Apoptotic cell clearance in Systemic Lupus Erythematosus (SLE)
Reefman, Esther

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2006

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Do apoptotic cells accumulate in the epidermis of patients with cutaneous Lupus Erythematosus after Ultraviolet irradiation?
Comment on the article by Kuhn et al

Esther Reefman\textsuperscript{1}, Pieter C. Limburg\textsuperscript{2}, Cees G.M. Kallenber\textsuperscript{1} & Marc Bijl\textsuperscript{1}
Departments of Rheumatology & Clinical Immunology\textsuperscript{1}, and Pathology & Laboratory Medicine\textsuperscript{2}, University Medical Center Groningen, University of Groningen.
Groningen, The Netherlands

Arthritis Rheum., 2006 Oct; 54(10):3373-4
LETTER TO THE EDITOR

We read with interest the recent article by Kuhn et al showing accumulation of apoptotic cells in the epidermis of patients with cutaneous Lupus Erythematosus (CLE) after ultraviolet (UV) irradiation (1). This is an interesting observation as it supports the “defective waste disposal hypothesis” in (S)LE pathogenesis (2). Although the authors conclude that apoptotic cells accumulate in the skin of CLE patients after UV irradiation, data should be interpreted with caution, as results are merely based on the TUNEL reaction and in situ nick translation (ISNT) for detecting apoptotic cells. Both methods detect DNA nicks and strand breaks and are not specific for apoptosis.

First of all, these methods can detect terminally differentiated keratinocytes present in the stratum granulosum of normal human skin (NHD) and CLE lesional skin. However, terminal differentiation in keratinocytes is a process distinct from apoptosis (3).

Secondly, false positive results can result from proliferation. Wrone-Smith et al reported, using pulsed field gel electrophoresis, that DNA fragmentation was absent in TUNEL positive cells in psoriatic skin. In addition, they showed that numerous TUNEL-positive keratinocytes were also positive for proliferating cell nuclear antigen (PCNA, expressed during proliferation and DNA repair) and Ki-67 antigens (4). Finally, TUNEL-positivity might also result from DNA repair. In myocytes, TUNEL-positivity did not result from apoptosis (TaqPol in-situ ligation negative) nor from proliferation but from increasing DNA repair activity, as cells were Ki-67 negative and PCNA positive (5).

In the studies of Kuhn et al, apoptosis was induced by UV irradiation, which is known to induce apoptosis, but also increases cell proliferation and DNA repair. Therefore, several discrepancies in their study may result from the a-specific nature of DNA nick labeling using TUNEL and ISNT. First, ‘apoptotic nuclei’ were frequently present in non-irradiated skin from normal healthy donors and their presence varied considerably (ranging from 9.0 (Fig 3) to approximately 15.0 per mm epidermis (Fig 1)). Furthermore, numbers of apoptotic nuclei detected by cleaved caspase-3 staining were much lower compared to the number of TUNEL positive cells (Fig 4 and 5, respectively). In our own studies on UV-induced apoptosis in SLE patients we stained skin by hematoxylin and eosin staining allowing the detection of the classical Sunburn cells. This method correlated very well with cleaved caspase-3 staining and did not show any apoptotic keratinocytes in non-irradiated skin from healthy controls or SLE patients (6).

In summary, we feel that the data of Kuhn et al should be interpreted with caution. Further studies are needed to analyze, using other apoptotic markers, the appearance and fate of apoptotic cells in SLE patients in vivo. For studies in SLE this is highly relevant, since there is no general agreement about the central defect leading to the accumulation of apoptotic cells in these patients: increased apoptosis, decreased phagocytosis, and/or influence of intervening humoral factors all might be involved.
Reference List


