Evaluation of Vascular Pattern in Mycosis Fungoides Lesions by Dermoscopy and Immunohistochemistry.

A Thesis
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Abstract

Background: Mycosis fungoides is the most common form of CTCL and accounts for around 60% of new cases. Angiogenesis is a highly ordered process required for the normal remodeling of the primary vascular plexus formed during vasculogenesis. Angiogenesis is involved in the development and progression of pathogenic processes in a variety of disorders and Angiogenesis plays a critical role in solid tumor development and metastasis.

Objectives: Evaluation of vascular pattern in mycosis fungoides and if such pattern would be due to vasodilatation or angiogenesis.

Methods: Twenty five patients with MF and twenty age and sex matched healthy controls were enrolled in the study. The MF lesions were evaluated by dermoscopy and skin biopsy was taken from all participants. Immunohistochemical (IHC) staining for CD34 was done for the specimen.

Results: The total number of blood vessels positive for CD34 (9.1±2.7) and endothelial buds (10.8 ±4.1) were significantly higher in MF patients than that of controls , (P= 0.000).

Dermoscopic evaluation showed that MF exhibts a characteristic dermoscopic pattern, where the dotted pattern of blood vessels was the most frequently encountered pattern in the MF lesions followed by the linear pattern.

Conclusions: Our findings support that neoangiogenesis is increased MF lesions and that the main dermoscopic feature of MF is dotted blood vessels followed by linear blood vessels.

Key words: Angiogenesis, dermoscopy, CD34, mycosis fungoides.

Contents

List of Abbreviations

Abbreviation	Word
Ang2	Angiopoietin-2
AHM	Amelanotic/hypomelanotic melanoma
BCC	Basal cell carcinoma
BCL-2	B cell lymphoma-2
BD	Bowen disease
B-FGF	Basic fibroblast growth factor
CLA	Cutaneous lymphocyte associated antigen
CLL	Chronic lymphocytic leukemia
CMV	Cytomegalovirus
CT	Computed tomography
CTCL	Cutaneous T- celllymphoma
DCs	Dentritic cells
DLBCL	Diffuse large B-cell lymphoma
EC	Endothelial cells
FasL	Fas with its ligand
FGF	Fibroblast growth factor
HIV	Human immunodeficiency virus
HTLV	Human T-cell lymphotropic virus
IEC	Intraepidermal carcinoma
IL	Interleukin
KA	keratoacanthoma
MCL	Mantle cell lymphoma
MF	Mycosis fungoides
MMP	Matrix metalloproteinases
Mrna	Messenger-RNA
MVD	Microvessel density
NHL	Non-Hodgkin lymphoma
NPSL	Nonpigmented skin lesion

NPST	Non pigment skin tumors
PCR	Polymerase chain reaction
PTCL	Peripheral T-cell lymphoma
PTEN	phosphatase and tensin homolog
SCC	Squamous cell carcinoma
SK	Seborrheic keratosis
SLL	Small lymphocytic lymphoma
TEs	Trichoepitheliomas
T regs	Regulatory T cells
TCRGR	T-cell receptor gene rearrangement
TIA1	T-cell intracellular antigen-1
VEGF	Vascular endothelial growth factor

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INTRODUCTION and AIM OF WORK

Angiogenesis is the production of new blood vessels from an existing vascular network ***(Mazur et al., 2004)***. It is a crucial process in the growth and progression of cancer, correlating with the metastatic potential in some neoplasms **(*Folkman , 1995)***.

Mycosis fungoides (MF), a low grade lymphoproliferative disorder, represents less than 1% of the total number of non-Hodgkin lymphomas; however, it is the most common cutaneous lymphoma. It usually has an indolent course and good prognosis when identified in its early stages ***(Willemze et al., 2005).***

Many techniques were developed for the assessment of angiogenesis in cancer. One of them is the determination of microvessel density by immunohistochemistry through measuring CD34, CD31 or von Willebrand factor expression ***(Mangi and Newland, 2000)***.

Dermoscopy is a useful tool that improves diagnostic accuracy in the preoperative evaluation of pigmented skin tumours ***(Argenziano et al., 2003)***. This technique may also be of value for the assessment of vascular structures and color variations that are not clinically visible; thus, dermoscopy may be regarded as an intermediate step between clinical examination and dermatopathology ***(Zalaudek et al .,2006 b)***.

Recently a study was done by ***(Lallas et al., 2013)***, in which dermoscopic images of lesions that were clinically equivocal between MF and contact dermatitis were evaluated for the presence of predefined morphologic-criteria.

In this study we aim to evaluate vascular pattern in mycosis fungoides lesions and to determine whether such pattern would be due to vasodilatation or angiogenesis.

CHAPTER I

MYCOSIS FUNGOIDES

Cutaneous T-cell lymphomas (CTCL) are a heterogeneous group of malignancies derived from skin-homing T cells. The most common forms of CTCL are mycosis fungoides (MF) ***(Wong et al., 2011)***.

Epidemiology:

MF is the most common form of CTCL and accounts for around 60% of new cases. It accounts for 3% to 5% of non-Hodgkin's lymphoma ***(Trautinger et al., 2006)***.

MF particularly affects male and female adults, with a male to female ratio between 1.6 and 2.1. These individuals are usually older than 50 years, but incidence has increased in children and adolescents ***(Cerroni et al., 2009)***. The survival percentage in the fifth year of follow-up ranges from 80% to 100% when MF and its variants are considered ***(Cerroni et al., 2009)***.

Clinical Presentations:

Three classical cutaneous phases of MF including patches, infiltrated plaques, and tumors ***(Keehn et al., 2007)***.

Early skin lesions may mimic eczema or papulosquamous eruptions such as tinea corporis, secondary syphilis, or psoriasis. Most investigators believe that large-plaque parapsoriasis represents an early form of MF. Sequential biopsies of such lesions may be necessary to establish or confirm a diagnosis of MF ***(Ackerman, 1996)***.

Patch-stage lesions are erythematous patches or slightly raised plaques with a fine scale. The lesions may be single or multiple and are

often located on the buttocks, thighs, and abdomen. Patch lesions may be intensely pruritic or entirely asymptomatic (Fig.1) ***(Keehn et al., 2007)***.

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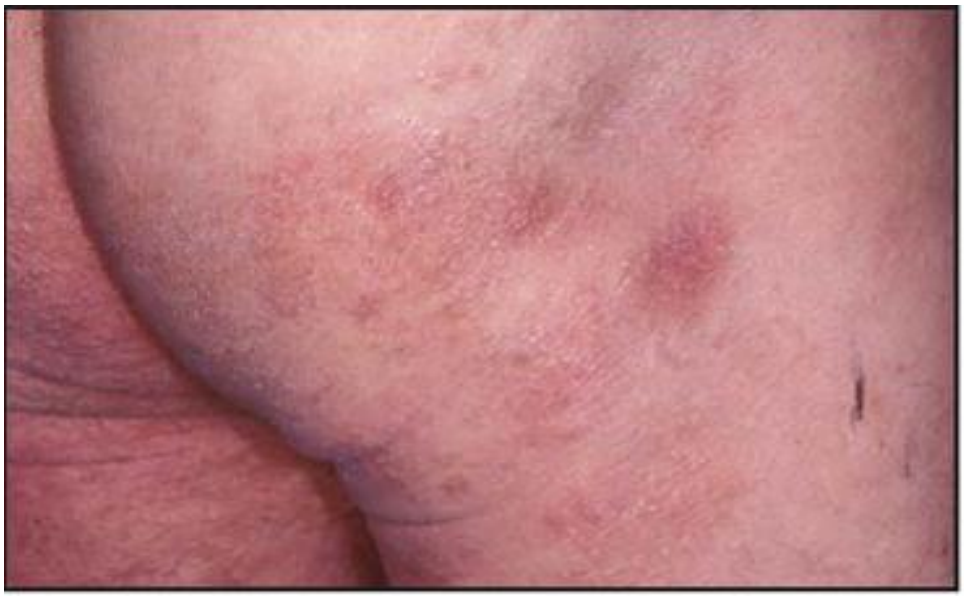

Fig. (1): Patch-stage MF ***(Keehn et al., 2007)***.

Poikiloderma atrophicans vasculare is a term used to describe patch lesions with cigarette-paper-like atrophy, telangiectasia, and mottled hyperpigmentation (Fig. 2) (***Keehn et al., 2007)***.

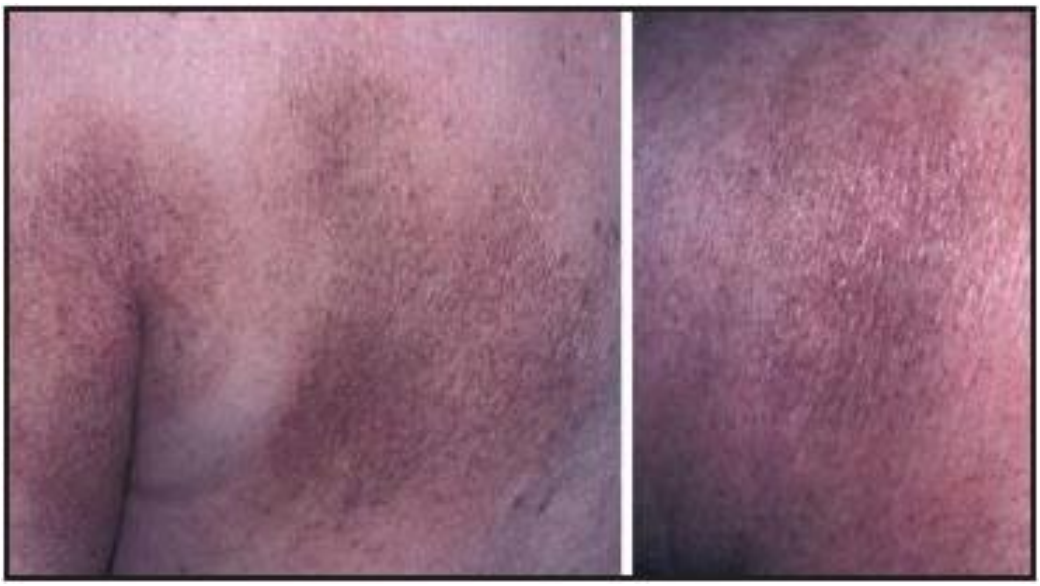

Fig. (2): Poikilodermatous variant of MF ***(Keehn et al., 2007)***.

Plaques of MF are elevated due to epidermal hyperplasia or significant neoplastic lymphocytic infiltrates (Fig. 3). These lesions may develop from preexisting patches or de novo. They are usually red-brown and sharply demarcated, but they may coalesce to form annular, arciform, or serpiginous patterns, sometimes with central clearing. Infiltrative plaques occurring on the face may result in leonine facies, and those appearing in hairy areas may produce alopecia or madarosis. Erythroderma (exfoliative dermatitis) may occur as a result of diffuse infiltration of the skin by neoplastic cells with or without scales ***(Michael et al., 2004)***.

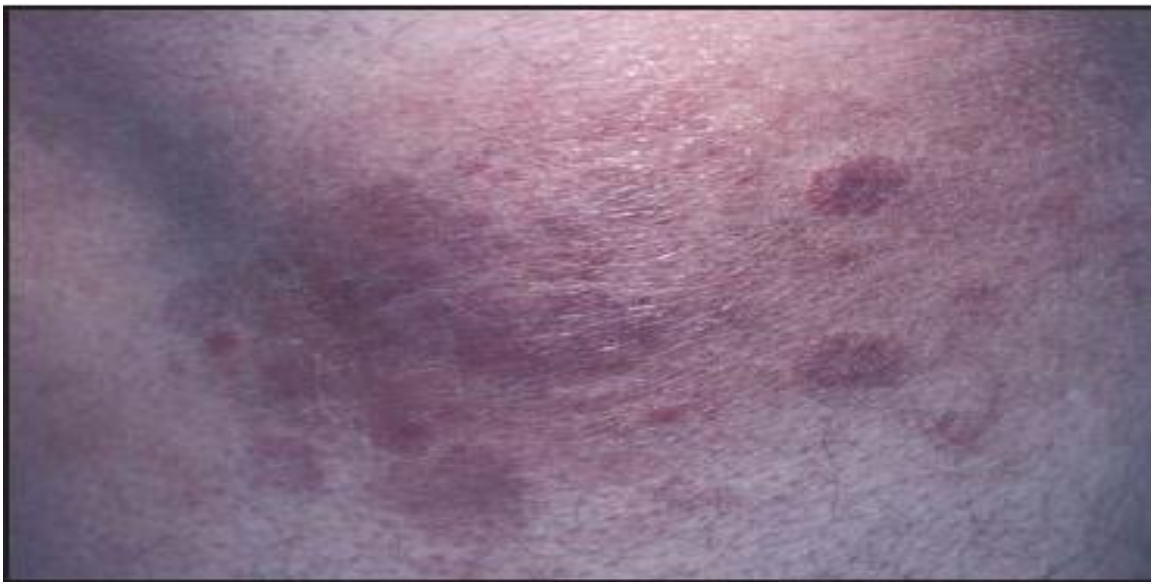

Fig. (3): Plaques of MF ***(Keehn et al., 2007)***.

The lesions of tumor-stage MF are typically violaceous, exophytic, mushroom-shaped tumors that preferentially affect the face and body folds (Fig. 4) ***(Keehn et al., 2007)***.

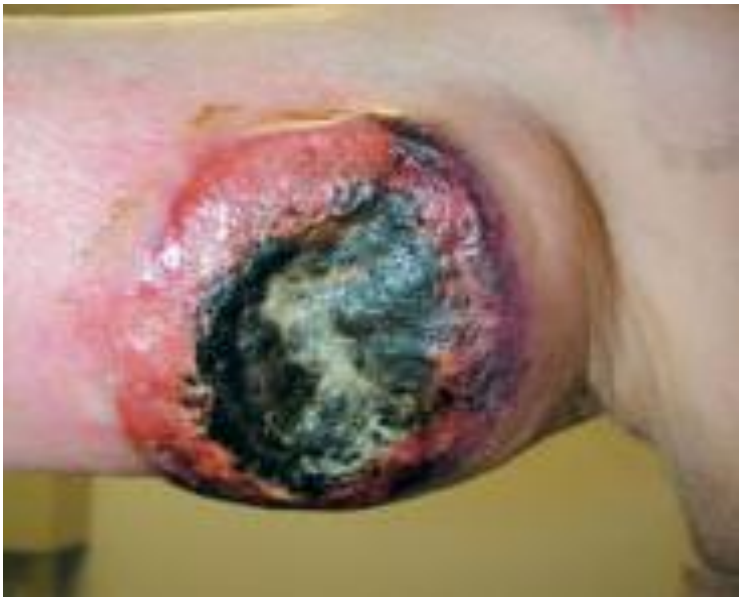

Fig. (4): Tumor-stage MF ***(Michael et al., 2004)***.

Pruritus is the most common symptom in patients with MF. Itching may be mild and easily controlled, but frequently it becomes so severe and