphous light eruption* je razmjerno česta erupcija na koži polimorfnog izgleda, a obično se pojavljuje u proljeće. Nepoznate je patogeneze, a vjerojatno je riječ o fotoalergijskoj reakciji. *Hydroa vacciniforme* je rijetka fotodermatoza nepoznate etiologije koja se pojavljuje ljeti, a ispoljava se vezikulobuloznom erupcijom, nakon koje preostaju neestetske varioliformne brazgotine.