



Review

Diagnosis and classification of psoriasis

Smriti K. Raychaudhuri^a, Emanuel Maverakis^b, Siba P. Raychaudhuri^{a,c,*}^a VA Sacramento Medical Center, Department of Veterans Affairs, Northern California Health Care System, Mather, CA, United States of America^b Department of Dermatology, School of Medicine, University of California, Davis, CA, United States of America^c Department of Medicine, Division of Rheumatology, Allergy and Clinical Immunology, School of Medicine, University of California, Davis, CA, United States of America

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ABSTRACT

Psoriasis is a chronic inflammatory multi organ disease with well characterized pathology occurring in the skin and often the joints. Although the disease has many characteristic and even pathognomonic features, no established diagnostic criteria exist for cutaneous psoriasis and there is no unified classification for the clinical spectrum of the disease. Prior approaches that have been taken to classify psoriasis include age of onset, severity of the disease, and morphologic evaluation. The latter has yielded plaque, guttate, pustular, and erythrodermic as subtypes of psoriasis. Unlike other autoimmune diseases, histopathological examination and blood tests are generally not valuable tools in making the diagnosis of psoriasis. However, on occasion, dermatopathologic evaluation may be helpful in confirming the diagnosis of psoriasis. Thus, in most cases the diagnosis of psoriasis is dependent primarily on pattern recognition that is morphologic evaluation of skin lesions and joints.

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1. Introduction

Psoriasis, a chronic skin disease is known to be the most prevalent autoimmune disease in humans [1,2]. Approximately 2%–5% of the world's population suffers from psoriasis [1,2]. According to the National Institutes of Health (NIH), as many as 7.5 million Americans have psoriasis [2]. The precise etiology of psoriasis remains poorly understood,

* Corresponding author at: Department of Medicine, Department of Veterans Affairs NCHCS, Division of Rheumatology, Allergy and Clinical Immunology, School of Medicine, UC Davis, 10535 Hospital Way, Mather, CA 95655 United States of America Tel.: +1 916 843 7096; fax: +1 916 366 5475.

E-mail address: sraychaudhuri@ucdavis.edu (S.P. Raychaudhuri).

but psoriasis is thought to result from a complex interplay between genetics, environment, skin barrier disruption, and immune dysfunction [1,3,4].

There is no cure for the spectrum of psoriatic diseases, which comprise various different subtypes of psoriasis and psoriatic arthritis. Psoriasis is associated with a high degree of morbidity and the current medications can have severe side effects. Several clinical studies have reported a strong association between psoriasis and atherosclerosis, type 2 diabetes, and metabolic syndrome, together the leading causes of mortality in the Western world [5]. In addition, patients with psoriasis, like those with other major medical disorders, have reduced levels of employment and income as well as a decreased quality of life [6,7]. The combined costs of long-term therapy and social costs of the disease have a major impact on health care systems and on society in general. According to the National Psoriasis Foundation, USA, total annual direct and indirect costs of psoriasis are over US \$11 billion, with missed workdays accounting for 40% of the cost burden [2].

The focus of this article is to discuss the clinical spectrum of psoriasis and how to diagnose the protean manifestations of psoriasis. An expert dermatologist should be able to diagnose plaque psoriasis and other clinical variants of psoriasis by evaluating their characteristic morphologic appearance. Neither histopathological examination nor any specific blood tests are recommended for the diagnosis of psoriatic disease. However histopathological and immunohistochemical features of psoriasis are unique and on rare occasions clinicopathological correlations may be helpful in diagnosis of psoriasis.

2. Pathogenesis and the pathology of psoriasis

In this section we will briefly review the histopathological features (Figs. 1 and 2) and immunopathogenesis of psoriasis. Both psoriasis and psoriatic arthritis (PsA) are complex genetic diseases. The genetic basis of psoriasis is supported from evidence from family and twin studies, linkage studies, and population-based association studies. These studies illustrate the importance of both keratinocytes and the

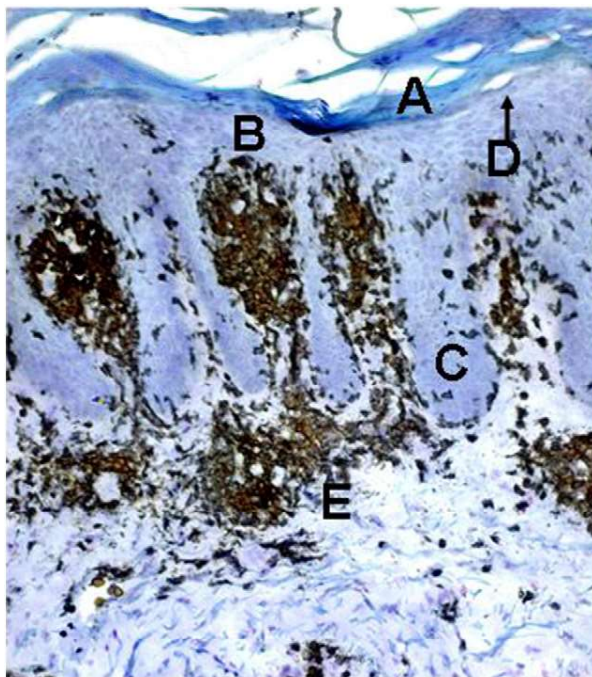


Fig. 1. A psoriasis plaque stained with an anti-CD3 antibody and counter stained with hematoxylin demonstrates unique histological features of psoriasis — A. Parakeratosis. B. Suprapapillary thinning. C. Elongated rete pegs. D. Loss of stratum granulosum (marked by the arrow). E. Diffuse infiltration of CD3⁺ T cells in the deep and superficial dermis along with the epidermotropism of CD3⁺ T cells.

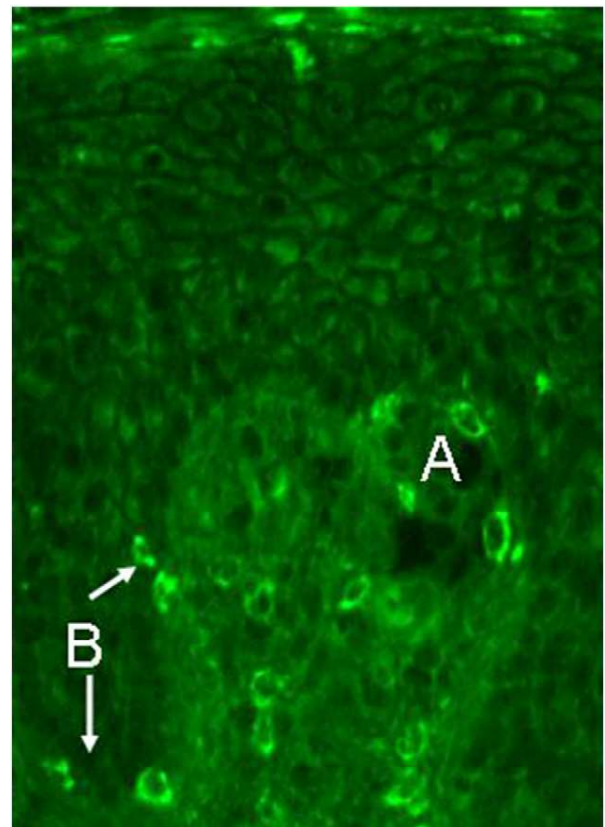


Fig. 2. A psoriasis plaque stained with an anti-CD8 antibody (immuno fluorescence microscopy) demonstrates epidermotropism of significant number of CD8⁺ T cells (A, B).

immune system in the pathophysiology of psoriasis. It has been reported that NF- κ B mediated responses in the skin are directed by CARD14 and that a subset of rare CARD14 variants leads to psoriasis and psoriatic arthritis [8,9]. Elder and his colleagues have reviewed the SNP analyses of several major studies in this field to provide collective information about an association between psoriasis and various loci of the immune system, such as the TH17 pathway (*IL12B*, *IL23A*, *IL23R*, *TRAF3IP2*, *TYK2*), innate immunity [NF- κ B and IFN] signaling pathways (*TNFAIP3*, *TNIP1*, *NFKBIA*, *REL*, *TYK2*, *IFIH1*, *IL23RA*) and β defensin, the TH2 pathway (*IL4*, *IL13*), and adaptive immunity involving CD8 T cells (*ERAP1*, *ZAP70*) [10].

Hyperproliferation and abnormal differentiation of keratinocytes are the two critical outcomes of the underlying patho-physiologic dysregulation in psoriasis. Histologically, there is marked thickening of the epidermis due to increased proliferation of keratinocytes in the interfollicular epidermis, and epidermal rete peg become very elongated [11–15]. Keratinocyte differentiation is also extensively altered in psoriasis, paralleling ‘regenerative maturation,’ an alternative cell differentiation program that is transiently expressed during wound repair. The granular layer of the epidermis, in which terminal differentiation begins, is greatly reduced or absent in psoriatic lesions [12–15]. Consequently, a stratum corneum forms from incompletely differentiated keratinocytes that aberrantly retain a cell nucleus (parakeratosis).

An active role of T cells in the pathogenesis is strongly substantiated by the following observations: (i) immunotherapy targeting the T cells or T cell cytokine such as IL-17 clears active plaques of psoriasis [16–20] and (ii) in SCID mice, transplanted nonlesional psoriatic skin converts to a psoriatic plaque following administration of intradermal administration of antigen-activated T cells [21]. In addition to traditional inflammatory mediators, experiments in the SCID mouse model, have demonstrated that Nerve Growth Factor (NGF) and substance P (SP) activated lymphocytes can also convert nonlesional psoriatic skin transplants to psoriasis [22]. Thus cytokines (Th1, Th17 and Th22), chemokines, adhesion

molecules, growth factors like NGF, neuropeptides, and specific T cell subpopulations along with their receptors all act in an integrated way to evolve into unique inflammatory and proliferative processes typical of psoriasis.

The inflammatory infiltrates in the skin and joints have been studied extensively. In both tissues there are prominent lymphocytic infiltrates localized to the dermal papillae in the skin and the sublining layer stroma in the joint. T cells, with a predominance of CD4⁺ lymphocytes, are the most significant lymphocytes in the tissues; by contrast, this ratio is reversed in the epidermis, synovial fluid compartment, and at the entheses, where CD8⁺ T cells are more common [23–25]. This differential tropism of CD8⁺ T cells suggests that CD8⁺ T cells may be driving the immune response in the joint and skin. This is supported by an association of psoriasis with human leucocyte antigen (HLA) class I [10].

To summarize the immunopathologic features of a psoriasis plaque are unique [26]. Histological features of plaque psoriasis are: marked thickening of the epidermis, elongated epidermal rete pegs, parakeratosis, loss of the granular layer, suprapapillary thinning, microabscess of Munro (collection of neutrophils in the stratum corneum), spongiform pustule of Kojog (epidermal spongiform pustule with neutrophilic infiltration), dermal/epidermal CD3⁺ T cell infiltrates with epidermotropism of CD8⁺ T cells (Figs. 1 and 2). The histology of psoriatic subtypes may share classic dermal and epidermal features of a plaque psoriasis however, they may also display distinct histopathologic characteristics [26–28].

3. Diagnosis of psoriasis — the clinical spectrum, classification and diagnosis of psoriasis

3.1. The clinical spectrum

Clinical manifestations of psoriasis are protean. The primary skin lesions may vary from macules, papules, plaques to pustules. The disease may not necessarily be restricted to skin and nails. About 30% of patients may develop an inflammatory arthritis; and on occasions patients with psoriatic disease may also develop uveitis and inflammatory bowel disease. Furthermore, the presentation can vary drastically from patient to patient. The skin manifestations may be limited or extensive, monomorphic or polymorphic, and can appear at any age. Thus, psoriasis can be viewed as a spectrum of disease and because of this variability in clinical appearance, there are yet to be definite diagnostic criteria for psoriasis.

3.2. Disease classification

The disease spectrum or clinical phenotypes have been classified based on various features of psoriasis such as age of onset, degree of skin involvement, morphologic pattern and predominant involvement of specific anatomic location of the body [29–32]. Table 1 outlines the various clinical phenotypes that can be seen [29–32].

Table 1
Clinical classification of psoriasis.

Classification criteria	Clinical phenotypes
1. Age of onset	Type I psoriasis — age of onset before 40 years Type II psoriasis — age of onset before 40 years
2. Degree of severity according to body surface area (BSA) involvement or number of sites	Mild psoriasis <5% BSA Moderate psoriasis 5%–10% BSA Severe psoriasis >10% BSA Localized psoriasis/widespread psoriasis
3. Pattern of distribution	Inverse, flexor, seborrheic
4. Morphology	Plaque, guttate, erythrodermic, pustular (generalized/localized), rupioid, elephantine
5. Anatomical site	Scalp psoriasis, palmoplantar psoriasis, genital psoriasis, nail psoriasis, anal psoriasis
6. Stage of development	Stable plaque psoriasis Unstable eruptive psoriasis

3.3. Diagnosis

Because there are no diagnostic criteria for psoriasis the diagnosis of psoriasis is made clinically through pattern recognition that is careful morphologic evaluation of a skin lesion. Based on the morphology of the cutaneous lesions and anatomical locations psoriasis has been classified into various clinical phenotypes (Table 1). Clinical features of the different psoriasis subtypes are described in detail by Farber and Nall [33]. In the next section we will briefly describe the tell-tale diagnostic features of these conditions.

4. Clinical phenotypes of psoriasis

4.1. Plaque psoriasis

This is the commonest form of psoriasis, representing almost 90% of psoriatic patients [34] and is also known as psoriasis vulgaris. The lesions usually begin as erythematous macules or papules, extend peripherally, and coalesce to form plaques. The lesions are characterized by dry, sharply demarcated round/oval plaques with loosely adherent silvery white scales (Fig. 3A). Psoriasis plaques can appear at any part of the body but are generally distributed symmetrically over elbows and knees (Fig. 3A, B, C); and scalp may be the most common site of involvement [32].

In a patient with psoriasis, new lesions may appear following direct cutaneous trauma, which is known as the Koebner phenomenon. Another well-known feature of plaque psoriasis is Auspitz phenomenon, where mild disruption of the superficial layer of the lesion results in pinpoint bleeding.

4.2. Guttate psoriasis

Guttate psoriasis is characterized by the acute onset of round erythematous exanthem of generally less than 1 cm size over the trunk and extremities in a centripetal fashion. The characteristic morphologic features are: the lesions appear as droplets ('gutta'), they are monomorphic and at the same stage of evolution. Guttate psoriasis frequently affects children and adolescents following a streptococcal infection or an upper respiratory tract infection [35,36]. Generally the disease is self limiting, but a certain percentage of individuals may progress to chronic plaque psoriasis [35]. Patients that do have complete recovery from an episode of guttate psoriasis, still have a significantly higher risk for developing plaque psoriasis in the future [37]. Thus, it is not surprising that chronic plaque psoriasis and guttate psoriasis are genetically similar, with a strong association with the PSORS1 genetic locus [38,39].

4.3. Pustular psoriasis

Pustular psoriasis is characterized by multiple tender sterile pustules with an underlying, blotchy, erythematous base (Fig. 4A). Histologically, the lesions show diffuse dermal neutrophilic infiltration and



Fig. 3. Plaque psoriasis and erythrodermic psoriasis. A. Localized plaque psoriasis. B. Stable widespread symmetrically distributed plaques. C. Unstable widespread psoriasis progressing to erythroderma. D. Erythrodermic psoriasis.

intraepidermal micropustules. Various forms of pustular psoriasis have been described. Among these generalized pustular psoriasis (von Zumbusch) and localized pustular psoriasis are most well recognized [40,41] (Fig. 4A–D).

Acrodermatitis continua of Hallopeau and palmoplantar pustulosis are two distinct forms of localized pustular psoriasis. Acrodermatitis continua (Fig. 4D) is characterized by the pustular eruption of the fingers and toes [42]. Subsequently, the pustules become confluent and may spread proximally to involve the dorsal aspects of the hands (Fig. 4C) and feet. Patients may develop osteolysis of the distal phalanx (Fig. 4C) and the pustules may become generalized. *Palmoplantar pustular psoriasis* manifests as pustules on the palms and soles on an erythematous base and scaling. It is frequently associated with psoriatic nail involvement. Plaque formation is not typically seen in palmoplantar pustulosis, but it may be associated with psoriasis vulgaris.

Generalized pustular psoriasis is rare and represents an active, unstable disease. It has been reported that 20% of chronic plaque psoriasis patients may have pustular lesions during the course of the disease [43]. Acute generalized pustular psoriasis may be precipitated

by an infection, pregnancy, drugs, hypocalcemia, after an irritant topical treatment of plaque psoriasis or due to abrupt corticosteroid withdrawal [40,41,43,44]. Onset of an acute generalized pustular psoriasis is often associated with fever, myalgia, nausea, leukocytosis and characterized by erythematous tender skin [40,41]. Within hours, innumerable pustules appear on an erythematous base (Fig. 4A) and later pustules may confluent to create sheets of superficial pus (Fig. 4B). The pustules eventually desiccate and the lesions slough off leaving a shiny erythematous surface where new crops of pustules might appear. There may be geographic tongue, polyarthritides and cholestasis associated with generalized pustular psoriasis [45]. Patients with generalized pustular psoriasis are often severely sick, require hospitalization and close monitoring of their liver function, hypocalcemia and hydration. With supportive care and aggressive treatment pustular psoriasis may go into remission. Infrequently, pustular psoriasis can appear during the first six months of pregnancy, which is then referred to as *impetigo herpetiformis* [46].

4.4. Erythrodermic psoriasis

The clinical presentation consists of generalized erythema involving the majority of the body surface area (Fig. 3D). Erythrodermic psoriasis generally develops if there is poor control of a patient's existing psoriasis; abrupt withdrawal of systemic medication, such as corticosteroids; as a response to a drug reaction, such as lithium; or due to an underlying systemic infection [47,48]. Erythrodermic psoriasis in a patient with preexisting psoriasis may not be difficult to diagnose. However erythroderma can be a life threatening condition and the following conditions should be considered in the differential diagnosis: drug rash, atopic dermatitis specially in children, air borne contact dermatitis, Sezary syndrome and pityriasis rubra pilaris. In an undiagnosed patient of erythroderma the nail changes may be indicative of erythrodermic psoriasis. Also skin biopsy may helpful for diagnosing psoriasis and to rule out other diseases as mentioned above.

4.5. Phenotypes of psoriasis according to involvement of anatomical location

4.5.1. Scalp psoriasis

The scalp is a well-known predilection site for psoriasis [32]. Scalp psoriasis around the hairline, can cause significant impairment in quality of life due to its visibility. Particular challenges in managing scalp psoriasis include choosing an appropriate treatment option, difficulties of applying topical treatments and deciding how to treat severe disease [49].

4.5.2. Inverse/flexural psoriasis

In contrast to its preferred external surfaces such as on knees and elbows psoriasis may appear on the flexor surfaces and in the skin folds such as on perineal, inframammary, axillary, inguinal, and intergluteal areas. As these areas are moist psoriasis is less scaly than the plaque form of psoriasis.



Fig. 4. Pustular psoriasis. Generalized pustular psoriasis (A and B). A. Initial discrete pustular lesions on an erythematous base. B. Generalized pustular psoriasis of von Zumbusch. C. Acrodermatitis continua — pustular psoriasis of hands with erythema, scaling and osteolysis of the distal phalanges in the right hand. D. Acrodermatitis continua — severe pustular psoriasis of the fingers.

4.5.3. Plamopllantar psoriasis

Painful fissures and thick scales in nonpustular palmoplantar psoriasis can be a disabling condition [50]. Treatment of recalcitrant palmoplantar psoriasis is a clinical challenge. Preventive measures such as use of emollients at night, and avoiding friction and irritants can reduce the morbidity of this condition.

4.5.4. Genital psoriasis

Psoriasis of the genitalia occurs in all age groups from infants to the elderly. Nearly one-third of patients with psoriasis suffer from genital psoriasis [51]. Special attention is required in this form of psoriasis as it significantly affects quality of life in both men and women.

4.5.5. Nail psoriasis

Nails are commonly involved in psoriasis and on occasion their characteristic changes can fetch the diagnosis of psoriasis [52]. Current treatment options for nail psoriasis are limited and often poorly efficacious [53]. Pitting of nails is the most characteristic feature whereas onycholysis or the detachment of the proximal part of the nail from the nail bed is the most common nail abnormality in psoriasis. Involvement of the nail bed is often represented by the appearance of “oil spots” or orange-yellow areas beneath the nail plate. Moreover, the nail plate may become, thickened, dystrophic, discolored and yellow, and keratinous material may collect under the nail plate, which is known as subungual hyperkeratosis.

5. Conclusion

Psoriasis is a multifactorial disease. Psoriasis may present in many different forms and may include extracutaneous manifestations. Currently there are no established diagnostic criteria for psoriasis [29]. Classification schemes are based on the various clinical phenotypes, on the age of onset, disease severity, and disease morphology. Despite such a broad clinical spectrum, a trained clinician is fully capable of diagnosing psoriasis and its various phenotypes. However, this does not mean that psoriasis as a disease does not need diagnostic criteria. We echo and endorse the views of Naldi and his group that there should be an internationally coordinated approach to develop standardized diagnostic criteria for psoriasis [29].

6. Contributions

SKR and SPR have designed the paper. SPR has provided the figures from his research work. SKR, EM and SPR have together written this manuscript. This material is the result of work that was supported by resources from the VA Northern California Health Care System, Sacramento, California. The contents reported/presented within do not represent the views of the Department of Veterans Affairs or the United States Government.

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