Time to Consider Psoriasis an Autoimmune Disorder?

Jashin J. Wu MD[a] and Young M. Choi BS

[a]Department of Dermatology, Kaiser Permanente Medical Center, Los Angeles, CA
[b]David Geffen School of Medicine at UCLA, Los Angeles, CA

Traditionally, psoriasis has been described as an inflammatory or an immune-mediated condition but not as an autoimmune disease. Four of the main dermatology textbooks (Dermatology, 3rd edition by Bolognia; Andrews' Diseases of the Skin, 11th edition by James; Fitzpatrick's Dermatology in General Medicine, 8th edition by Goldsmith; and Rook's Textbook of Dermatology, 8th edition by Burns) do not describe psoriasis as an autoimmune condition. Online references like UpToDate and Emedicine do not have any mention of autoimmunity. According to MedLinePlus (http://www.nlm.nih.gov/medlineplus/ency/article/000816.htm), there are more than 80 different types of autoimmune disorders. Is it now time to add psoriasis to this list?

We found that patients with psoriasis were more likely to have at least one autoimmune disease (odds ratio [OR] 1·6; 95% confidence interval [CI] 1·5-1·7) and to have at least two autoimmune diseases (1·9; 95% CI 1·6-2·4).[1] Prevalent psoriasis without psoriatic arthritis has also been associated with a higher prevalence of inflammatory bowel disease (1·4 [95% CI: 1·2-1·6]), ulcerative colitis (1·3 [95% CI: 1·1-1·6]), and Crohn's disease (1·6 [95% CI: 1·4-2·0]).[2]

It is known that autoimmune diseases tend to cluster around other autoimmune diseases. Genome-wide association studies have identified a large number of major loci with many shared associations between various autoimmune diseases.[3-5] A recently published meta-analysis of independent psoriasis and Crohn's disease patients confirmed four genetic loci known to be shared by the two diseases (IL23R, IL12B, REL, and TYK2), as well as identified seven further shared loci (JAK2, ZMIZ1, PRDX5, SOCS1, STAT3, FUT2, and YDJO).[6] These in addition with others (NFKBIA, TNFAIP3, TNFRSF9, ERAP1, ERAP2, IFIH1, TAGAP) brings the total number of shared loci between psoriasis and Crohn's disease to eighteen.[7]

Likely, more and more genes for psoriasis will be found to be shared with commonly accepted autoimmune disorders. Understanding the genetic basis of psoriasis is critical in elucidating the disease process and ultimately developing novel therapies. Currently, many of the most effective therapies for psoriasis, including methotrexate, cyclosporine, TNF inhibitors, ustekinumab, and IL-17 inhibitors are considered immunosuppressants. Not surprisingly, the vast majority of autoimmune disorders are treated with some form of immunosuppressive therapy.

Despite the growing genetic evidence, the lack of a specific autoimmune target has been a main obstacle in considering psoriasis an autoimmune disease. Review articles have described the initiation of psoriasis, broadly, as an interaction between genetic and environmental factors.[8] However, the presence of clonal T cell populations in lesions, as well as the chronic inflammatory activity seen in psoriasis, suggest the presence of an antigenic trigger. Possible triggers that have been postulated include peptide antigens produced by keratinocytes (heat shock proteins or S100A12) or environmentally acquired Toll-like receptor (TLR) agonists.[8]

The strongest evidence for an autoimmune target for psoriasis was demonstrated by the work of Ganguly et al.[9] They discovered that self-DNA and self-RNA molecules, when bound to the peptide LL37, could be abnormally transported into the endosomal compartment of plasmacytoid dendritic cells (pDCs) and myeloid dendritic cells (mDCs). Subsequent activation of TLR7, TLR8, and TLR9 led to the secretion of IFN-α, TNF-α, and IL-6. These self-DNA-LL37 and self-RNA-LL37 complexes were found in psoriatic tissues.

In conclusion, we believe we are slowly marching towards the conclusion that psoriasis is in fact an autoimmune disorder, by definition a "clinical syndrome caused by the activation of T cells or B cells, or both, in the absence of an ongoing infection or other discernible cause."[10] Genetic studies are increasingly linking psoriasis with other autoimmune disorders, and recent studies are promising for a possible self-DNA and self-RNA autoimmune target for psoriasis.

Disclosure

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AUTHOR CORRESPONDENCE

Jashin J. Wu MD
E-mail:.. jashinwu@hotmail.com