Guest Editorial

A Burning Issue: Burns and Other Triggers in Pemphigus

Sarah Brenner, MD; Yonit Wohl, MD

Pemphigus is a multifactorial autoimmune disorder for which certain individuals have a genetic predisposition that is triggered or exacerbated by exogenic factors. Many exogenic factors have been identified as possible stimuli for the immune system. Drugs from different chemical groups are among the culprits: thiol drugs such as penicillamine and captopril; phenols such as rifampin or aspirin; and other drugs such as calcium-channel blockers, angiotensin-converting enzyme inhibitors, and nonsteroidal anti-inflammatory drugs. Other possible inducers include infectious agents such as organisms from the Herpesviridae family; organophosphates and organochloride pesticides; certain phenolic, thiol, or tannin (polyphenolic) compounds found in foods such as those in the allium group of vegetables; hormones such as estrogens; and malignancies, mostly those that are lymphoproliferative.

Certain physical triggers are implicated as well in the development of pemphigus: UV radiation,[2] trauma, surgical and cosmetic procedures,[3,4] x-ray radiotherapy,[5] and thermal burns.[6,7] An article in this issue adds electric burns to this list.[8]

This plethora of etiologies led us to suggest the acronym PEMPHIGUS as an aid in the diagnosis and treatment of the disease: pesticides, malignancy, pharmaceuticals, hormones, infectious agents, gastronomy, UV radiation, and stress. Removal of the inciting agent often results in rapid resolution of the disease, though it may persist.[1]

Speculating on possible pathogenic mechanisms for the development of pemphigus, we looked for the common sequelae that all traumatized skin undergo regardless of the particular insult. In 1877, Köbner described an isomorphic response to many forms of environmental stress on the skin of patients with psoriasis, sarcoidosis, lichen planus, lupus erythematosus, and autoimmune dermatoses including pemphigus vulgaris.[9,10] The biologic mechanism underlying the Köbner phenomenon is the capacity of cutaneous trauma to turn on the regulatory components of the immune system that are needed to activate and perpetuate an immune response.[11]

The same immunologic and pathophysiologic mechanisms are true for physically-induced pemphigus. When burns injure the skin, they result in cellular necrosis, which generates cryptic epitopes or peptides, creates neoantigens, and results in epitope spreading. These reactions can elicit the stimulation of the immune system in a 2-step fashion. First, the innate immune system is activated with the formation and release of a wide array of nonspecific inflammatory cytokines, such as interleukins 1 and 6, TNF-α, ICAM-1, and IFN-γ (some of which have been implicated in the development of pemphigus vulgaris).[12] Next, the adaptive T-cell arm is recruited, leading to disease-specific reactions including the formation of pathogenic immunoreactants to different sites in the skin, which explains the intercellular deposition and the acantholytic process in pemphigus.[13,14]

Drs. Brenner and Wohl are from the Department of Dermatology, Tel Aviv Sourasky Medical Center, Israel. Dr. Brenner also is from Sackler Faculty of Medicine, Tel Aviv University.
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Reprints: Sarah Brenner, MD, Department of Dermatology, Tel Aviv Sourasky Medical Center, 6 Weizmann St, Tel Aviv 64239 Israel (e-mail: derma@tasmc.health.gov.il).

When we realize that pemphigus is in fact a complex immunologic reaction to different internal or external stimuli, we can expect to observe its development in the right context.

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