Etiology and Pathogenesis of Psoriasis

Wolf-Henning Boehncke, MD[a,b,*]

KEYWORDS

• Psoriasis • Genome-wide association study • Etiology • Pathogenesis • IL-17 • T lymphocytes • Dendritic cells • Keratinocytes

KEY POINTS

- Psoriasis is characterized by the parallel appearance of epidermal hyperproliferation, inflammation, and angioneogenesis.
- Psoriasis is driven by an intimate interplay between the innate and the adaptive immune systems.
- The central axes of psoriatic inflammation comprise the nuclear factor-κB, interferon-γ, and interleukin (IL)-23 signaling pathways as well as antigen presentation.
- Biologic therapies targeting tumor necrosis factor-α, IL-23, or IL-17 are highly effective, underlining the clinical importance of these inflammatory mediators.
- Recent genetic and clinical observations allow differentiation of generalized pustular psoriasis as a distinct entity.

INTRODUCTION

Given the prevalence of around 2% in most populations studied so far, psoriasis is a common disease. In its most typical type, the disease manifests as well-demarcated, red, scaly plaques about the size of a palm. These lesions highlight already clinically the 2 pillars of its pathogenesis, namely epidermal hyperproliferation (scaling) and inflammation (infiltrated, red lesions; **Fig. 1**). Genetic analyses, particularly genome-wide association studies, identified key players in these processes, namely cells as well as mediators. Proof for their relevance in patients arises from the successful use of biologic drugs targeting these crucial components, resulting in unparalleled efficacy in relief of the signs and symptoms of psoriasis.

Disclosures: The author has received honoraria as a speaker or advisor for Abbvie, Biogen Idec, Celgene, Covagen, Galderma, Janssen, Leo, Lilly, MSD, Novartis, Pantec Biosolutions, Pfizer, and UCB.

[a] Department of Dermatology and Venereology, Geneva University Hospitals, Rue Gabrielle-Perret-Gentil 4, Genève 14 CH – 1211, Switzerland; [b] Department of Pathology and Immunology, University of Geneva, Rue Michel-Servet 7, Geneva CH – 1206, Switzerland
* Department of Dermatology and Venereology, Geneva University Hospitals, Rue Gabrielle-Perret-Gentil 4, Genève 14 CH – 1211, Switzerland.
E-mail address: wolf-henning.boehncke@hcuge.ch

Rheum Dis Clin N Am 41 (2015) 665–675
http://dx.doi.org/10.1016/j.rdc.2015.07.013 **rheumatic.theclinics.com**
0889-857X/15/$ – see front matter

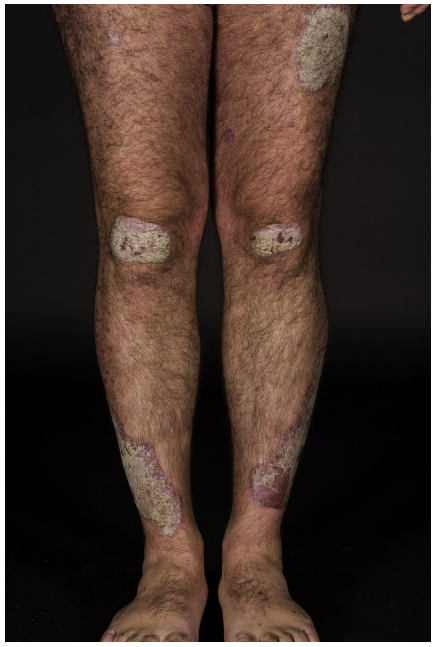

Fig. 1. Chronic plaque-type psoriasis. Well-demarcated, red, scaly plaques symmetrically distributed on the legs of a patient.

Noteworthy, pustular forms of psoriasis also exist. These forms do not respond to many of the drugs proven effective in chronic plaque-type psoriasis. Recent genetic studies suggest that at least generalized pustular psoriasis should be viewed as a distinct entity distinct from what formerly was regarded as "psoriasis."

This review provides an overview of the etiology of psoriasis, followed by a more in-depth discussion of pathogenesis, the need to differentiate between "psoriasis" and "generalized pustular psoriasis," and a discussion of the concept of "psoriatic disease" extending beyond the level of the skin.

ETIOLOGY

Psoriasis is a multifactorial disease with extrinsic as well as intrinsic factors playing major roles, as evidenced by the so-called Koebner phenomenon: nonspecific—extrinsic—triggers induce the manifestation of typical psoriatic lesions locally in the skin of patients, intrinsically "set" to develop such lesions. In addition, numerous triggers for a general aggravation have been described. Among the factors known to induce or worsen psoriasis, are:

- Mild localized trauma, such as scratching, piercings, tattoos, sunburns, chemical irritants ("classical" Koebner phenomenon)
- Drugs,[1] including β-blockers, lithium, antimalarials, and nonsteroidal antiinflammatory drugs
- HIV infection[2]
- Streptococcal pharyngitis.[3]

The climate in general and exposure to natural sun light in particular are discussed as additional extrinsic factors with clinically important impacts on disease activity.