

Pustular Psoriasis: A Comprehensive Review on Dermatological Diagnosis and Management

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Abstract

Psoriasis is an enigmatic, chronic, autoimmune disease exhibiting in different clinical forms and varied appearance, and involve a complex interplay of genetic, immunological and environmental factors. Hence, a thorough knowledge on accurate distinction between different clinical types is necessary to initiate an effective treatment of the disease. In this review, we discuss the various aspects of pustular psoriasis including its clinical types, pathophysiology and its association with other comorbidities. Moreover, we enlighten the diagnostic and therapeutic challenges associated with this emerging disease, due to its physical and mental components, which play a crucial role in influencing the quality of life of psoriasis patients. As an emerging elusive disease characterized by varied symptoms and predisposing factors, the dermatologists and other respective clinical practitioners have a great responsibility and challenge in implementing guidelines for diagnosis, criteria for severity assessment and therapeutic outcomes assisting in improving the quality of life among the patients. Finally, we recommend that psoriasis patients, especially those with severe disease, must receive a more holistic, multitarget therapeutic and management approach that encompasses both medical and psychological measures in order to improve their quality of life.

Keywords: Psoriasis; Pustular Psoriasis; Clinical Spectrum; Diagnostic Challenge; Dermatology; Quality of Life

Abbreviations

GPP: Generalized Pustular Psoriasis; ACH: Acrodermatitis Continua of Hallopeau; PPP: Palmoplantar Psoriasis; PsA: Psoriatic Arthritis; PASI: Psoriasis Area Severity Index; QoL: Quality of Life

Introduction

Psoriasis, exhibiting in different clinical forms and varied appearance is a chronic autoimmune disease characterized by erythematous, scaly patches, that usually affects the skin and joints. Psoriasis is reported world-wide among all age groups with an estimated global incidence rate of 2 to 4%, but the prevalence varies considerably worldwide and among different ethnic and age groups [1].

Psoriasis, literally meaning “itching” (“psora” = “itch”), has been known since ancient times, and for quite some time now was considered as the most common human skin disease, and as a variant of leprosy. Since the past four decades, advances in diagnostic techniques, genome analysis and therapeutic measures on psoriasis have made a significant contribution to unravel the knowledge and pathogenic mechanism of this multifactorial disorder which runs in families with a high genetic predisposition. Many other predisposing factors play a key role in this immunologically mediated inflammatory disease such as obesity and vitamin deficiency [2]. Psoriasis causes a significant physical and psychological imbalance among patients with strong social stigma, especially with genital lesions in pustular psoriasis that affect the quality of life among individuals [3].

Even though psoriasis is generally characterized by inflammatory symptoms that lead to proliferation and dysfunctional differentiation of keratinocytes with cellular inflammatory infiltrates associated with joints and skin, it is not always limited to these tissues and has been shown to affect major organ systems in the body [4,5]. This peculiar feature of psoriasis draws more clinical attention, apart from considering it as a dermatologic disease.

Histologically, psoriatic lesions are presented as acanthosis with characteristic epidermal hyperplasia with inflammatory infiltrates and immune cells from active inflammatory pathways [4]. Pustular psoriasis is a rare form, typically presenting as widespread abnormal skin pustules characterized by scaly, red, itching spots that can affect any age group [6]. The yellowish pustules may often be surrounded with erythema and the center of the pustule may have a clear and sterile fluid indicating no evidence of infection.

Psoriasis, often appearing as a chronic relapsing disease may often require long-term therapeutic management. Even though, complete cure is considered ‘far away from reality’, several treatment options are available that can affect the clinical course of the disease and alleviate the symptoms [4]. The various therapeutic modalities include both systemic and topical immunosuppressive drugs and steroid-based creams, in addition to phototherapy or vitamin D analogs prescribed to patients based on their clinical conditions of the severity of symptoms and the location and extent of lesions. Moreover, the choice of therapy for psoriasis is determined by disease severity, comorbidities, and access to health care, mainly because psoriasis is reported to be associated with an increased risk of developing psoriatic arthritis, cardiovascular disease, Crohn’s disease, and lymphomas that may deteriorate their quality of life [7]. Additionally, various psychological conditions may also be encountered as co-morbid with psoriasis in youngsters such as stress associated depression, smoking and alcohol consumption, microbial infections and some drugs such as beta-blockers and anti-malarial drugs [8].

The thorough knowledge on accurate clinical distinction between different types and sub-types of psoriasis is necessary to initiate the treatment and management of the disease (Table 1). In this review, we discuss the various aspects of Pustular psoriasis including its different clinical types, pathophysiology, association with other comorbidities and a small account on its diagnostic challenges which may help the dermatologist to implement an accurate therapeutic management of this disease. We aim to enlighten the diagnostic importance of this challenging disease which is lacking standardized guidelines due to a paucity of randomized controlled trials. Moreover, stress is on implementing proper management of this disease which may help the patients to recover from the associated social stigma and to overcome its negative impact on normal life of patients with this chronic disease.

Clinical spectrum of psoriasis classification

The dermatologic manifestations of psoriasis are varied; psoriasis vulgaris (also called plaque-type psoriasis or scaling psoriasis) is the most prevalent type, and this subtype is one of many subtypes, some of which are less common clinical types such as pustular, inverse, erythrodermic, and guttate, which accounts for only 10% of the cases) [9]. In most literature, the different forms of psoriasis, such as pustular psoriasis and psoriasis vulgaris are used interchangeably, even though distinct morphological characteristics are evident between these subtypes. Psoriasis vulgaris is clinically presented as discrete keratotic erythema on the skin with silvery scaling erythematous plaques in addition to nails and scalp region [10].

Types of Psoriasis	Clinical findings	Pathological findings	Site of lesions
1. Psoriasis vulgaris	Red papules become sharply demarcated erythema by silver-white scales.	Munro’s microabscess, club-shaped epidermal rete ridges, capillary vasodilation	Elbows and knees, scalp, lumbosacral region, umbilicus
2. Guttate psoriasis	Same severity of Psoriasis vulgaris. The size of erythema is about 1 cm in diameter.	Munro’s microabscess, club-shaped epidermal rete ridges, capillary vasodilation	mainly over the trunk and proximal limbs.
3. Pustular psoriasis	Sterile pustules on erythema, fever, malaise	Kogoj’s spongiform pustules	Throughout the body depending on subtypes
3.1 Acute Generalized (von Zumbusch type)	Fever, anorexia, nausea with myriads of pinhead-sized confluent pustules producing lakes of pus.	Pustules dry out, skin peels off with glazed, smooth erythematous surface	Generalized throughout body, but mainly in folds
3.2 Localized Pustular Psoriasis	Categorized into two sub-types: Acrodermatitis continua and Palmoplantar pustulosis	Pustules with pus	Fingers, hands and feet
3.2.1 Acrodermatitis continua	Pustular eruption of the fingers and toes, localized trauma starting at the tip of a single digit	Pustules with pus	Fingers, Toes and Tips of digits
3.2.2 Palmoplantar pustulosis	Hyperkeratosis and clusters of pustules over the ventral aspects of hands and/or feet	Pustules with pus	Ventral aspect of Hands and feet, base of thumb or sides of the heel
4. Psoriatic erythroderma	Diffuse flushing, severe scaling, itching, and pain that affects most of the body	Inflammatory phase of Erythematous plaques	Whole body surface
5. Nail psoriasis	Inflammation of the nail matrix and/or nail bed with pitting and distal onycholysis	Paronychia, subungual hyperkeratosis, onycholysis, and severe onychodystrophy	Nail, nail bed and nail matrix
6. Psoriatic arthritis	Seronegative arthritis accompanied by psoriasis in DIP joints and vertebra	Focal bone erosions mediated by osteoclasts at the bone-pannus junction	Progressive destruction and inflammation of bones in joints

Table 1: Types and clinical findings of psoriasis.

Pustular psoriasis is a rare chronic disease with all its variants showing similar clinical presentations characterized by superficial pustular eruptions with an erythematous base that can affect any age group. Unlike the classical type of psoriasis (psoriasis vulgaris), pustular psoriasis is commonly associated with pain over the involved spots [11] and on physical examination, the dermatologist may note the characteristic tenderness over the pustule area. As shown in table 1, Pustular psoriasis is broadly classified into generalized pustular psoriasis (GPP) and localized pustular psoriasis (LPP). Many clinical variants of GPP and LPP are characterized based on the nature of symptoms and patients, such as acute GPP, pustular psoriasis of pregnancy, and infantile pustular psoriasis in GPP groups and palmoplantar psoriasis and acrodermatitis continua of Hallopeau (ACH) in LPP group [12].

Pustular psoriasis

Pustular psoriasis, even though considered as the rarest and unstable clinical type among all psoriasis, a population survey had reported the development of pustular lesions during the clinical course of psoriasis among 20% of cases [13]. Conversely, a very small percentage (up to 5%) of cases only are presented clinically with predominant pustules and are definitely diagnosed as pustular psoriasis type.

All clinical variants of pustular psoriasis are presented with similar clinical picture involving superficial pustular eruption with erythema. Histopathology of pustular psoriasis lesions shows inflammatory infiltration with mononuclear cells and neutrophils which may lead to extensive edema and hyperplasia in the epidermis [14].

The pathological features indicative of pustular psoriasis includes spongiform pustules of Kogoj, Munro's micro-abscesses and hyperplasia of supra-papillary capillaries [15]. As shown in table 1, Pustular psoriasis is classified into two major clinical types, such as Acute generalized (von Zumbusch type) and Localized type which is again sub-classified into Acrodermatitis continua and Palmoplantar pustulosis.

Generalized pustular psoriasis (von Zumbusch)

Most patients with acute generalized pustular psoriasis are cases with preexisting plaques complicated after treatments including topical application of irritant lotions or patients who had withdrawn corticosteroids [16]. Acute onset of generalized pustular psoriasis is triggered within hours with eruption of innumerable pustules studded with the erythematous background, which may become confluent, filled with pus and characterized by systemic symptoms like fever, anorexia and nausea.

Patients may require hospitalization for careful management of symptoms such as polyarthritis and cholestasis, and the pustules may often dry and lead to exfoliation to form the new generation of crops of pustules over the same area [17]. Clinicians should distinguish the pustules of GPP from acute generalized exanthematous pustulosis (AGEP) appearing as self-limiting, toxic pustuloderma characterized by non-follicular pustules in folded skin which is also associated with drug reactions. The pathognomonic features of GPP include necrotic cells and eosinophils in the epidermis and evident vascular changes in the dermis, and with remission of acute stage, signs of erythroderma and plaque-like lesions appear. Impetigo herpetiformis, a rare form of pustular psoriasis may appear during the first two trimesters of pregnancy [18].

Localized pustular psoriasis

The localized form of pustular psoriasis includes two main clinical types: palmoplantar pustulosis (PPP) and acrodermatitis continua of Hallopeau (ACH).

Palmoplantar pustulosis

Palmoplantar psoriasis (PPP), also known as palmoplantar pustulosis was initially described as "dermatitis repens", is now classified as localized pustular psoriasis, characterized by hyperkeratosis and clusters of pustules with scaling over the ventral aspects of hands and/or feet. Classification of palmoplantar pustulosis within the spectrum of psoriasis is controversial, as several authors propose that PPP is a distinct entity, while others consider PPP is a variant of psoriasis [9,19]. The most common sites where pustules appear are on the palm and soles corresponding to the regions such as the base of the thumb in the palm (thenar area), and the little finger area (hypothenar) and the central areas of palms and soles. In severe cases, the lesions may coalesce and extend to the wrists and heels from the initial site of infection [19,20].

PPP is often reported highly among females with a predominance rate of more than 70% and are most common among reproductive age group [20] mainly due to the multiple precipitating factors such as smoking, stress, and trauma, which may increase the expression levels of inflammatory mediators through IL-17 [21,22]. Sensitivities to metals are other precipitating factors with the most common metal sensitivity reported is to nickel and occurs in 3% of patients with PPP [20], in addition to metal allergies caused by chrome and cobalt. Tonsillitis is also recognized as a precipitating factor for PPP indicated through substantial evidence by Takahara, *et al.* in their study, where tonsillectomy in PPP patients has significantly improved the disease in 88% of cases [23]. Seasonal variations with hot and humid climatic conditions also are reported to influence the onset of PPP with worsened exacerbations [24]. Many studies have reported that stressful psychological conditions such as anxiety, worry, and psychosomatic disorders may also impact the onset and worsening of PPP [22].

Palmoplantar forms of psoriasis are well-known for their refractory to conventional therapy. The first-line topical therapy involves corticosteroids under occlusion, which has been described as successful for treatment and for the prevention of new pustule formation [25]. Much second-line topical therapy is followed after first-line therapy, such as photodynamic therapy, PUVA, calcipotriene, and tacrolimus, which may often lead to remissions, and called for first-line and second-line systemic therapy with acitretin and cyclosporine respectively [25]. Biological agents are universally accepted and are used for the treatment of recalcitrant PPP. Monoclonal antibody-based drugs aimed for blocking TNF-, such as adalimumab, etanercept, and infliximab, have been reported to be successful in the treatment of PPP [21,26].

Acrodermatitis continua of Hallopeau (ACH)

Acrodermatitis continua is also known with other clinical terminologies such as acrodermatitis perstans, dermatitis repens, acropustulosis and pustular acrodermatitis, is considered as a rare form of pustular psoriasis mainly showing eruption of fingers and toes, and results from trauma at the tip of the finger or toe [27]. ACH often presents as painful and extensive sterile pustules on the most distal portions of the fingers and toes leading to onychodystrophy or anonychia [14]. Clinical presentation of ACH resembles other pustular disorders of the hands and feet, especially palmoplantar pustulosis, thus a clinical distinction of this form of psoriasis is necessary for therapeutic intervention. Additional distinguishing features of ACH include predisposition for the periungual areas, higher predominance in middle-aged females, and confinement to a limited area without extensive spreading to other regions on the digits for a long time [28].

ACH is also notoriously recalcitrant to many therapies same as Palomar-plantar pustulosis. Owing to the rarity of the disease, treatment is primarily based on data from case reports, which include antibiotics and tar. Current first- and second-line treatment is the same as PPP, however, these medications often could not prevent the relapses and further systemic medications may be necessary to control the disease. Limited epidemiological study data is available for ACH due to its rarity of disease [29].

Diagnostic challenges in psoriasis

Although much advanced clinical characteristics and pathognomonic features of various types of psoriasis are established, diagnostic criteria for definitive and early diagnosis of cutaneous psoriasis and a unified strategy for its clinical classification of the spectrum of disease is still lacking. Previously, psoriasis was classified based on the age of onset and severity of the disease, and morphological evaluation of the lesions of the disease. Morphologic evaluation of the disease has aided definite classification and identification of various clinical types of psoriasis. Even though definite autoimmune pathophysiology exists in psoriasis, unlike other autoimmune diseases, histopathological examination and blood tests are generally not valuable tools in making the diagnosis of psoriasis [12]. However, on occasion, dermatopathologic evaluation, depending primarily on pattern recognition of skin lesions and joints may be helpful in confirming the diagnosis of psoriasis.

Primary care practitioners and dermatologists play an increasingly important role in the management and care of psoriasis [30]. Thus, thorough knowledge about the various clinical types and presentation of symptoms of the disease is mandatory to differentiate between common myths and facts related to diagnosis and treatment of psoriasis and associated comorbidities. A collaborative working atmosphere between the primary care practitioners and dermatology health professionals and other clinical specialists can facilitate more interactive discussion regarding the various clinical and psychological aspects of the patients and their treatment preferences and symptom relief, so that they may be better able to work with the patient to optimize treatment adherence.

Psoriasis comorbidities

Psoriasis affecting mainly the skin and joints due to inflammatory reactions has also been associated with a number of other different organ systems, largely resembling systemic disease rather than a solely dermatological disease [4]. These disease conditions referred to as psoriasis comorbidities mainly include obesity or other metabolic diseases, autoimmune conditions, cardiovascular diseases, psychiatric diseases, malignancy and sleep disorders [7,8]. Psoriatic patients exhibited parameters of metabolic disorders of diabetes and coro-

nary heart diseases such as increased BMI, hypertension, hyperlipidemia. Recently, psoriasis was reported to be associated with increased mortality due to stroke in cardiovascular disease and is reported as an independent risk factor of myocardial infarction in young patients [31,32]. Additionally, overactivity of the sympathetic nervous system leads to more cases of psoriatic arthritis and anxiety/depression syndrome [33].

Higher prevalence of metabolic disorders such as diabetes and coronary diseases were positively correlated with psoriatic disease severity and was reported to be two times more frequent compared to control groups [34,35]. In addition to a prime risk factor for cardiovascular diseases, a recent study using the General Practice Research Database suggested that severe psoriasis is an independent risk factor for atherosclerosis, myocardial infarction, and stroke [36]. Psoriatic arthritis (PsA) results from inflammatory reactions in the joints and is usually reported to be associated with prior skin manifestations which are characterized by chronic spreading inflammation requiring systemic therapies due to serious impairment. The statistics report shows that psoriatic arthritis develops in up to 40% of psoriasis patients [37] and around 15% of psoriasis patients are thought to have undiagnosed PsA [38].

A higher prevalence of chronic kidney diseases and gastrointestinal symptoms were also reported to be associated with psoriasis in addition to cardiovascular diseases. Genetic studies based on the sharing of susceptibility locus of the genes and imaging studies have confirmed the association of psoriasis and IBD with Crohn's disease and mild liver diseases [39,40]. The risk factor assessment of psoriasis with chronic kidney diseases, end-stage renal diseases, cardiovascular diseases suggests that all these life-threatening comorbidities may critically influence the quality of life of patients and their disease burden. Impact of psoriasis on psychological and mental health is important as the cumulative effect on the psychological quality of life equal to cancer and depression, which may lead to anxiety and suicidal ideation.

Treatment and management of psoriasis

The initial step in the management of cases of pustular psoriasis is the exact dermatological diagnosis of the clinical type of psoriasis and the identification of the triggering factors. Certain clinical types of generalized psoriasis-like, von Zumbusch, may require hospitalization and the underlying systemic symptoms including fever and joint pain will require treatment with antipyretics and anti-inflammatory medications [41]. As all clinical forms of psoriasis is a chronic relapsing disease, it often necessitates a long-term therapy, and the choice of therapy is determined by several factors, such as disease severity, comorbidities, and access to health care facilities. Depending on the clinical severity of lesions, the percentage of affected body surface area, and patient quality of life, patients are frequently categorized into two groups: mild or moderate to severe psoriasis before initiating therapeutic management of cases.

Treatment strategies followed in each group may vary widely and the assessment of response to treatment is evaluated through the grading system after the therapy is initiated. One of the popular and extensively used scoring systems in clinical trials is the psoriasis area severity index (PASI) score [42]. According to the criteria, mild to moderate cases can be treated using topical applications with a combination of glucocorticoids, vitamin D analogs, and phototherapy [4].

Moderate to severe psoriasis may often require systemic treatment along with topical drug therapy. The management of psoriasis cases in the presence of comorbidities such as psoriasis arthritis, cardiovascular diseases, genital psoriasis infections, Crohn's disease, lymphomas, depression is also highly relevant in treatment selection. The first-line disease-specific medications include systemic retinoids (acitretin, isotretinoin), methotrexate, cyclosporine, and infliximab in adults; and acitretin, cyclosporine, methotrexate, and etanercept in pediatric age groups. Many complicated cases which lead to severe systemic manifestations often require second-line drug therapeutic options like etanercept and adalimumab or topical treatments like corticosteroids, calcipotriene, and tacrolimus. The second-line drug medications can be administered as monotherapy or in combination with the first-line options [43].

Topical therapy based on topical ointment medications might cause toxic complications in more sensitive subjects, which can be substituted with a more targeted approach with new drugs having greater efficacy in the management of psoriasis. Lesions in specifically

difficult locations to treat are preferred with the drugs having a targeted approach compared with their traditional systemic alternatives. Phototherapy is another treatment option and should be considered if any of the treatments as mentioned earlier fail [44]. Phototherapy (including PUVA and NB-UVB) is also considered as a first-line therapeutic method in treating lesions over the hands and feet. Although drawbacks of phototherapy such as visibility after treatment, limited effectiveness, and multiple hospital visits have been reported, some advanced phototherapeutic technique using excimer lasers have shown better results but is expensive and not widely available [45].

Biological therapy with systemic drugs is used as an alternative when standard therapies fail and are reported to be more efficient in faster clearance of skin lesions, than other currently available therapies [45]. Newer biologic therapy based on monoclonal antibodies such as secukinumab, ustekinumab, and ixekizumab is efficiently used in treating PPP [46]. Recent reports indicate that the use of IL-1 receptor antagonists (e.g. anakinra) has shown efficacy in treating cases of pustular psoriasis. Also, tocilizumab, a monoclonal antibody, has also shown efficacy in some recalcitrant cases of pustular psoriasis. Another important therapeutic management suggested is by tonsillectomy in patients suffering from guttate psoriasis and plaque psoriasis, which has been validated by a number of case series reports [47,48].

Conclusions and Recommendations for Clinical Practice

It is a well-known fact that many cases of psoriasis were associated with significant psychological stress leading to psychiatric morbidity, because of which patients may experience stigmatization and reduced quality of life (QoL). It was indicated that the significant negative impact of psoriasis on QoL is almost similar to the impact of other chronic diseases, such as heart disease, diabetes, and cancer. Moreover, the negative impact on QoL is further worsened by the presence of psoriatic arthritis, psychiatric disorders, and other co-morbidities in such patients [49]. Hence it is highly recommended that both the symptomatic component associated with clinical measures as well the stigmatization component associated with the mental stability should be considered while diagnosis and management of psoriasis.

Dermatologists usually follow a strategical symptom-based diagnosis for their patients and often concentrate on investigating the superficial skin rather than bringing out the deep emotional and psychological stress the patient is experiencing. Hence, they should be encouraged to differentiate and identify patients who perceive such high levels of discomfort and social rejection, irrespective of gender and of the severity of clinical manifestations [50]. In clinical practice, dermatologists have a great responsibility to improve both the well-being and quality of life of the psoriasis patients, by implementing specific therapeutic measures that leads to long-lasting remission of all symptoms that can be achieved by addressing both the physical and psychosocial effects of psoriasis.

Conflicts of Interest

All authors have declared that they have no conflict of interest.

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