SKIN AFFECTION IN RHEUMATOLOGICAL DISEASES

Essay

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Master Degree in ***Internal Medicine***

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بسم الله الرحمن الرحيم
وَأَنْزَلَ اللهُ
عَلَيْكَ الْكِتَابَ
والْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ
تَكُنْ تَعْلَمُ
وَكَانَ فَضْلُ
اللهِ عَلَيْكَ
عَظِيمًا
صدق الله العظيم
سورة النساء آية
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List of Abbreviations

Abbrev.	Full term
ACLE	Acute cutaneus lupus erythematosus
ALT	Alanine transaminase
ANA	Antinuclear antibody
ANCA	Antineutrophil cytoplasmic antibody
AP	Alkaline phosphatase
AST	Aspartate transaminase
ATP	Adenosine tri-phosphate
C1q	Complement-1q
c-ANCA	Cytoplasmic ANCA
CBC	Complete blood culture
CCLE	Chronic cutaneus lupus erythematosus
CCS	Churg-strauss syndrome
CK	Creatine kinase
CLE	Cutaneus lupus erythematosus
CRP	c- reactive protein
CSVV	Cutaneus small vessel vasculitis
CTL	Cytotoxic T-lymphocytes
CV	Cutaneus vasculitis
DAF	Decay accelerating factor
DGI	Dissiminated gonococcal infection
DIF	Direct immunoflurescence
DLE	Discoid lupus erythematosus
DNA	Deoxy-ribonucleic acid
ESR	Erythrocyte sedimentation rate
GM-CSF	Granulocyte-monocyte colony stimulating factor
HLA	Human leucocytic antigen
HSP	Henoch-schoenlein purpura
HV	Hypersensitivity vasculitis
IFN	Interferon

LIST OF ABBREVIATIONS (CONT...)

Abbrev.	Full term
IG	Immunoglobulin
IL	Interlukin
IVIG	Intravenous immunoglobulin
KC	Keratinocytes
La\SSB	La-ssb antigen
MHC	Major histocompitability cells
MMPs	Matix metalloproteinases
MPA	Microscopic polyangitis
NK	Natural killer
p-ANCA	Peri-nuclear ANCA
RA	Rheumatoid arthritis
RNA	Ribonucleic acid
Ro\SSA	Ro\ssa antigen
SLE	Systemic lupus erythematosus
SNP	Single nucleotide polymorphism
TGF	Transforming growth factor
THc	T-helper cell
TNF	Tumor necrosis factor
UV	Ultraviolet rays
VCAM	Vascular cell adhesion molecule

INTRODUCTION

The skin is a systemic organ which is one of the most commonly involved tissues in rheumatic autoimmune diseases ***(Drosera et al., 2008).***

The exact pathogenesis of the various skin manifestations is complex and incompletely understood in autoimmune diseases ***(Eriksson et al., 2005*).** Different mechanisms are thought to be implicated in the pathogenesis of skin lesions such as the release of inflammatory cytokines by keratinocytes which initiate an inflammatory cascade in cutaneus lupus erythematosus (CLE) ***(Drosera et al., 2008).***

Several lines suggest that there is also a role of tumor necrosis factor-α (TNF-α), nitric oxide (NO), t-cell mediated injury, ultraviolet (UV) light in promoting the release of cytokines, they also induce apoptosis in keratinocytes contributing in induction of skin lesios in CLE ***(Flendri et al., 2005 and Drosera et al., 2008).***

Plasmacystoid dendritic cells appear to be an important source of type 1 interferon (IFN) which is involved in the pathogenesis of dermatomyositis (DM) skin lesions ***(Wenzel et al., 2008).***

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Studies also suggest that IL-1alpha and TNF-alpha may be responsible for the increased ICAM-1 expression on endothelium in microvessels resulting in vascular injury in cutaneus vasculitis ***(Hayashi et al., 2009).***

CXCL16 levels were increased in patients with Systemic sclerosis (SSc), and correlated with the extent of skin sclerosis, suggesting that CXCL16 may have a role in the development of skin fibrosis in SSc ***(Yanaba et al., 2008).***

Blockage of (TNFalpha) antagonists have also been shown to significantly reduce rheumatic skin lesions, especially in rheumatoid arthritis (RA) ***(Kary et al., 2008).***

AIM OF THE WORK

To highlight the pathogenesis, clinical manifestations, and management of skin involvement in different autoimmune rheumatological diseases.

BASIC SKIN STRUCTURE

The skin is complex morphologically. The challenge in recent years has been to locate precisely its structure ***(Naik et al., 2006).***

The skin consists of an outer epidermis, the dermis, and the hypodermis. It includes nerves, blood vessels, glands and hair follicles (figure-1) ***(Prost-Squarcioni et al., 2005).***

Epidermis

The epidermis is an stratified squamous keratinized epithelium, not vascularized innervated. It consists of four cell types: keratinocytes, the original epidermis, the melanocytes from neural crest, cells of Langerhans, marrow-derived hematopoietic and Merkel cells. Keratinocytes represent 80% of epidermal cells, migrating, and differentiating itself from its depth to its surface, they give their morphological characteristics (stratification, superficial squamous cells and enucleated), the 20% of other types of cells are scattered among the keratinocytes ***(Turesson et al., 2005).***

a- Keratinocytes (KC)

Keratinocytes provide three major functions related to structures histologically identified: the cohesion of the epidermis, through their cytoskeleton and their systems,

junction barrier function between the indoor and outdoor environments, in connection with their terminal differentiation and finally, protection against light radiation ***(James et al., 2006).***

b- Melanocytes

Melanocytes are, by their number, the 2nd cell population of the epidermis, Their function is the synthesis of melanin, eumelanin and pheomelanin, which gives skin its color constituent, also they have a photoprotective role, Hemidesmosomes with the extracellular matrix, However, they possess focal contacts (***Naik et al., 2006).***

c- Langerhans cells

Langerhans cells represent 3% to 8% of epidermal cells. They belong to the group of dendritic cells presenting antigen to T lymphocytes. In the epidermis, their function is to capture the exoantigens through endosomes, and to prepare them to reexpress surface molecules with class II major histocompatibility complex (MHC) ***(Naik et al., 2006).***

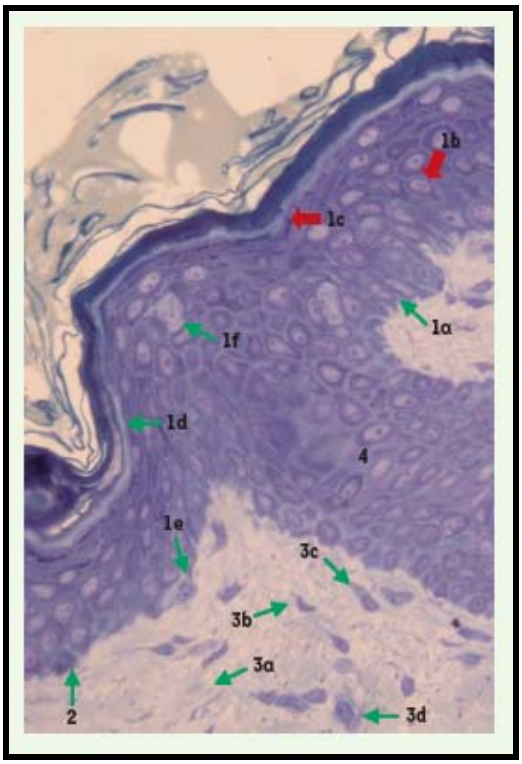

Figure (1): Cup semi-thin, stained with toluidine blue. 1. Epidermis, with in 1a: the basal layer, consisting of a single layer of columnar cells, in 1b: SPINEUSE layer consisting of keratinocytes polygonal, rounded stone, bristling of "thorns" ((-> m / s 2006 , No. 2, p. 144) in 1c: the granular layer, formed of flattened keratinocytes containing "grain" ((-> m / s, 2006, No. 2, p. 144) in 1d: the stratum corneum which keratinocytes become corneocytes have lost their nucleus (orthokératose) in 1st, a melanocyte, clear cell in the basal layer, and 1f: Langerhans cell, clear cell nucleus notched the granular layer. 2. Junction dermo-epidermal 3. papillary dermis, with in 3a: oxytalanes elastic fibers in 3b: "collagen fibers" in 3c: a fibroblast and 3d: a macrophage; 4. isthmic portion overlying a follicle pilosebaceous -sebaceous layer. 2. Junction dermo-epidermal 3. papillary dermis, with in 3a: oxytalanes elastic fibers in 3b: "collagen fibers" in 3c: a fibroblast and 3d: a macrophage; 4. isthmic portion overlying a follicle pilosebaceous –sebaceous. ***Adapted from (Gerami et al., 2006).***

d- Dendritic cell (DC)

Dendritic cells (DCs) are immune cells that form part of the mammalian immune system. Their main function is to process antigen material and present it on the surface to other cells of the immune system, thus functioning as antigen-presenting cells ***(McKenna et al., 2005).***

Dendritic cells are present in small quantities in tissues that are in contact with the external environment, mainly the skin (where there is a specialized dendritic cell type called Langerhans cells) ***(Ohgimoto et al., 2006).***

The dendritic cells are constantly in communication with other cells in the body. This communication can take the form of direct cell-to-cell contact based on the interaction of cell-surface proteins. An example of this includes the interaction of the receptor B7 of the dendritic cell with CD28 present on the lymphocyte. However, the cell-cell interaction can also take place at a distance via cytokines ***(Liu et al., 2005).***

For example, stimulating dendritic cells in vivo with microbial extracts causes the dendritic cells to rapidly begin producing IL-12. IL-12 is a signal that helps send naive CD4 T cells towards a Th1 phenotype ***(Ohgimoto et al., 2007)***.