1. Introduction

Mycosis fungoides (MF) is the most common form of cutaneous T-cell lymphoma (CTCL) accounting for almost 50% of all primary cutaneous lymphoma ***(Prince et al., 2003).***

Typically, MF affects older adults (55-60 years) with male-to-female ratio about 1.6-2:1, but may occur in children and adolescents ***(Kim et al., 2003).*** MF has an indolent clinical course with slow progression over years, from patches to more infiltrated plaques and eventually to tumors. In some patients, lymph nodes and visceral organs may become involved in the later stages of the disease. The initial skin lesions have a predilection for sun-protected areas ***(Willemze et al., 2005).***

Histologically, early MF patch lesions show superficial lichenoid infiltrates, mainly consisting of lymphocytes. Atypical cells with small- to medium-sized, highly cerebriform, and sometimes hyperchromatic nuclei are few, and mostly confined to the epidermis "epidermotropism" ***(Smoller et al., 2003).*** In typical plaques, epidermotropism is generally more pronounced than in the patches. The presence of Pautrier micro abscesses is a highly characteristic feature, but is observed in only a minority of cases ***(Nickoloff, 1988).*** With progression to tumor stage, the dermal infiltrates become

more diffuse and epidermotropism may be lost. Conventionally, the neoplastic cells in MF have a mature CD3+, CD4+, CD45RO+, CD8- memory T-cell phenotype ***(Diamandidou, 1998).***

Early diagnosis of MF remains of crucial interest in clinical practice ***(El Bedewi et al., 2010).*** In early stages, clinical and histopathological diagnosis of MF is difficult and may be indistinguishable from chronic dermatitis in a high proportion of patients ***(Lallas et al., 2013).***

Dermoscopy is a noninvasive diagnostic technique for the in vivo observation of skin lesions ***(Lacarrubba et al., 2010).*** Dermoscopes are modified magnifying devices that permit the visualization of pigmented structures or vessels in the epidermis and superficial dermis and generally employ x10 magnifications ***(Micali et al., 2011).*** Their use has gained great popularity for aiding the diagnosis of pigmented skin lesions ***(Akay et al., 2010).***

The use of dermoscopes has been applied for the diagnosis of non-pigmented skin lesions including, hair diseases, skin tumors and inflammatory dermatoses ***(Zalaudek et al., 2006).***

Lallas et al. (2012) reported that the dermoscopic features in dermatitis more commonly showed yellow scales and dotted vessels in a patchy arrangement. Recently, **Lallas et al. (2013)** reported that there are specific dermoscopic findings for early MF cases.

Marwah (2014) concluded that fine short linear vessels, spermatozoa-like vessels, dark globules, and light brown multifocal pigmentation on a pink homogenous background are highly suggestive of MF.

Bosseila et al., (2015) studied 25 patients complaining of early stage of MF. Dermoscopic evaluation of these patients exhibited characteristic vascular pattern consisting mainly of dotted blood vessels and linear blood vessels. Orange yellow patch areas were seen in only a few cases.

Establishing the dermoscopic features of MF could be of help as a rapid diagnostic screening non-invasive tool to differentiate chronic eczema cases from the clinically simulator MF.

2. Aim of the Work

The aim of the current study is to establish the dermoscopic features of the early stage MF and to evaluate the predictive value of dermoscopy in differentiating early stage MF from chronic eczema.

3. MYCOSIS FUNGOIDES

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

3.1 Epidemiology:

Mycosis fungoides 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)***.

Mycosis fungoides 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. 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)***

3.2 Clinical Presentations:

There are 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)***.

The lesions commonly affect the breasts, buttocks and flexures of extremities and may be asymptomatic transitory and disappearing spontaneously without leaving scar. The patch stage of MF may last for months or years before it progress to the plaque stage ***(Christine et al., 2014).***

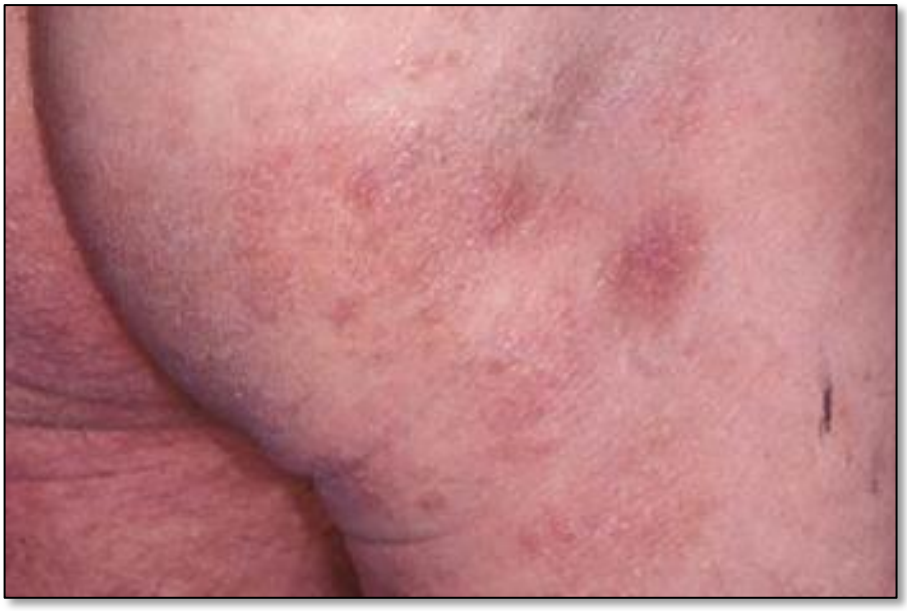

Fig (1): Patch-stage MF ***(Keehn et al., 2007)***.

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

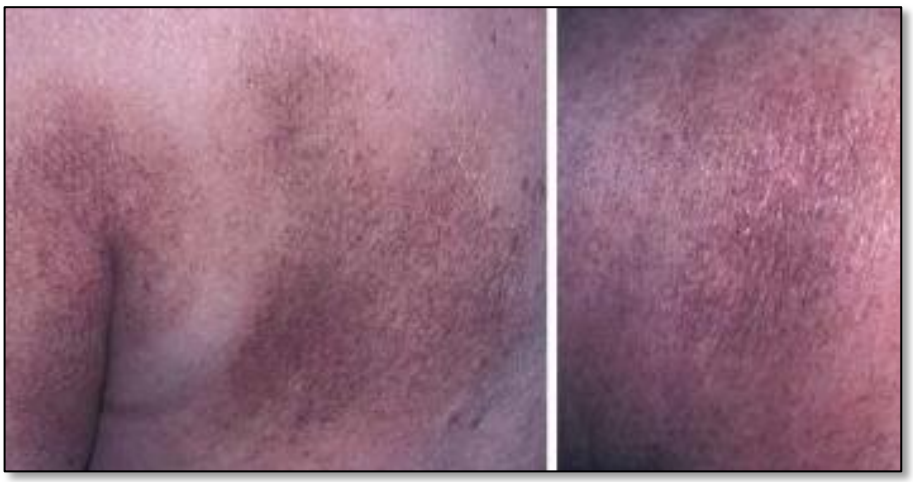

Fig. (2): Poikilodermatous variant of MF ***(Keehn et al., 2007).***

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 ***(Keehn et al., 2007).***

Typical patches usually observed contiguous to plaques or at other sites ***(Christine et al., 2014).***

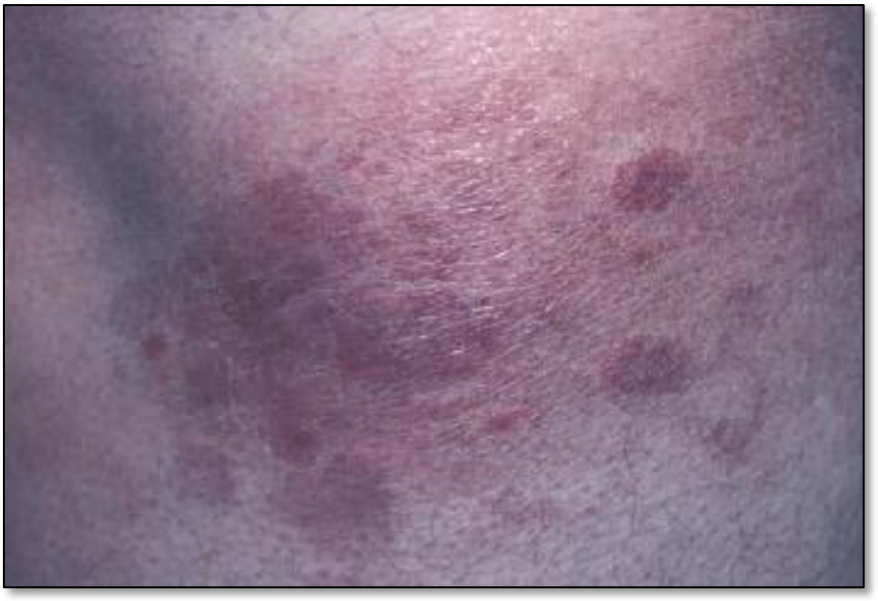

Fig. (3): Plaques of MF ***(Keehn et al., 2007).***

The lesions of tumor-stage MF are typically violaceous, exophytic, mushroom-shaped tumors ***(Michael et al., 2004).***

Tumors are the main finding in this stage of MF, but in most cases plaques and patches are also present. The tumors are characterized by an exaggerated vertical growth phase resulting in large reddish-brown or bluish-red smooth-surfaced nodules which may ulcerate. Tumors can be seen on previously involved or unaffected skin and have a predilection for the face and body folds such as the groin, axillae, neck, antecubital fossae and inframammary areas in women ***(Christine et al., 2014).***

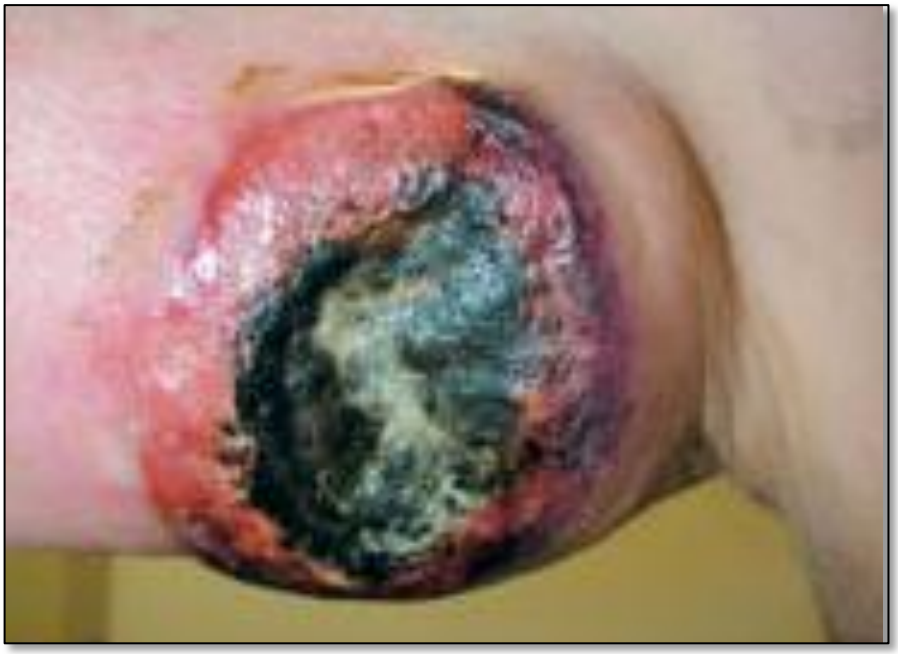

Fig. (4): Tumor-stage MF ***(Michael et al., 2004).***

Pruritus is the most common symptom in patients with MF. Itching may be mild and easily controlled, but frequently it becomes so severe and intractable that it interferes with sleep and disrupts daily activities. Unless the disease is advanced, patients usually do not experience constitutional symptoms such as fever, fatigue, weight loss, and night sweats ***(Parker and Bradley, 2006).***

Other rare presentations include bullous, follicular, hyperpigmented, hypopigmented, verrucous/hyperkeratotic, pustular, lichenoid, papular, psoriasiform, palmoplantar, granulomatous and acanthosis nigricans-like variants. Variants with distinctive clinicopathological features include folliculotropic MF, pagetoid reticulosis and granulomatous slack skin ***(Willemze et al., 2005)***.

Lesions often undergo ulceration or necrosis and secondary infection. Over 50% of deaths from MF are caused by *Staphylococcus aureus* or *Pseudomonas aeruginosa* sepsis. Tumors may undergo transformation into clusters of differentiation (CD) 30 positive large-cell anaplastic variant of CTCL with an aggressive biological behavior. Transformation has been reported to range between 8% and 55% of tumor-stage MF. In contrast to the primary CD30+ anaplastic large-cell lymphomas that generally have a good prognosis,the prognosis for secondary CD30+ lymphomas developing in association with MF is poor, with median survival from transformation ranging from 11 to 36 months ***(Vergier et al., 2000).***

Sezary Syndrome (SS) is a distinctive (leukemic) form of CTCL in which patients have significant blood involvement with Sézary cells, erythroderma and lymphadenopathy. Additional clinical findings commonly seen in SS include keratoderma, nail dystrophy, alopecia, ectropion, and skin edema (especially in the legs). These patients often experience intractable itching (pruritus), which can be the most significant life-altering symptom, and therefore treatments that can successfully reduce pruritus even without measurable objective response may still be a valuable option ***(Kim et al., 2006).***

3.3 Etiology:

3.3.1 Antigen stimulation hypothesis:

The cause of CTCL is unclear. Several theories have been reported, the predominant theory is that MF most likely develops secondary to chronic antigenic stimulation by multiple factors in a process involving oncogenes mutations as well as certain DNA repair genes mutations ***(Mirvish et al., 2011).***

The various risk factors for chronic inflammation and malignant diseases, including alcohol consumption, nicotine use, and excessive exposure to UV radiation association with MF remains uncertain ***(Morales-Suarez-Varela et al., 2006).***

Together with specific antigens, bacterial superantigens such as Staphylococcus aureus (S.aureus) may also be a cause of continuous stimulation of T cells ***(Vonderheid et al., 2005).*** Studies however, suggest that S.aureus appears more relevant for exacerbation in advanced stages than for the etiology of MF. In summary, no specific antigen or carcinogen has yet been identified as being essential to MF development ***(Beyer et al., 2011).***

3.3.2 Viral Induction Theory:

Many epidemiologic studies suggested associations of CTCL with viral infectious origin. Viral infection of Langerhans cells is the initial event leading to CTCL carcinogenesis ***(MacKie, 1981).***

3.3.2.1 Retroviruses: **Van der Loo ET al., (1979)** observed retrovirus-like particles in Langerhans cells residing within the skin and lymph nodes of patients with MF and SS.

The notion of retroviral involvement in CTCL was further propelled by the discovery of human T-lymphotrophic virus (HTLV) the retrovirus that causes adult T-cell leukemia and lymphoma. As CTCL bears significant clinical and histopathological similarities to its nodal correlate, HTLV became a subject of close scrutiny as a putative causative factor of CTCL.

In a cell line derived from a patient with SS retrovirus-like particles and reverse transcriptase activity were detected. The investigators isolated a novel retrovirus related to HTLV-I and HTLV-II, which they named HTLV-V. However, no subsequent data confirmed the existence of HTLV-V ***(Manzari et al., 1987).***

Zucker-Franklin et al., (1992), found HTLV-like inclusions in the peripheral blood mononuclear cells of patients with CTCL and HTLV proviral sequences and reverse transcriptase activity in some cell lines derived from peripheral blood mononuclear cells of patients with MF and SS.

3.3.2.2 Herpes virus:

There is a significantly higher rate of CMV seropositivity in patients with MF and SS than in age-matched control subjects ***(Herne et al., 2003).***

Evaluating MF tumors for evidence of the recently discovered MCV yielded negative findings ***(Mirivish et al., 2011).***

There is a higher rate of positivity for EBV nucleic acids in a small sample of cutaneous lesions excised from patients with a variety of CTCL subtypes ***(Shimakage et al., 2001).***

In contrast to these findings **Kreuter et al., (2008)** found that MF cutaneous lesion samples were uniformly negative for EBV DNA and protein by real-time PCR and immunohistochemistry, respectively.

Trento et al., (2005) found a high prevalence of KSHV/HHV-8 infection in patients with large plaque

parapsoriasis, which is often considered to be a precursor lesion for CTCL.

Possible explanations for these inconsistent findings include various forms of contamination (eg, viral genomic contamination of PCR reactions); misdiagnosis of virus-associated cancers (eg, adult T-cell leukemia/lymphoma) as CTCL; and the limitations of current molecular and immunologic diagnostic techniques, which may be unable to fully differentiate between the various disease subtypes collectively characterized as CTCL. Most studies have probed possible associations with retroviruses and herpesviruses ***(Mirivish et al., 2011).***

3.3.3 Fas Ligand Expression Failure Theory:

The failure of the fas ligand expression is another theory under investigation. The latter is partially responsible of the T-cell apoptosis, thus its failure of expression may explain how the T lymphocytes avoid the immune surveillance ***(Gu et al., 2013).*** Immuno histochemical analyses of skin biopsies in MF have shown that the epidermal tumor cells in the early stages are Fas-positive, while during the tumor stage the expression of Fas is diminished ***(Zoi-Toli et al., 2000).***