Psoriasis as Autoinflammatory Disease

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KEYWORDS

• Psoriasis • Autoinflammatory disease • Genetics • Immunopathogenesis • TH cells • TNF-α • Cytokines • Inflammasome

KEY POINTS

- Psoriasis immunopathogenesis.
- Inflammatory cycle.
- Psoriasis causes and genetic and clinical features.
- Autoinflammatory versus autoimmune.
- Role of Th1-Th2 activation and balance on psoriasis.
- T-cell activation.
- Pathogenic mechanisms of self-immunity.
- Immune links of psoriasis to autoinflammation.
- Inflammasome-mediated inflammation.

INTRODUCTION

This article presents a summary of the evidence that can be used to establish a link between the recently introduced autoinflammatory diseases (AIDs) and psoriasis, a member of the papulosquamous disorders, the primary lesions of which are characterized by scaly plaques. These entities have some common characteristics among their phenotypic features, genetic components, and the mechanism of tissue damage exerted through intricate immunopathologic pathways and players.

The main concepts regarding the disease state of psoriasis are discussed and these lead to the establishment of a link that can change the perspective on the clinical and pathophysiologic nature of psoriasis as a chronic, recurrent disease with important genetically defined features, and an associated or concomitant systemic inflammatory state that involves a multifactorial cellular and molecular network, transforming the old perception of psoriasis as a localized autoimmune skin disease, to the new perspective of psoriasis as a systemic inflammatory disease with autoinflammatory features and severe associated comorbid conditions.

The extension of the skin lesion to a systemic inflammatory stage, as shown in several studies and publications, manifests in different body systems, creating the need for a more comprehensive approach to the affected patients.

From the point of view of several investigators, the concurrent inflammation seen in the different types of psoriasis compromises innate and adaptive immune system components and has a well-defined network of chemokines and messengers that can be compared with the cellular and chemical networks found in the patient with AID, requiring the identification of the possible links between them and the subsequent potential consideration of psoriasis as an AID.

Several years of intense studies of the pathogenic components, immune mediators, and involved

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pathways of psoriasis enhanced knowledge about the disease state and its clinical associated conditions. The concept of activated T cells has gained a key role, suggesting autoimmunity as a basic mechanism of the disease. In later publications and discoveries, after evaluating the different psoriasis phenotypes, analysis of the variable course of the disease with periodic outbreaks, as well as results from immunotyping studies, justified an extension of the autoimmunity concept. Current evidence establishes that innate immunity and autoinflammation play significant roles.

AIDS: A NEW CATEGORY

The AIDs, a concept recently introduced in the medical literature, are a category of illnesses characterized by seemingly unprovoked episodes of inflammation, without high-titer autoantibodies or antigen-specific T cells, in which, as in the autoimmune diseases, the capability of self-recognition is disturbed, initiating an attack on the body's own tissues. The distorted and abnormal response generates a cellular network with the implicated chemokine chain reaction that, in turn, generates an inflammatory response. The mechanisms for which the inflammation is generated and the abnormal action of the innate immune system are currently not completely understood. In 2008, Yao and colleagues[1] proposed the new classification, with the identification of the genes underlying hereditary components associated with gene mutations for the periodic fever syndromes. Soon after the new nosology was proposed, Masters and colleagues[2] published an article in which 6 categories of AIDs were defined: interleukin (IL)-1β activation disorders (inflammasomopathies), nuclear factor (NF)-κB activation syndromes, protein misfolding disorders, complement regulatory diseases, disturbances in cytokine signaling, and macrophage activation syndromes. More conditions, mostly included because of their clinical manifestations, have recently been added to the classification, with a special consideration of their complexity and their heritable linkage.[3–5] Details of the newest classification are discussed elsewhere in this issue by Abramovits. The diseases are characterized by spontaneous activation of cells of innate immunity in the absence of ligands. Autoantibodies are usually not found.[6]

AUTOIMMUNE VERSUS AUTOINFLAMMATORY

Differentiated by the absence or presence of specific antibodies, the activation of different immune systems, and their genetic features, the disorders share common characteristics in that both result from the immune system targeting and aggressively injuring self-tissues, with a resulting increased inflammation as an expression of the tissue damage mechanisms. These common grounds could create confusion in diagnosis. This conceptualization was defined by The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), a part of the US Department of Health and Human Services, National Institutes of Health (NIH), in March 2010[7] (discussed later). Their publication established several different types of AID.

The mechanism for which the local or systemic damage is produced in autoinflammatory syndromes is complex, involving cellular and cytokine networks, and probably involves a systemic disruption of the molecular basis of mediating and controlling inflammation. These disorders were defined, until recently, by phenotypic features, including recurrent attacks of fever, abdominal pain, arthritis, or cutaneous signs, which occasionally overlap inducing doubts and consequently an inaccurate diagnosis. To date, the improved knowledge of the pathophysiology, the mechanisms of the disease, and the molecular effects of the mediators has allowed an expansion of their classification.

Autoimmune disorders are a consequence of an inappropriate immune response of the body against substances and tissues whose presence is recognized as normal in the body. The immunologic hallmark is the formation of specific antibodies against the target organ or tissue; the immune system mistakes some part of the body as a pathogen and attacks its own cells. This response may be restricted to certain organs (eg, in autoimmune thyroiditis) or involve a particular tissue in different places (eg, Goodpasture disease, which may affect the basement membrane in both the lung and the kidney).

It is important not to confuse autoinflammatory syndromes with autoimmune diseases, which are caused by the body's adaptive immune system developing antibodies to antigens that then attack healthy body tissues.[7] Autoimmunity and autoinflammation share some common characteristics: both lead to self-directed inflammation, but with different mechanisms. Although autoimmunity involves adaptive immune activation, autoinflammation involves innate immune activation. Autoinflammation is genetically related to perturbations of innate immune function, including proinflammatory cytokine signaling abnormalities, or bacterial sensing, or local tissue abnormalities. The clinical and pathophysiologic expressions of autoinflammation are determined