PSORIASIS : IS IT VIRAL-INDUCED ?

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ABSTRACT

The etiology of psoriasis as a disease is still not clear. In many other chronic diseases of previously unknown etiology a genetic and/or viral background has been proved or seems likely to be proved [1,2,3,4,5]. It seems reasonable to consider psoriasis in the same way. This paper gives a review of articles that support a viral etiology of psoriasis based on genetic susceptibility [6,7,8].

INTRODUCTION

Gillhou et al in 1978 [6] first suggested that a slow virus infection could be the cause of the abnormal immune responses and keratinocyte proliferation in psoriasis. That article and others published subsequently were reviewed for their molecular findings, data supporting a viral background, evidence from therapeutic trials and experimental and/or investigational data supporting a viral background.

RESULTS

Our review found that electron microscopy of specimens from psoriatic plaques demonstrated virus-like particles and cell cultures established from psoriatic plaques released particles showing the morphological features of a retrovirus [9].

Sub cellular particles resembling retroviruses in morphology, density and protein composition have been isolated from urine of psoriatic patients [10,11,12]. These particles cross-reacted with antiserum raised against virus-like particles from cultured psoriatic epithelial cells [12]. The major internal protein of these particles, P27, was found also in extracts of psoriatic scales and formed circulating immune complexes with anti-P27 antibodies. Similar immune complexes were detected in the serum and synovial fluid of patients with psoriatic arthritis [10]. Virus-like particles were found also in phytohemagglutinin-stimulated lymphocyte cultures from psoriatic patients [13].

HIV-RNA transcripts were detected in psoriatic plagues in HIV-infected psoriatic patients by using in situ hybridization together with confocal laser scanning microscopy. The transcripts were found predominantly in CD4+cells, factor XIIIa positive dermal dendrocytes. Skin of normal appearance from HIV-infected patients did not show these HIV transcripts [14].

Published clinical data reported a psoriatic spectrum in HIV-infected individuals with Reiter's disease being the most severe manifestation [15,16,17]. Psoriasis may be the initial symptom of HIV infection and AIDS may exacerbate psoriasis [18,19,20].

Evidence from Therapeutic trials showed that psoriasis in HIV-infected patients improved with azidothymidine (AZT) treatment [21,22,23] and that HIV-induced retinoid resistant psoriasis also responded to AZT [24,25]. HIV-negative psoriatics improved with AZT and with peptide-T and patients with psoriatic arthritis responded to peptide-T [26,27,28,29].

Experimental work has demonstrated that mice transgenic for HIV provirus will develop an epidermal hyperplasia and acanthosis that resembles psoriasis [30].

DISCUSSION

Epidemiological and histocompatibility studies have shown chronic psoriasis to be an inflammatory disease with a genetic background [31,32] and multifactorial stimuli [33]. Viral involvement is one such factor that will precipitate psoriasis in an individual with an appropriate genetic background. Prior to 1991 virus-like particles had been reported in proriatic plaques, in immune complexes in the serum and joints of patients and in activated lymphocytes from psoriatics [9,10,11,13]. The demonstra-

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tion of HIV-RNA viral transcripts in the psoriatic skin of HIV-infected patients but not in the normal skin of such patients or in HIV-negative psoriatics confirms the involvement of the virus in psoriasis-associated HIV infection [14].

If HIV-negative psoriatics improve on other antiviral agents this suggests the possibility of another retrovirus being the cause. For example, the improvement of psoriasis with peptide-T treatment may be because the putative retrovirus has similarities to HIV. Peptide-T is known to improve AIDS as well as HIV-associated psoriasis through binding to the CD4+ T-cell receptors, thus blocking the HIV attachment to these receptors [34,35].

Indirect immunofluorescence using S-100 antiserum on biopsies of the psoriatic plaque has shown a decrease in the number and even the disappearance of epidermal Langerhan's cells (LCs) while the dendritic cells in the dermis increased and clustered around the vascular structures. Administration of peptide-T resulted in a rearrangement of these S-100 positive dendritic cells so that the number in the epidermis increased while the number in the dermis decreased as in normal skin. This was accompanied by an improvement of the psoriasis [36].

It can be hypothesized that, in an individual with a certain genetic constitution, the putative psoriasis-causing virus acts in the following way :

a) the virus is directed towards the CD4+ recep tors on the epidermal LCs according to a particular HLA-phenotype.
b) the LCs then migrate to the dermis carrying the virus, presenting it to the CD4+ helper T-cells causing the dendritic S-100 positive cells to decrease in the epidermis and in crease in the dermis of the psoriatic plague as described above [36].
c) these T-cells are activated and also infected because the virus or its particles will be ac cepted by their CD4 + receptors.
d) these activated infected cells release their cytokines (IL-1 and gamma IFN) [37,38] that are augmented by, and that mutually inter act with, the inflammatory mediators of the LCs (IL-IB) and keratinocytes (IL-8) [39,40].

The end result of these persistent inflammatory mediators is vascular dilatation, the first histopathological change in psoriasis [41], with neutrophil chemotaxis and epidermal proliferation, the basic pathological changes in a psoriatic lesion.

Peptide-T, through its ability to combine with CD4 + receptors of both the LCs and the T-helper cells, is capable of reversing the inflammatory process in psoriasis by blocking its initiation. The beneficial effect of Zidovudine in psoriatics without AIDS is possibly due to inhibition of a putative causative virus and, through its inhibitory effect on DNA the drug is able to inhibit keratinocytic proliferation [42].

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