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Polymorphous Light Eruption: a Review

Christina E. Artz[1] · Caitlin M. Farmer[2] · Henry W. Lim[2]

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Abstract

Purpose of Review To update readers on the current understandings of polymorphous light eruption (PMLE) in regard to epidemiology, clinical findings, pathophysiology, treatment, and prognosis.

Recent Findings PMLE is known to be the most common photodermatosis seen in individuals with light skin types; however, recent evidence shows that it is also commonly observed in individuals with skin of color. Resistance to UV-induced immunosuppression is now known to be an essential part of pathogenesis; this could be secondary to unique cytokine or antimicrobial peptide expressions in these patients. Photohardening, done at the onset of sunny season for patients living in temperate climate, is a commonly used and effective management.

Summary PMLE is the most common photodermatosis. Lesions occur within hours after sun exposure, varying from urticarial papules, pinhead papules, to vesicles; they resolve in days to weeks without scarring. Resistance to UV-induced immunosuppression is thought to be an important contributor to the pathophysiology. Management includes photoprotection and photohardening. A 7–10-day course of oral corticosteroids is an appropriate prophylaxis for patients who plan to go to sunny locale for vacation. Though PMLE is chronic, many patients show improvement over years.

Keywords PMLE · Polymorphous light eruption

Introduction

Polymorphous light eruption (PMLE), also known as polymorphic light eruption, is an immunologically mediated photodermatosis with a high prevalence of up to 10–20%, making it the most common photodermatosis worldwide [1–4]. PMLE most often affects young women, of all skin types, in the second to third decades of life [3, 5]. The condition is characterized by minimally pruritic, non-scarring polymorphic lesions on sun-exposed skin that develop usually several hours after the first exposure to sunlight in spring and early summer, often leading to its mistaken description as a "sun allergy" [1–3]. These lesions subside in a few days with avoidance of sun exposure.

Epidemiology

PMLE is the most common photodermatosis with a wide geographic distribution [1, 3]. High latitudes have a high prevalence of the condition with highest prevalence in Scandinavia (22%) and northern USA and UK (15%) and lower prevalence in Australia (5%) [1, 3]. These differences are attributed to the varied amounts of ultraviolet (UV) light seen in these regions and the greater variation of UVB radiation between summer and winter in high latitude locations [1]. Overall, prevalence is likely to be underestimated as patients with mild disease may not seek medical attention [6, 7].

PMLE chiefly affects women, with a four-time greater incidence compared to men [1, 3, 5]. Onset commonly occurs in the second to third decades of life, though childhood onset occurs with 20% of patients diagnosed [8]. PMLE affects all races and skin types, including Asians, Africans, Hispanics, and Native Americans [8–11]. A large European study by Rhodes et al. in 2010 showed that prevalence of PMLE in

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✉ Henry W. Lim
hlim1@hfhs.org

[1] University of South Alabama College of Medicine, Mobile, AL, USA

[2] Department of Dermatology, Henry Ford Hospital, New Center One, 3031 West Grand Blvd, Suite 800, Detroit, MI 48202, USA

highest among Fitzpatrick classification type I skin type in both women and men; the prevalence declines sequentially with darkening skin type with lowest prevalence among skin types IV or higher [12]. However, a more recent American study by Nakamura et al. in 2013 demonstrated a higher proportion of PMLE in African-Americans compared to Caucasians [10].

Genetics is thought to play a role in PMLE, though the exact mechanism remains unclear [3, 13–17]. Twin studies have suggested a multifactorial and polygenic model of inheritance for PMLE with both genetic and environmental components [14, 15]. Estimates of prevalence of PMLE in monozygotic and dizygotic twins were similar at 21% and 18%, respectively; however, concordance of disease presence or absence among monozygotic twins was significantly higher than that of dizygotic twins, supporting a strong genetic influence [14]. Also, evidence of family clustering has been demonstrated as 12% of affected twins with PMLE had a positive family history, while only 4% of unaffected twins had a positive family history [15]. Overall, family history of photosensitivity in PMLE patients is estimated from 15 to 56% of patients [14–17].

Clinical Features

Lesions present with variable morphology. Erythematous and urticarial papules are the most commonly seen morphology in light skinned individuals (Fig. 1), while pinhead papules predominate in dark skinned individuals (Fig. 2). Small (2–3 mm) vesicles can be seen following intense sun exposure, especially in early spring. Erythema multiforme (EM)-like lesions have also been described. While morphology may vary from patient to patient, the lesions present in a single individual are generally monomorphic [3, 5]. This is supported by a 7-year follow-up evaluation of PMLE patients, which reported 76% of patients had consistent lesion morphology throughout the follow-up period [18]. Lesions are classically found in areas of sun-exposed skin that are covered during the winter months, including the external forearms and arms, lower anterior neck, V area of chest, and dorsal hands [2]. Areas exposed to continuous sunlight throughout the year (i.e., the face) are often spared, though it can be affected in some cases [2]. Associated edema, bullae, and vesicles are possible [2]. Stinging, burning, pain, and sleep difficulties, though uncommon, have also been described [19].

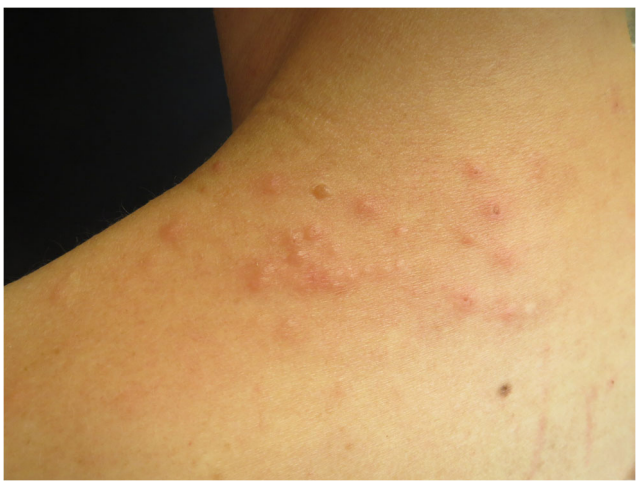

Fig. 1 Erythematous papules and papulovesicles on sun-exposed skin of a Caucasian patient

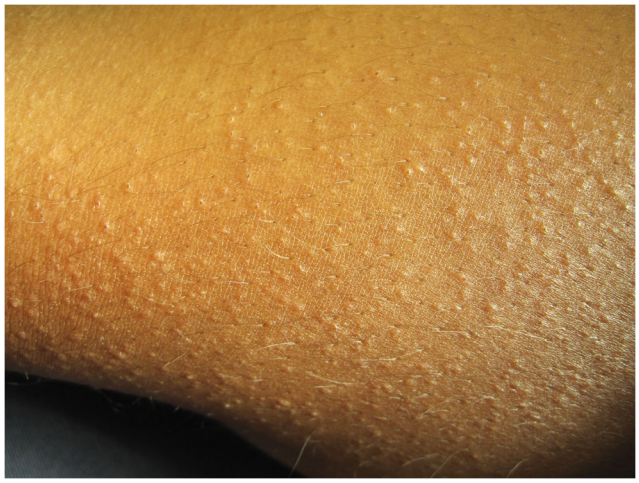

Fig. 2 Multiple pinpoint flesh-colored papules on sun-exposed skin of a patient with Fitzpatrick skin type IV

Symptoms are worse in spring or early summer and tend to fade as the seasons progress due to the "hardening" phenomenon [1–3]. When exposed to the first intense UV radiation of the season, the eruption develops within minutes, hours, or, less commonly, days. The lesions persist for days or occasionally weeks if there is continued exposure [1–3]. When the patient limits sun exposure, the eruption will steadily fade over a few days or weeks and heal without scarring [1–3]. Outdoor winter activities and recreational tanning use can stimulate eruptions outside of the classic spring/summer time frame [20]. Typically, the same skin sites are affected in a given patient with each eruption. A wide variety of disease severity exists with some patients experiencing frequent attacks throughout the spring and summer and other patients experiencing attacks only during particularly sunny vacations [21, 22].

In darker-skinned patients, a pinpoint variant of PMLE is the most commonly morphology, with 1–2-mm papules appearing most commonly on the arms or dorsum of hands. These pinhead papules may resolve leaving shiny, minimally hypopigmented macules [12, 23••, 24, 25]. Another more localized but uncommon form of PMLE, called spring and summer eruption of the elbows (SSEE), presents as erythematous and pruritic papules, papulovesicles, or plaques overlying the

bilateral elbows following the first intense UV exposure of the season [26]. Lesions of SSEE resolve spontaneously but can be symptomatically treated with topical corticosteroids and/or oral antihistamines [26]. Juvenile spring eruption is a more commonly reported localized PMLE variant that affects boys and young men with diffuse erythema and pruritus on helices of ears, beginning hours after bright sunlight exposure with blisters and papules forming 24–48 h later [27–29]. These lesions also resolve spontaneously in a few days. Another uncommon variant, polymorphic light eruption with severe abnormal phototesting sensitivity (PLESAPS), was recently reported [30••]. While monochromatic phototesting is normal in many PMLE patients, it is severely abnormal in patients with PLESAPS. These patients also experience more facial involvement and higher prevalence of contact allergies compared to classic PMLE; therefore, patch testing should be considered [30••]. A rare variant of PMLE, known as polymorphic light eruption, sine eruption, presents with sun-induced pruritus in the absence of visible skin lesions [31, 32]. Other reported skin eruptions suspected to be variants of PMLE include the following: Mallorca acne [33], solar purpura [34, 35], and benign summer light eruption [32].

Pathophysiology/Histology

Since its first description, the pathophysiology of PMLE is now better understood. A decreased ultraviolet radiation (UVR)-induced immunosuppression to antigen recognition and presentation has been established as a central theory [36–38]. This decreased immunotolerance to normal photoinduced antigens allows for a delayed type hypersensitivity (DTH) response to occur [37]. Normally, UVR induces large changes in cytokine production and influx of several cell types in the dermis and epidermis [39]. In PMLE, Langerhans cells are relatively resistant to UVR and remain within the epidermis to further potentiate the DTH reaction; this is likely due to lack of critical cytokines such as IL-1, TNF-α, and IL-18, which are essential for immunosuppression in the skin [39, 40]. The DTH pathophysiology is supported by the presence of similar inflammatory mediators in both PMLE and allergic contact dermatitis, a proven DTH reaction [41, 42••]. IL-36, a proinflammatory cytokine in the IL-1 family, is present in increased numbers in the skin and peripheral blood of PMLE patients, indicating an activation of local and systemic immune response, further supporting the loss of immunosuppression in PMLE [43].

The photoinduced neoantigen that stimulates the immune reaction, however, is largely unknown. A recent hypothesis suggests the antigen forms due to a failure in apoptotic cell clearance [44••]. Because of this impaired clearance, apoptotic cells and proteins accumulate and are potential sources of auto-antigens to fuel the immune reaction [44••]. A recent genome-wide expression analysis found that 14 genes associated with apoptotic cell clearance were less expressed in PMLE patients compared to healthy controls [44••]. Another theory suggests that this immune reaction is stimulated by antimicrobial peptides (AMPs), small amino acid residues that neutralize invading microorganisms [45••, 46, 47]. PMLE patients have been shown to have a unique expression pattern of AMPs upon UV exposure. Patra et al. hypothesized that UV-induced damage to microbes and microbial elements contribute to the unique AMP expression pattern that helps explain the pathogenesis of PMLE [45••]. Furthermore, a prospective case–control study by Lembo et al. demonstrated a significantly decreased prevalence of PMLE in patients with a history of UV-induced skin cancer (basal cell carcinoma, squamous cell carcinoma, and melanoma) as well as a trend towards fewer of these skin cancers in patients with PMLE. As UV-induced immunosuppression contributes to the development of skin cancer, the authors proposed that the increased immune surveillance and resistance to UV-induced immunosuppression in PMLE could contribute to these findings [48].

The histology seen in PMLE depends on the clinical morphology of the lesions. The histological features are characteristic, but not diagnostic due to the lack of specificity [1, 47]. The papular form of PMLE demonstrates a perivascular lymphocytic infiltrate in the upper and middle dermis composed of chiefly lymphocytes with variable neutrophils and eosinophils [49]. Dermal edema and endothelial cell swelling are also common features [9]. A band-like infiltrate in the upper dermal layers is observed in the plaque type of PMLE, while more prominent dermal edema is seen in the EM-like type of PMLE [47]. The papulovesicular form of PMLE has numerous neutrophils; the vesiculobullous form has intense subepidermal edema with spongiotic vesicles; and the eczematous form has parakeratosis, spongiosis, sporadic dyskeratosis, and acanthosis [29, 49].

Diagnosis

PMLE is usually diagnosed by its typical clinical history, evolution, and morphology of lesions. Neither phototesting nor skin biopsy is routinely performed. Photoprovocation testing, which involves repeatedly exposing the skin daily for 4–5 days with suberythemal doses of UVA, UVB, or solar-simulated UVR, can confirm the diagnosis [50–52]. Ideally, two symmetrical areas of previously involved skin should be tested as to avoid false-negative results if uninvolved skin is used. Also, testing should not be performed late in the season (late spring or summer) as tolerance with natural photohardening can lead to false-negative results [9]. Estimates suggest 60 to 90% of PMLE lesions can be reproduced by photoprovocation depending on the specific method used [9, 50–52]. In practice, due to lack of insurance

coverage and the need for patients to repeatedly return to the clinic, this is not commonly done.

Provocative phototesting studies demonstrate that the majority of patients with PMLE are sensitive to UVA alone [51]. However, lesions may be provoked by UVB alone, UVA plus UVB, and even visible light [3, 51, 53, 54]. Though these studies support induction of PMLE by a broad UV waveband action spectrum, UVA is thought to play a critical role in lesion formation. This concept is supported by the sensitivity of PMLE patients to sunlight through window glass and the failure of UVB-absorbing sunscreens to protect many patients from developing an eruption [47, 55].

Differential Diagnosis and Associated Conditions

Differential diagnoses include lupus erythematosus, solar urticaria, photocontact allergic dermatitis, and other photoaggravated dermatoses (e.g., atopic dermatitis, seborrheic dermatitis) [1, 29, 47]. Lupus erythematosus (LE) is the most important differential diagnosis both clinically and histologically [29, 47]. In contrast to PMLE, photoinduced lesions of LE develop several days after sun exposure and last for weeks; hardening is not observed in LE [47]. Also, they are accompanied by positive direct immunofluorescence and serologies [29]. It should be noted that while patients with PMLE may have positive ANA, there is no evidence that PMLE progresses to LE [56].

Management

Prevention and prophylaxis are two important management strategies for PMLE [1]. Basic photoprotective measures with shades, broad-spectrum sunscreen, protective clothing, and wide-brimmed hat and should be implemented. Often, mild cases respond fairly well to these basic measures [57].

PMLE patients with more severe eruptions may also receive prophylactic photohardening in the spring just before the first intense sun exposure of the year [1, 58–60]. Narrowband UVB (NB-UVB), broadband UVB (BB-UVB), and psoralen plus UVA (PUVA) photochemotherapy have all been employed as photohardening modalities, with NB-UVB being the most commonly used light source [3]. More recently, beneficial outcomes have also been seen with ultraviolet A1 (UVA1) [61].

Photohardening therapy can be directed to sun-exposed sites alone or to the entire body [62••, 63••]. In our center, it is usually administered 2–3 times a week for a total of 15 treatments. To prevent flaring of PMLE, in patients who are exquisitely sensitive, prednisone (0.5–1.0 mg/kg/day) can be given during the first week of hardening. Ninety-one percent of subjects in a recent 5-year case series by Aslam et al. found that phototherapy was effective and showed no loss of efficacy in subsequent courses [62••]. While many requires yearly hardening treatment, in some patients, hardening can be discontinued as the PMLE resolves [62••].

When an acute PMLE eruption occurs, topical corticosteroids and oral antihistamines can be given [9, 57, 64]. Oral corticosteroids can be used in short courses for moderate to severe PMLE flares or prophylactically to prevent flares while on sunny winter vacations (prednisone, 0.6–1.10 mg/kg for 7–10 days) [64–67]. Other systemic therapies that have been used for severe forms of PMLE include azathioprine and cyclosporine [68–70].

More recent studies have investigated the effects of afamelanotide and other short oligopeptides involved in melanogenesis as treatments for PMLE [71••, 72, 73, 74]. Afamelanotide increases the production of eumelanin by stimulating melanocortin 1 receptor (MCR1), thereby creating photoprotection against UVR and visible light [74]. A pilot trial of afamelanotide in 36 PMLE patients by Minder et al. in 2017 showed a reduction in the severity of symptoms [71••]. *Polypodium leucotomos* extract, an over the counter oral supplement with antioxidant and photoprotective properties, has also emerged as a potential therapy for PMLE [75, 76••, 77, 78]. Many recent open-label studies have demonstrated reduction in the severity, frequency, and rapidity of onset of PMLE reactions with this supplement [79–81]. In one open-label trial by Tanew et al. in 2012, *P. leucotomos* increased the cumulative UVR threshold dose for PMLE induction, but further investigation is needed [81]. A double-blinded placebo-controlled intraindividual half-body trial by Gruber-Wackernagel et al. also demonstrated significantly reduced PMLE symptoms following photoprovocation in patients treated with a topical 1,25-dihydroxyvitamin D3 analogue [82].

Prognosis

PMLE is often chronic with slow improvement over time, though the prognosis remains variable. In a 7-year follow-up study by Jansen et al., a majority (57%) of patients experienced alleviation of sun sensitivity complaints and 11% of these patients completely cleared [18]. A 32-year follow-up study by Hasan et al. demonstrated that 51% of patients had reduced symptoms, with 24% of patients considered cured. However, 24% of patients also reported equal or stronger symptoms than before [33]. Of note, a few patients did have temporary symptom-free periods of 1–3 years in duration [33].

In many PMLE patients, the psychosocial impact leads to a notable loss of quality of life and discomfort during the spring and summer months [19, 83, 84]. High levels of depression and anxiety have been reported in PMLE [84]. Patients with facial involvement or young age of disease onset may require

more rigorous psychological management [84]. In order to assess the degree of disease impact, PMLE severity scores have been established to better standardize disease extent [21, 22, 83]. The Polymorphous Light Eruption Severity Index (PLESI) assesses symptoms, recurrences, body location affected, outdoor restrictions, etc., allowing for better quantification of the disease impact of PMLE on a particular patient to help direct further management [22].

Conclusions

PMLE is the most prevalent photodermatosis worldwide [1, 3]. It most commonly affects women in the third and fourth decades of life but varies among skin types and races and can affect a wide range of age groups [1–3, 5, 9]. The eruption occurs after an intense sun exposure, usually in spring or early summer. The pathogenesis involves the production of UV-induced neoantigens combined with lack of cutaneous immunosuppressive capacity allowing for a delayed type hypersensitivity reaction to occur in the skin [1]. Skin lesions are variable with reports of papular, pinhead papular, papulo-vesicular, plaque, insect bite-like, and EM-like morphologies often accompanied by erythema and pruritus on sun-exposed areas of skin. PMLE can be prevented or improved photoprotection and, if need be, with prophylactic photohardening [58–60]. Short courses of oral corticosteroids can be used for severe acute eruption or as prophylaxis during sunny vacation in the winter. While PMLE tends to be chronic, patients should be educated that many will show slow improvements over time with possible disease remission [18, 33].

Compliance with Ethical Standards

Conflict of Interest Christina E. Artz and Caitlin Farmer declare no conflict of interest.

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Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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