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PSORIASIS AND ITS COMORBIDITIES: A REVIEW

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ABSTRACT

Psoriasis is a common chronic systemic inflammatory disease that not only affects the skin but also other body systems. Studies show that psoriasis can leave individuals vulnerable to other diseases. The purpose of this review is to show the correlation between psoriasis and its comorbidities. The pathophysiology that links psoriasis with other diseases such as psoriatic arthritis, cardiovascular diseases, gastrointestinal disorders, autoimmune diseases, and psychiatric and neurological disorders. Psoriasis patients have been reported to have a higher prevalence of these conditions than non-psoriasis patients. The identification of the presence of comorbidities is essential for finding the best choice of therapy for psoriasis and ensuring that the treatment of psoriasis does not conflict with the management of its comorbid conditions and vice versa.

KEYWORDS: Psoriasis, Comorbidities, Systemic inflammation, Cardiovascular disease, Psoriatic arthritis, Obesity.

INTRODUCTION

Psoriasis represents a chronic, immune-mediated inflammatory disease classically manifesting as well-demarcated erythematous plaques with silvery scales on the skin surface.[1] While traditionally regarded as a purely dermatologic condition, extensive research over the past two decades has fundamentally transformed the understanding of psoriasis into a systemic disorder with far-reaching consequences beyond cutaneous involvement.[1,2] The disease pathogenesis involves a complex interplay of genetic susceptibility (particularly polymorphisms in HLA-Cw6 and IL23R genes).[3,4] environmental triggers (such as stress,

infections, and trauma).[5,6] and dysregulated immune responses characterized by Th17 cell activation and overexpression of proinflammatory cytokines including IL-17, IL-23, and TNF-α.[7]

This systemic inflammation underlies the significant comorbidity burden observed in psoriatic patients, particularly those with moderate-to-severe disease.[8] Robust epidemiological evidence demonstrates strong associations between psoriasis and cardiovascular diseases (including a 3-fold increased risk of myocardial infarction).[3] metabolic disorders (notably a 4-fold elevated risk of type 2 diabetes mellitus)[3,9] autoimmune conditions (especially psoriatic arthritis occurring in approximately 30% of patients).[10] and psychiatric comorbidities such as depression and anxiety disorders.[11] The metabolic dysregulation in psoriasis patients frequently manifests as a distinct cluster including central obesity, atherogenic dyslipidemia, insulin resistance, and non-alcoholic fatty liver disease (NAFLD), creating a proatherogenic milieu that substantially amplifies cardiovascular risk.[5]

Alarmingly, population-based studies from the United Kingdom reveal that patients with severe psoriasis may experience reduced life expectancy by approximately six years compared to matched controls, primarily attributable to accelerated cardiovascular morbidity.[12] This mortality gap appears particularly pronounced in elderly populations, where psoriatic patients over 65 years demonstrate markedly increased prevalence of hypertension, left ventricular hypertrophy, and abnormal glucose metabolism, with nearly half presenting with at least three major comorbidities.[3] The cumulative impact of these systemic manifestations necessitates a paradigm shift in clinical management from purely dermatologic care to comprehensive risk stratification and multidisciplinary intervention.[13] Current guidelines emphasize the importance of early disease detection, regular screening for associated conditions particularly cardiovascular and metabolic disorders, and selection of systemic therapies that simultaneously address cutaneous inflammation while mitigating systemic comorbidities, such as IL-17 inhibitors which may improve both psoriatic plaques and endothelial dysfunction.[14]

PSORIASIS AND OBESITY

Psoriasis and obesity fuel each other in a harmful cycle where each condition worsens the other.[15] Research shows that obesity can trigger the development of psoriasis, while the

chronic inflammation from psoriasis contributes to weight gain.[14] Breaking this cycle requires addressing both conditions together.

How Inflammation Connects Psoriasis and Obesity

The key link lies in how fat tissue functions. Fat isn't just an inert storage depot—it acts as an active organ that releases inflammatory signals.[12] In obesity, fat cells produce excessive amounts of pro-inflammatory molecules (such as leptin and resistin).[12] while reducing beneficial anti-inflammatory ones (like adiponectin).[3] These changes trigger immune responses that worsen psoriasis flare-ups.[12] At the same time, psoriasis creates its own inflammatory cascade.[12] The same immune proteins responsible for skin inflammation (including IL-17 and TNF-α) also interfere with the body's ability to metabolize sugars and fats.[12] This double burden of inflammation explains why people with both conditions often experience more severe symptoms and poorer treatment responses.[3,12]

Key statistics

- People with obesity have a nearly 50% higher risk of developing psoriasis.[16]
- Severe psoriasis (i.e. >20% body surface area) has an even stronger association with obesity.[3]

Research shows that people with mild psoriasis are 46% more likely to be obese than the general population.[15] For people with severe psoriasis, the risk soars: they have more than double the odds (123% higher) of being obese.[15]

Research also suggests that psoriasis patients are 18% more likely to develop obesity as their condition advances even if they didn't initially have obesity.[15] Over time, chronic inflammation, decreased exercise because of joint pain or even psychological stress could cause the balance to shift.[15]

Weight loss can lead to significant improvements in psoriasis.[12] Studies show dramatic skin clearance in patients after gastric bypass surgery.[5] Even moderate lifestyle changes—such as a healthier diet and regular exercise—can reduce psoriasis severity while lowering the risk of related conditions like diabetes and heart disease.[5]

PSORIASIS AND PSORIATIC ARTHRITIS

Psoriasis and psoriatic arthritis (PsA) closely related conditions that often go hand in hand.[10] Research shows that about 1 in 3 people with psoriasis will eventually develop PsA, a painful joint condition that can significantly impact quality of life.[10]

At their core, both conditions stem from similar overactive immune responses.[10] Scientists have identified several key players: the same inflammatory chemicals (IL-23, IL-12B [5]) drive both skin and joint symptoms, certain genetic markers make people more susceptible to developing both conditions.[17]

For most patients, psoriasis comes first - typically by about 12 years.[17] But some important patterns have emerged: people with more extensive skin involvement are at much higher risk, those with nail or scalp psoriasis are particularly likely to develop joint problem.[13] Sometimes, PsA cases occur without noticeable skin symptoms, making diagnosis tricky. About 15% of patients suffering from psoriasis have undiagnosed PsA.[18]

Psoriatic arthritis is diagnosed using the CASPAR (Classification Criteria for Psoriatic Arthritis) criteria which utilise unique clinical cues like psoriatic nail changes (eg, pitting or separation), a negative rheumatoid factor serum test, swelling of whole fingers or toes (dactylitis) and X-ray evidence for bone growth abnormalities (bone spurs) adjacent to joints.[14] While CASPAR is incredibly specific (99.1%)—so much so that it's generally considered to be one of the definitive tests for confirming whether a patient has PsA—it has moderate sensitivity (87.4%), meaning it could miss some early-stage cases.[14] Consequently, it works best as a diagnostic confirmation mechanism, not as an initial screen.[14] It aids clinicians in differentiating psoriatic arthritis from other forms of arthritis, such as rheumatoid arthritis or osteoarthritis.[14]

There are, currently, about 17 targeted therapies which are used to address and manage PsA.[19] Medications targeting IL-12 or IL-23 show particular promise while traditional TNF inhibitors (TNFi) continue to be effective options.[19]

PSORIASIS AND NONALCOHOLIC FATTY LIVER DISEASE(NAFLD)

Current evidence demonstrates a significant association between psoriasis and nonalcoholic fatty liver disease (NAFLD), with a bidirectional relationship mediated by shared inflammatory pathways and metabolic disturbances.[5] Studies indicate that psoriasis patients

exhibit more risk of developing NAFLD compared to the general population, while the presence of NAFLD may exacerbate psoriasis severity.[17]

Systematic reviews report NAFLD prevalence of 47% in psoriasis populations versus 28% in matched controls.[20]

Pathophysiological Mechanisms

Three primary pathways underlie this association

1. Inflammatory Mediators:

- Elevated IL-17, TNF-α, and IL-23 promote both hepatic steatosis and keratinocyte proliferation.[13]
- Dysregulated adipokines (increased leptin, decreased adiponectin) contribute to insulin resistance.[12]

2. Metabolic Dysfunction:

- Characteristic lipid abnormalities include elevated triglycerides and reduced HDL cholesterol.[3]

3. Genetic Predisposition

- Polymorphisms in IL-23R genes increase susceptibility to both conditions.[13]

Ultrasound or transient elastography (FibroScan®) recommended for high-risk patients and regular monitoring advised for patients with metabolic risk factors.[5] TNF-α inhibitors may improve both dermatological and hepatic parameters.[15] IL-17/23 inhibitors demonstrate favorable safety profiles in NAFLD.[15] Methotrexate requires careful hepatotoxicity monitoring.[17] and lifestyle modification remains cornerstone therapy.[5]

PSORIASIS AND CARDIOVASCULAR DISEASE

Emerging research has established that psoriasis represents a systemic inflammatory disorder with important implications for cardiovascular health[1] Psoriasis patients face substantially higher risks of developing coronary artery disease, experiencing heart attacks, and suffering strokes, independent of traditional risk factors.[1] This connection arises from overlapping inflammatory processes, genetic factors, and metabolic disturbances that affect both conditions.[1]

Patients with severe psoriasis experience about 53% greater likelihood of major cardiovascular events compared to those with mild psoriasis or healthy individuals.[15]

Patients with severe psoriasis have, according to meta-analyses, a 70% increased risk of myocardial infarction (heart attack), a 56% greater risk of stroke and a 39% higher risk of dying from cardiovascular causes.[15] In addition to these acute events, psoriasis is associated with chronic vascular disease.[15] For instance, psoriasis patients have 78% greater risk of ischemic heart disease and over 2 times greater risk of arteriosclerosis than the general population.[15]

The hazards extend to heart rhythm disorders and cerebrovascular events.[15] Patients with severe psoriasis have almost double the risk of atrial fibrillation (97% higher incidence) and more than twice the risk of ischemic stroke (123% higher incidence) compared to healthy individuals.[15] Even mild psoriasis raises these risks, though to a lesser extent.[15]

Two primary mechanisms explain this association

1. Shared Inflammatory Pathways

The same immune system overactivity that drives psoriasis (particularly through IL-12 and TNF-α) also damages blood vessels and promotes dangerous plaque formation in arteries.[17] Additionally, imbalances in fat-derived hormones (like elevated leptin and reduced adiponectin) worsen both skin inflammation and vascular health.[3]

2. Proinflammatory Cytokines

Proinflammatory cytokines like IL-1, IL-6, IFN-gamma and TNF-α, increase susceptibility to both psoriasis and coronary artery disease.[3]

Notably, psoriasis patient's "good" HDL cholesterol often doesn't function properly, failing to protect against artery clogging.[12]

Standard cardiovascular risk calculators often underestimate risk in psoriasis patients, making advanced imaging like coronary calcium scoring valuable for early detection.[15] TNF inhibitors (e.g., adalimumab) may reduce cardiovascular risk while treating skin symptoms, while IL-17/23 inhibitors (e.g., secukinumab) appear heart-safe but require long-term study.[12] Even methotrexate shows potential cardiovascular benefits, underscoring the need for personalized treatment selection.[17]

CONCLUSION

Psoriasis is much more than just a skin disease; it is a systemic inflammatory disease with significant multisystem consequences. The robust associations with cardiovascular disease,

metabolic syndrome, psoriatic arthritis, and NAFLD underscore the need for a multidisciplinary approach to patient care. Timely diagnosis and treatment of these comorbidities is imperative as focused treatment can result in improvement in both cutaneous and systemic manifestation. Future studies aimed to investigate common pathogenic mechanisms might help to optimize therapeutic strategies and alleviate the burden of comorbidities responsible for the significant morbidity and mortality in psoriatic patients. Such holistic and patient-centered approaches integrating perspectives from both dermatology and internal medicine will be necessary to enhance long-term outcomes.

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