Clinical, Histopathological and Immunohistochemical Study of Cases Presenting with Erythroderma

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Abstract

Background:

Erythroderma is a morphologic presentation of a variety of cutaneous and systemic diseases. Diagnosing erythroderma is very challenging mainly as regards the differentiation between neoplastic and benign (inflammatory) causes.

Aim of work:

This work aimed at studying cases presenting with erythroderma, clinically, histopathologically and immunohistochemically in order to develop criteria that help in reaching a final diagnosis and in differentiating between benign (inflammatory) and neoplastic causes of this condition.

Patients and methods:

Thirty patients with erythroderma aged more than 12 years old were included. Each was subjected to complete medical history, thorough general and cutaneous examination as well as laboratory investigations. Accordingly, a provisional clinical diagnosis was reached. Two Skin biopsies were examined blindly to any clinical data and a histopathological diagnosis was defined. Cases with mismatched provisional clinical and histopathological diagnoses as well as histopathologically unsettled cases were subjected to further clinical correlation and immunohistochemical study of the expression of CD2, CD5, CD7, CD4 and CD8 to verify the diagnosis. Immunohistochemistry was also done for cases representing both inflammatory and neoplastic conditions in order to characterize their immunophenotypic profile.

Results:

Based on the constellation of clinical, histopathological and immunohistochemical data, the final diagnoses of studied cases included: 15 cases (50%) of ***erythroderma due to a pre-existing dermatosis*** namely: 12 cases of psoriasis (40%), 2 cases of atopic dermatitis (6.7 %), and 1 case of pemphigus foliaceus (3.3%). The remaining 15 cases were diagnosed as ***drug induced erythroderma*** in 7 cases (23.3%), 1 case (3.3%) of ***papuloerythroderma of Ofuji*** and 7 cases (23.3%) of

erythrodermic CTCL which included 1 case (3.3%) of Sézary syndrome and 6 cases (20%) of erythrodermic MF.

On clinical basis, a diagnosis of psoriasis was significantly associated with fiery red erythema, dry white silvery scales, absent oozing, palmoplantar scaling and erythema (P value =0.003, <0.0001, =0.031 and 0.007 respectively). A diagnosis of CTCL was significantly associated with dusky red erythema, fine branny scales, infiltrated areas, alopecia and palmoplantar keratoderma (P value =0.003, <0.0001, =0.043, =0.015 and 0.007 respectively). Eosinophilia was significantly seen in cases of drug induced erythroderma (P value = 0.015).

On histopathological basis, psoriasiform hyperplasia, hypogranulosis and superficial perivascular infiltrate were significantly seen in cases of psoriasis (P value < 0.0001, = 0.011, =0.005 respectively). Irregular hyperplasia, epidermotropism, the presence of atypical lymphocytes in the infiltrate, band like infiltrate, dense infiltrate and wiry fibrosis in the papillary dermis were significantly seen in CTCL (P value = 0.001,= 0.002, <0.0001, =0.045, 0.027 and 0.001respectively). The presence of vacuolar degeneration along the dermoepidermal junction was significantly seen in cases of drug induced erythroderma (P value = 0.007).

Immunohistochemical results showed variable expression of CD4 and CD8 in malignant cases with tendency towards loss of pan T cell markers and a CD8-ve profile while inflammatory conditions mainly showed a CD8+ve profile.

Conclusion:

Diagnosis of cases of erythroderma is a complex process that depends on a proper constellation of clinical, histopathological and immunohistochemical data. Multiple biopsies from different sites as well as repeated biopsies in chronic cases are highly recommended. Although immunohistochemistry is helpful, it has many limitations.

Keywords: Erythroderma, Clinical, Histopathology, Immunohistochemistry, Psoriasis, Eczema, CTCL, MF, Drug reaction.

List of Abbreviations

HIV	Human immunodeficiency virus
CTCL	Cutaneous T cell lymphoma
ICAM-1	Intercellular adhesion molecules-1
ICAM-2	Intercellular adhesion molecules-2
VCAM-1	Vascular cell adhesion molecule-1
ELAM-1	Endothelial leukocyte adhesion molecule- 1
CD	Clusters of differentiation
GMP-140	Granule membrane protein-140
TNF	Tumor necrosis factor
VPF	Vascular permeability factor
VEGF	Vascular endothelial growth factor
Th1	T helper 1
Th2	T helper 2
g/d	Gram per day
DRESS	Drug rash with esinophilia and systemic symptoms syndrome
PUVA	Psoralen combined with ultraviolet A treatment
mg/Kg	Milligram per kilogram
AD	Atopic dermatitis
PRP	Pityriasis Rubra Pilaris
SCARD	Severe cutaneous adverse reactions to drugs
SJS	Stevens-Johnson syndrome
TEN	Toxic epidermal necrolysis
E-CTCL	Erythrodermic cutaneous T cell lymphoma
SS	Sézary syndrome
E-MF	Erythrodermic mycosis fungoides
MF	Mycosis fungoides
NOS	Not otherwise specified
IgE	Immunoglobulin E
AIDS	Acquired immunodeficiency syndrome
CBC	Complete blood count
ESR	Erythrocyte sedimentation rate
ECG	Electrocardiogram
KOH	Potassium hydroxide

List of Abbreviations, continued

PCR	Polymerase chain reaction
ELISA	Enzyme-linked immunosorbent assay
ANA	Antinuclear antibody
Anti-DNA	Anti double stranded DNA
H&E	Hematoxylin and Eosin
IFN-γ	Interferon gamma
CLA	Common leukocyte antigen
IL	Interleukin
IV	Intravenous
SDF-1	stromal cell-derived factor 1
CXCR4	C-X-C chemokine receptor type 4
TCR	T cell receptor
Mm	Micrometer
ISCL	International Society for Cutaneous Lymphomas
FC	Flow cytometry
Vβ	V beta
DNA	Deoxyribonucleic acid
SD	Standard deviation
NAD	No abnormality detected
PPK	Palmoplantar keratoderma
TLC	Total leukocytic count
BSA	Body surface area
HSM	Hepatosplenomegaly
PF	Pemphigus foliaceous
DEJ	Dermoepidermal junction
BM	Basement membrane

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INTRODUCTION

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Introduction

Erythroderma refers to a generalized or nearly generalized sustained erythema of the skin, involving more than 90% of the body surface accompanied by a variable degree of scaling ***(Khaled et al., 2010)***. It is actually a clinical syndrome that represents the morphologic presentation of a variety of cutaneous and systemic diseases, thus a thorough workup is essential to reach the diagnosis and establish the management in order to avoid serious complications and metabolic burden ***(Okoduwa et al., 2009).***

According to ***Xiao-Ying and colleagues*** in ***2010***, erythrodermic patients are categorized into four groups: erythroderma due to pre-existing dermatoses, drug induced erythroderma, malignant erythroderma and idiopathic erythroderma.

Most studies of erythroderma did not correlate the presenting clinical features of erythroderma with the etiology, as they are usually not specific ***(Hafeez et al., 2010)***, however the classic inflammatory clinical picture can be modified according to individual causes giving some clues for diagnosis ***(Kraft and Lynde, 2008).***

Skin biopsy is one of the corner stones in the diagnosis of erythroderma, but interpretation of such specimens is difficult, due to the fact that the histopathological expression of the underlying disorder is more subtle in the setting of erythroderma , hence, in many cases, the microscopic changes are not diagnostic ***(Walsh et al., 1994 and Wolff et al., 2010)*** and only few series addressed the issue of its histopathological features ***(Wolff et al., 2010)*** with conflicting results regarding the diagnostic value of skin biopsies ***(Rym et al., 2005).***

The main difficulty in diagnosis of erythroderma is distinguishing benign (inflammatory) from malignant cases (mainly cutaneous T cell lymphoma) with overlapping histopathological features. As a result, recent immunohistochemical studies focus on the expression of the T cell markers, where neoplastic cells have aberrant expression of various T-cell markers compared with normal cells ***(Nagler et al., 2011).***

According to ***Vonderheid (2006)***, malignant T cells show: loss of pan-T cell markers defined as loss of CD2, CD3 or CD5 expression on more than 50% of T cells of the infiltrate in skin biopsies of erythrodermic patients. Also they show a CD4:CD8 ratio greater than 10 and a CD4+CD7- ratio of at least 40 %. All these criteria are helpful rather than definitive tools in the diagnosis of erythrodermic cutaneous T cell lymphoma ***(Nagler et al., 2011).***

Another tool for diagnosis is T cell receptor rearrangement, where PCR evidence of a T-cell clone in a skin biopsy that is otherwise non-specific (non-diagnostic histology and absence of an aberrant immunophenotype) strongly suggests the diagnosis of CTCL in an erythrodermic patient, and if an identical clone is also present in the blood, the diagnosis can be rendered with certainty ***(Nagler et al., 2011).***

Aim of work

To evaluate cases of erythroderma as regards clinical presentation, histopathological features as well as immunohistochemical expression of the following T cell markers: CD4, CD8, CD2, CD5 and CD7, in order to sum-up a constellation of findings that help in differentiating inflammatory from lymphomatous causes.

REVIEW OF LITERATURE