A review on Clinical Complication and Treatment Challenges In the management of psoriasis

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Psoriasis is a chronic, immune-mediated inflammatory skin disorder characterized by hyperproliferation of keratinocytes and systemic comorbidities. This review critically examines the clinical complications and therapeutic challenges associated with psoriasis, focusing on psoriasis vulgaris, the most prevalent form. The pathogenesis of psoriasis involves a complex interplay between genetic predisposition, environmental factors, and dysregulated immune responses, particularly the IL-23/Th17 axis. The review outlines the various clinical phenotypes, epidemiological patterns, and comorbidities such as psoriatic arthritis and cardiometabolic diseases. It also evaluates conventional treatments, including topical corticosteroids, vitamin D analogues, calcineurin inhibitors, and keratolytics, as well as systemic and biologic therapies for moderate to severe cases. A detailed exploration of vitamin D analogues highlights their mechanisms, clinical efficacy, safety profiles, and limitations. The findings underscore the need for individualized treatment strategies, long-term disease monitoring, and further research into safer and more effective therapies targeting underlying immunological pathways.

Keywords:

Psoriasis vulgaris, skin biology, pathophysiology, IL-23/Th17 axis, chronic inflammation, skin microbiota, epigenetics, targeted therapy, immune cells, dendritic cells, SALT (skin-associated lymphoid tissue), transcriptomics, autoimmune skin diseases, cytokine pathways, comorbidities, murine models.

Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disease that significantly impacts the physical and psychological well-being of affected individuals. It is primarily characterised by keratinocyte hyperproliferation, epidermal thickening, and erythematous, scaly plaques,

most commonly observed in psoriasis vulgaris—the most prevalent form of the disease. The underlying pathophysiology involves a complex interaction between genetic predisposition, environmental triggers, and dysregulated immune responses, particularly those mediated by T cells and dendritic cells.

Recent research has revealed that psoriasis is not merely a localized skin condition but a systemic disorder with various comorbidities, including psoriatic arthritis, cardiovascular disease, and metabolic syndrome. This has positioned psoriasis as a significant public health concern due to its chronic nature, potential for systemic involvement, and substantial burden on patients' quality of life.

The immune system plays a central role in psoriasis pathogenesis. Aberrant activation of the innate and adaptive immune pathways leads to sustained inflammation and pathological changes in skin architecture. Key players include epidermal keratinocytes, which act as both targets and mediators of inflammation, and immune cells such as Th17 cells, which secrete pro-inflammatory cytokines like IL-17 and IL-23. These insights have paved the way for the development of targeted biologic therapies that offer improved outcomes compared to traditional treatments.

This review aims to provide a comprehensive overview of the clinical features, complications, and therapeutic challenges associated with psoriasis. Special emphasis is placed on the efficacy and safety of vitamin D analogues, as well as the evolving landscape of topical and systemic therapies. By examining the immunological mechanisms, treatment modalities, and associated risks, this work seeks to contribute to a better understanding of psoriasis management and highlight the need for continued innovation in therapeutic approaches

Aetiology

A British dermatologist named Willan is credited with providing the first exact description of psoriasis, which helped to identify the condition. due to leprosy. One of the few skin conditions that is frequent and different enough for medical students (and the majority of clinicians) to notice it, psoriasis is still somewhat of a mystery. Understanding the natural history and prognosis of the illness, as well as defining the clinical phenotypes of psoriasis, have received very little study. We now have a far better grasp of the genetics and path mechanisms of psoriasis than we had 25 years ago. The question of whether psoriasis is an autoimmune condition is still up for debate. Psoriasis causes a significant reduction in quality of life, which has only recently been acknowledged by academics and physicians, leading to an

understanding that the condition has a significant negative impact on productivity in individuals who are affected.

Clinical features

90% of all instances of psoriasis are of the most common kind, psoriasis vulgaris, in which papulosquamous plaques are clearly separated from the surrounding normal skin. The plaques can be thick, thin, huge, or little, and are red or salmon pink in hue. They are coated in white or silvery scales. In quickly growing lesions, the normal skin may be annular in shape and more active near the edges. The extensor surfaces of the elbows and knees, the scalp (although they seldom extend below the hairline), the lumbosacral area, and the umbilicus are where plaques most frequently develop. The Koebner phenomenon, wherein new lesions appear at locations of stress or pressure, is what distinguishes active inflammatory psoriasis.

There are regional variations in psoriasis vulgaris. Sebopsoriasis, which can be mistaken with seborrheic dermatitis, contains greasy scales and affects the eyebrows, nasolabial folds, postauricular area, and presternal sites. Flexural (inverse) psoriasis is glossy, red, and often without scales in intertriginous sites. It is likely that there is multiple closely related but genetically and phenotypically diverse forms of psoriasis vulgaris,4 which might explain the variation in therapeutic response, particularly with T-cell focused biological agents.

Known as guttate psoriasis (from the Latin gutta, meaning droplet), children and adolescents can develop an acute form of psoriasis in which papules less than 1 cm in diameter appear on the trunk two weeks after contracting a viral infection or a haemolytic streptococcal infection, such as tonsillitis or pharyngitis. Although the long-term prognosis of guttate psoriasis is uncertain, it is self-limiting and resolves within 3–4 months of initiation. According to one research, only one-third of those with guttate psoriasis progress to conventional plaque disease.

Epidemiology

Because there are no standardised diagnostic criteria, it is difficult to determine the prevalence of psoriasis. Additionally, rates differ significantly among individuals from different ethnic backgrounds: The majority of cases of psoriasis are found in white individuals, although the condition is thought to affect only 3% of the population overall in China and is either nonexistent or extremely rare in some isolated tribes.

Latitude also appears to have an impact on prevalence, most likely as a result of the beneficial effects of sunshine on the illness. However, psoriasis is thought to affect both men and women

equally throughout Northern Europe and Scandinavia, with prevalence rates between 5% and 3% of the general population. Estimated incidence rates for white people are 60 incidences for every 100,000 people annually.

The onset of psoriasis can occur at any age. However, psoriasis vulgaris was recently found to have a mean onset age of 33 years, with 75% of cases developing before the age of 46.14 According to some research, the beginning is bimodal, with peaks occurring between the ages of 16 and 22 and later, between the ages of 57 and 60. Women appear to have symptoms at a little younger age than do males.

Although psoriasis can appear at any age, there is a bimodal age distribution for psoriasis presentation between the ages of 18 and 39 and also between the ages of 50 and 69.12The age at which psoriasis first appears may be influenced by environmental and genetic variables. As an illustration, the human leukocyte antigen (HLA)-C*06 allele is connected to early age of psoriasis onset.

Genetic factor:

The examination of the relationship between psoriasis and genetic markers (i.e., seroepidemiologic research) has also been done using the case-control technique. These studies have undergone several reviews. The primary predictor of psoriasis vulgaris is the PSORS1 locus in the major histocompatibility complex area. Recent research has shown that whereas palmoplantar pustulosis does not share the same connection with PSORS1, guttate psoriasis does.

Genetic approaches, based on statistical models of the distribution of genetic features in the general population and in chosen family members, enable a more systematic examination of genetic determinants and inheritance patterns when compared to epidemiologic study. When a multifactorial model of inheritance is proposed, heritability, a statistic based on statistical methods of analysis of variance, estimates the total contribution of genetic components, i.e. A linear relationship between independent genetic and environmental variables determines phenotypic. The statistical model makes the assumption that the risk of illness is determined by an underlying continuous attribute (referred to as "liability") while the phenotypic is discrete (i.e., afflicted vs unaffected). Heritability is measured as a ratio with values between 0 and 1.0. Based on population data and an investigation of twin concordance, measures of the heredity of psoriasis have been published.

Personal habits:

The use of alcohol and smoking have drawn considerable attention recently. The more persuasive evidence comes from studies that look at the exposure before to the development of psoriasis and account for the link between the exposure factors, namely alcohol and smoking. A case-control study of 216 individuals with palmo plantar pustulosis in Scotland found that the risk for smokers was substantially higher than the risk for non-smokers. It's unclear how this illness is related to psoriasis.

Drugs and infections:

Many medications, including lithium salts, beta-adrenergic blockers, antimalarials, NSAIDs, and the discontinuation of steroids, have been reported to cause the onset or exacerbation of psoriasis. To the best of my knowledge, there are just two formal studies that evaluate pharmacological hazards. The first one is the cohort research on the pill that the Royal College of General Practitioners undertook with 23,000 users and a comparable number of non-users. The study disproved a strong link between the pill and psoriasis. Another study suggests that calcium channel blockers may be linked to the start and/or worsening of psoriasis. It had 150 patients and 150 controls.

Symptoms

The most prevalent kind of psoriasis is plaque psoriasis. Dry skin plaques coated in scales are one of its symptoms. They can appear anywhere on your body, but they typically appear on your elbows, knees, scalp, and lower back. The plaques may itch, hurt, or have both. Your skin surrounding your joints may break and bleed if the condition is severe.

Some common symptoms are:

- A patchy rash that appears quite differently on each individual, ranging from little areas of dandruff-like scaling to significant eruptions across a large portion of the body.
- Variable-colored rashes with a preference for purple hues with grey scale on brown or black skin, and pink or red with silver scale on white skin.
- Small areas of scaling (often noticed in youngsters).
- Bruising skin that is dry and cracked.
- Soreness, burning, or itching.
- recurring rashes that peak for a few weeks or months before going away.

Clinical presentation

Depending on the psoriasis variant, psoriasis clinical characteristics vary. Plaque, guttate, erythrodermic, and pustular psoriasis are some of the several types of psoriasis. Different variants may coexist in a person at any given time, even though one variant typically predominates in a given person. Erythema, thickness, and scale are the three main clinical characteristics that the majority of psoriasis types share. The clinical appearance of plaque psoriasis is highlighted in this study since it is the most prevalent kind.

Plaque psoriasis

Plaque psoriasis, the most prevalent kind of psoriasis, results in scale-covered, dry, elevated skin patches (plaques). They might be few or numerous. They typically show up on the scalp, lower back, elbows, and knees. Depending on the skin tone, the patches have different colours. On dark or Black skin, the afflicted skin may recover with transient colour changes (postinflammatory hyperpigmentation). Approximately 80% to 90% of all psoriasis manifestations are plaque psoriasis. Sharply defined, erythematous, scaly plaques or patches are the hallmarks of plaque psoriasis. While plaque psoriasis can affect any part of the body, the scalp, trunk, gluteal fold, and extensor surfaces like the elbows and knees are frequently affected. Large thick plaques and small erythematous and scaly papules are both possible lesions in plaque psoriasis. Affected regions are often well defined and frequently symmetrical. New psoriasis lesions may appear at the site of trauma, such as scratching, wounds, or pressure, in the case of the Koebner phenomenon. An Auspitz sign may develop as a result of localised bleeding that happens when the scale is removed from the plaque. Patients with moderate to severe psoriasis or during an exacerbation may have significant itching.

Plaque psoriasis, also known as inverse psoriasis, refers to psoriasis affecting the skin folds, such as the axillary, inframammary, and vaginal regions, and has a disproportionately negative impact on quality of life when it affects specific areas, such as the face, palms and soles, nails, or intertriginous areas. Intertriginous psoriasis lacks the usual scales observed with psoriasis in nonintertriginous places due to the wet skin environment in which it develops, and it is sometimes mistaken for a fungal infection. About one-third of people with psoriasis develop genital psoriasis, which is associated with a significantly lower quality of life. Patients who have plaque psoriasis on their palms and soles develop painful, thick, scaly plaques that impair their ability to use their hands and feet normally. Pitting, onycholysis (separation of the nail

plate from the nail bed), and dystrophy of fingernails and toenails are all symptoms of psoriasis that can damage the nail apparatus. The causes of psoriasis in the majority of people remain unknown.

Objective

The primary objective of this review is to comprehensively explore the clinical complications and therapeutic challenges associated with the management of psoriasis, with a special focus on psoriasis vulgaris. By examining the pathophysiology, genetic and environmental triggers, and comorbidities linked with the disease, this study aims to shed light on the complex interplay of immune-mediated processes driving psoriasis. Furthermore, it seeks to evaluate the efficacy, safety, and mechanisms of current treatment modalities, especially topical therapies like vitamin D analogues, corticosteroids, and newer biological agents. A particular emphasis is placed on the role of vitamin D analogues in regulating keratinocyte proliferation and differentiation. This review also aims to highlight emerging therapeutic approaches that may offer improved outcomes and fewer side effects for patients with moderate to severe psoriasis.

Discussion

Psoriasis is a chronic, immune-mediated inflammatory skin disorder characterized by the abnormal proliferation and differentiation of keratinocytes, primarily driven by dysregulated T-cell activity and dendritic cell interactions. Among its various clinical forms, plaque psoriasis (psoriasis vulgaris) is the most prevalent, affecting up to 90% of diagnosed cases. The onset and severity of psoriasis are influenced by multiple factors, including genetic predisposition (notably HLA-Cw6), environmental triggers (such as infections, trauma, and stress), and lifestyle habits like smoking and alcohol use.

A significant development in the understanding of psoriasis pathophysiology is the identification of IL-23/Th17 axis as a major driver of chronic inflammation. This has led to the introduction of biologic agents that specifically target cytokines such as TNF-α, IL-17, and IL-23, offering improved clinical outcomes for patients with moderate to severe psoriasis. However, these treatments are costly and may be associated with systemic immunosuppression, limiting their use in broader populations.

Topical therapies remain the cornerstone of treatment for mild to moderate psoriasis. Among these, vitamin D analogues, particularly calcipotriol and calcitriol, have emerged as safe and

effective options. These agents exert their therapeutic effects by inhibiting keratinocyte hyperproliferation and enhancing their differentiation, while also modulating local immune responses. Clinical studies demonstrate that calcipotriol, when used within recommended dosages (not exceeding 100g per week), provides significant symptom relief with minimal risk of systemic side effects such as hypercalcemia. Combining calcipotriol with corticosteroids has also been shown to improve efficacy while reducing irritation.

Despite the efficacy of vitamin D analogues, several limitations remain. Skin irritation, especially in sensitive areas like the face and folds, can restrict their use. Moreover, the long-term safety of these treatments, although promising, requires further large-scale studies. For more severe cases, systemic therapies and biologics are preferred. However, treatment adherence, cost, and side effect profiles continue to pose challenges.

Another layer of complexity in psoriasis management lies in its comorbidities, particularly psoriatic arthritis, cardiovascular diseases, and psychological disorders such as depression and anxiety. These associations highlight the systemic nature of psoriasis and necessitate a holistic, multidisciplinary approach to treatment.

Conculsion

Psoriasis is an inflammatory skin condition that significantly lowers patients' quality of life and is linked to other comorbidities. The mainstay of treating mild psoriasis continues to be topical treatments. Therapeutic breakthroughs for moderate to severe plaque psoriasis include oral phosphodiesterase 4 inhibitors and biologics that suppress TNF-, p40IL-12/23, IL-17, and p19IL-23. The most easily treatable and well-known condition affecting humans is psoriasis vulgaris. by DCs and T cells. The availability of certain immune antagonists and the capacity to assess cellular and molecular inflammatory pathways in sick human tissue Compared to disorders like rheumatoid arthritis, Crohn's disease, or multiple sclerosis that are less accessible, relevant disease-related pathways have made it possible to deconstruct pathogenic circuits to a considerably greater extent. The common p40 subunit of IL-12/-23, the p19 subunit that identifies IL-23, and the IL-23 receptor are particularly well matched with components of hereditary risk and are therefore prime targets for both existing and new therapeutic immune antagonists.

To sum up, it has been shown that psoriasis is an immunological condition, and current results suggest that HLA-Cw*0602 may have a significant pathogenic impact on the majority of

psoriasis sufferers. It is suggested that the primary effector cells are cross-primmed antigenspecific CD8+ T cells that recognise the autoantigen(s), although CD4+ T cells are important for initiating and maintaining the illness. Additionally, it is hypothesised that CD8+ T cells regulate the Th1 polarisation seen in psoriasis lesions and that variations in psoriasis severity, including the frequent spontaneous remissions of guttate psoriasis, can be attributed to shifts in the ratio of CD4+ to CD8+ effector and regulatory cell subsets.

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