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Research Communication

Pathogenesis of Psoriasis: Focus on Autoinflammation

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Psoriasis is a common, immune-mediated, inflammatory disease mainly involving the skin and joints, that is genetically determined, strongly influenced by epigenetic mechanisms, and possibly triggered by environmental factors [1, 2].

Pathogenesis of psoriasis is extremely complex and fascinating: the studies on its main clinical subtypes, but also of its stages and corresponding histopathological features, have recently pointed out the involvement of autoinflammation, that is to say, a state of sterile inflammation, not mediated by circulating autoantibodies and autoreactive T cells [3, 4].

The clinical development of early lesions in psoriasis would be linked to periodic waves of autoinflammation, represented by burst of neutrophils and cytokines related to the interleukin-1 (IL-1) family, such as IL-1α, IL-1β, and IL-36, capable to initiate the disease [3].

Initiating events of the disease arise from a complex interplay between genetic and environmental factors (e.g., drugs, stress, smoking, trauma, microorganisms). In more detail, in genetically predisposed individuals, in these initial phases of the disease, cells from the innate immune system are activated by the above triggers, most notably via effectors of the innate immunity like the Toll-like receptors, and accumulate in the skin and in the other affected organs.

Keratinocytes are also activated, thus becoming in turn immune system cells, and release a number of chemokines further recruiting neutrophils and amplifying the inflammatory network.

Indeed, from a histopathological point of view, during the early stages of the disease as well as in its recurrent pustular flares, an infiltrate of cells of the innate immunity predominates in skin lesions, while cells from adaptive immunity like T lymphocytes are rare.

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This first flare is rapidly followed by an accumulation in the lesional skin of T-helper (Th) 17 cells that produce proinflammatory cytokines such as IL-17 and IL-22 crosstalking with the IL-12/IL-23 axis. The clinical background of this phase is represented by papulo-pustulous lesions of psoriasis.

In the late stages of the disease, clinically characterized by plaque psoriasis, the inflammatory process is shifted to a classical Th1 cell-mediated immune response, with predominance of Th1 cell-related cytokines like tumor necrosis factor (TNF)-α and interferon (IFN)-γ [3].

Thus, in its initial events, psoriasis seems to reproduce exactly the pathogenetic model of classic autoinflammatory diseases, such as pyogenic arthritis, acne, and pyoderma gangrenosum (PAPA) syndrome, and neutrophilic dermatoses, such as idiopathic pyoderma gangrenosum, which are due to mutations of genes regulating the innate immunity and share with psoriasis the same cascade of cytokine release and cell activation [4–7].

As well, the link between psoriasis and different autoinflammatory conditions is also given from the clinical ground, as the occurrence of a severe erythrodermic and pustular presentation of psoriasis is present in several syndromes such as Deficiency of IL-1 Receptor Antagonist (DIRA) and Deficiency of IL-36 Receptor Antagonist (DITRA) [8, 9].

The aforementioned physiopathological model may support the view on psoriasis as a paradigm of skin disease with systemic involvement and hallmarked by an important autoinflammatory component.

A comprehensive knowledge of the complex interplay among the genetic/epigenetic factors and immunological mechanisms of autoinflammation should contribute to the development of novel targeted therapeutic strategies.

Disclosure Statement

The authors have no conflicts of interest to declare.

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