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# Cutaneous T-Cell Lymphoma - Review Of Literature With Reference To A Case Report

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**ABSTRACT**— Cutaneous T cell lymphomas (CTCL) are a diverse group of extranodal non-hodgkin's lymphomas defined by a skin infiltration of neoplastic monoclonal T cells. Adults between the ages of 55 and 60 are most commonly affected, with a yearly incidence of roughly 0.5 per 100,000. The most frequently occuring subtypes of CTCL include mycosis fungoides, Sézary syndrome, and primary cutaneous peripheral T cell lymphomas not otherwise specified (PCTCL-NOS). CTCL is a difficult disease to understand in terms of etiology, pathogenesis, diagnosis, treatment, and clinical outcome. In this paper, we give a case study and highlight the progress made in these sectors.

**KEYWORDS:** T-cell, lymphoma, skin, recent, update, sezary, non-hodgkin’s

## 1. INTRODUCTION

Alibert first defined mycosis fungoides (MF) as lymphocyte infiltration of the skin in 1806. The terminology “cutaneous T cell lymphomas” (CTCLs) was used by Edelson in 1974 to describe MF and its leukemic variation, Sézary syndrome (SS), which are the two most frequently occurring kinds of CTCL [1]. CTCLs are a diverse category of extranodal non-lymphomas Hodgkin's that are defined by infiltration of neoplastic monoclonal T cells in the epidermis [1- 3]. Extranodal locations are involved in around 25-40% of non-lymphoma Hodgkin's patients. After the gastrointestinal system, the skin is the most prevalent location [4]. CTCL has an annual incidence of around 0.5 per 100,000, with males being more affected than women [1]. They usually affect people between the ages of 55 and 60 [1], [5]. The North American Mycosis Fungoides Cooperative Study Group categorized CTCLs for the first time in 1975, using the TNM method. Following that, the CTCL workshop changed and revised the categorization to what is now called the Bunn and Lambert system [1]. MF and SS were categorized by the International Society for Cutaneous Lymphoma/European Organization for management and research of this tumor based on clinical, pathological, biological, and immunological characteristics [6]. MF, SS, and PCTCL-NOS are the most common CTCL subtypes [7], [8]. MF is the most frequent kind of CTCL, amounting for 44-62% of all cases [9]. In sun-protected body locations, MF limited to the skin progresses indolently from patch and macule stage to infiltrating plaque and tumor stage [5], [10- 12]. SS is a leukemic-phase variant of MF with erythematous skin lesions and widespread lymph node enlargement that is clinically characterized by erythroderma and generalized lymphadenopathy [13]. PCTCL-NOS may manifest as a single red fiery tumor nodule on any portion of the body, or as scattered multifocal or diffuse nodules that become ulcerated and infected. This subgroup of CTCL is characterized by rapid cutaneous spread and systemic involvement [8]. CTCLs are often misdiagnosed as benign skin diseases in their early stages [1], [9], [13- 17]. The diseases include all types of eczema and dermatitis, psoriasis, parapsoriasis, adverse drug reactions, lichen planus, panniculitis, folliculitis, morphea, pityriasis lichenoides chronica, Vitiligo, pityriasis lichenoides et varioliformis acuta, pigmented purpuric dermatoses and lymphomatoid papulosis [14], [16], [17]. The

histologic characteristics of CTCL are usually modest, making it difficult to distinguish these illnesses from benign inflammatory diseases [18], [19]. Histologic sections of MF show haloed lymphocytes, epidermotropism, exocytosis, Pautrier's microabscess, massive hyper convoluted, hyperchromatic lymphocytes in the epidermis, and lymphocytes localizing within the basal layer [16], [20]. In terms of etiology, pathogenesis, diagnosis, treatment, and prognosis, CTCL is a difficult subject. We've compiled information on the most recent advancements in these domains along with presenting a case report.

## 2. Case report

A 61-year-old female patient presented with multiple large reddish papules all over her body including trunk and peripheral areas, for the past few weeks [Fig1-Fig5]. Skin biopsy submitted shows thinned out epidermis, with hyperkeratosis. There is evidence of epidermotropism. The dermis shows diffuse sheets of large lymphoid cells [Fig6-Fig8]. These cells appear anaplastic with round to oval, irregular nuclei. Some show prominent eosinophilic nucleoli and around cytoplasm. These cells are admixed with lymphocytes, eosinophils and histiocytes. A diagnosis of cutaneous lymphoma was made and immunohistochemistry was carried out. The tumor cells were strongly positive for CD3, CD4 and CD8 indicating cutaneous T-cell lymphoma [Fig9] confirming the diagnosis of CTCL.

## 3. Discussion

### *3.1 Etiopathogenesis*

Despite extensive research into the etiopathogenesis of CTCL over the past several decades, the specific mechanism of origin and development of this condition is still unknown [4], [10], [21]. Although various genes and signaling pathways have been found to be dysregulated in CTCLs, their precise function in the etiology of these illnesses is unclear [2], [3], [13], [22- 34]. The majority of these abnormalities are found on chromosome 10 [35]. CTCLs have been shown to have abnormal expression of cancer testis genes in recent research. This gene seems to act by suppressing apoptosis, causing resistance to different treatment strategies, and playing a role in carcinogenesis by affecting tumor suppressor genes like p53 [12]. Negative regulators such as protein tyrosine phosphatases have been linked to the dysregulated Jak-3/STAT pathway and malignant T cell division that is not reliant on interleukin (IL). By boosting the production of IL-10, IL-5, IL-17F, and IL-17A, modifying angiogenic agents, and interrupting histone deacetylase inhibitor (HDACI) treatment resistance, the Jak-3/STAT pathway aids in the battle against CTCLs [25]. Another study found that the NOTCH1 signaling pathway has a detrimental role in the etiology of SS13. NOTCH is a transmembrane receptor family that regulates cell maturation and proliferation [31].

Absence of phosphatase and tensin homolog (PTEN) heterozygosity in MF has been observed, however the relevance of the discovery is unknown. From patch to plaque stage, there was a significant reduction in the proportion of cells maintaining PTEN and less intensity of staining in MF, although this reduction was not very significant in tumor stage compared to plaque lesions [32]. In SS, but not in other forms of CTCLs, expression of a subgroup of receptor tyrosine kinase (RTK) mRNA is found to be elevated [13]. The transcription factor, TOX, regulates the expression of RUNX 3, a known tumor suppressor gene, and contributes to the development of helper T cells. Overexpression of TOX and its protein product has been linked to wider MF lesions, disease progression, and a worse prognosis in studies. In addition, deregulation of this gene has been found in SS lesions and circulating mononuclear cells [22]. CTCL patients have a unique microRNA (miRNA) expression profile. MiR-21 and miR-155, according to studies, are linked to bad prognosis and increased aggression by interfering with apoptosis and encouraging malignant growth, respectively. Another tumor suppressor miR-22 expression, is found to be reduced in SS. The decrease of miR-22 expression seems to be caused by Jak-3/STAT [25]. Another non-coding microRNA, miR-16, is

downregulated in CTCLs33 and causes cellular senescence. Many oncogenes, including MAX, MYCBP, cyclin-dependent kinase-6 (CDK-6) and nuclear receptor coactivator-1 (NCOA-1) have been found to be inhibited by miRNAs [25].

The genesis of CTCLs has been linked to IL-2Rgc-signaling chemical mediators such as IL-21, IL-15, IL-7 and IL-4 [25]. IL-12 acts as a powerful anti-tumor agent. During tumoral-stage MF, its expression is reduced [36]. Elevated expression of IL-9, which is controlled by STAT3/5, and interruption of STAT5 have been described in CTCL lesional skin. Increased expression of the CC chemical mediator receptors 6 (CCR6) and CCR has also been seen in CTCLs, and is thought to be the reason for the dissemination of neoplastic T cells to sentinel lymph nodes, the circulation, and distant organs. Chemokine (C-X-C motif) ligand12 (CXCL12) is a member of the chemokine (C-X-C motif) ligand12 (CXCL12) superfamily that is present on stromal and endothelial cells in several organs. CXCR4, the chemokine's receptor, is expressed by the majority of hematopoietic cells, including CD4+ T cells and CD34+ progenitor cells. Chemotaxis, angiogenesis, invasion, and proliferation are all aided by this receptor. The relevance of the CXCR4/CXCL12 axis in the pathophysiology of MF has been suggested [10]. Malignant T cells in CTCLs show activation of the TCR path, which results in TCR-dependent T helper 2 (Th2) chemokines like IL-13 and IL-4 and defiance of natural anti-proliferative methods like Fas cell surface death receptor (FAS) facilitated apoptosis and TGF-beta regulated growth reduction [12]. Regulatory T lymphocytes with the phenotype CD4+ CD25+ make up around 5-10% of circulating T cells and have a part in tumor immune mechanisms. The function of these lymphocytes in CTCLs is debatable. The majority of research has shown that a large number of FOXP3+ regulatory T cells in CTCLs is associated with a better prognosis. This observation contradicts previous research on the significance of these cells in other solid malignant tumors [27].

CD26 has been demonstrated to be able to split and disable CXCL12, hence its absence in CTCLs resulted in increased CXCL12 regulated chemotaxis. CD164, on the other hand, is highly expressed on CD4+ cells in SS. This component seems to be a diagnostic parameter as well as a possible treatment target in SS [39]. These zinc relied enzymes have been linked to gene regulation and the control of various cellular processes, including cell division, maturation, migration and apoptosis. CTCLs have been shown to have abnormal enzyme activity as well as mutations in these enzymes [1]. In MF, tumor cells move to the skin through utilizing lig- and E-selectin molecules on endothelial cells, as well as the presence of cutaneous lymphocyte-associated antigen (CLA), a skin specific marker. Specific chemokine receptor-ligand interactions are required for CLA to promote leukocyte localisation in the skin. One of these connections is via the chemokine receptor CCR4, which has been shown to be overexpressed in CTCL patients in leukemic stage [1]. Granulysin is a cytotoxic, antimicrobial, and proinflammatory substance found in the granules of cytotoxic T lymphocytes and natural killer cells, together with granzymes and perforin. It has been demonstrated to be implicated in the advancement of MF [27] and has a part in innate immunity and chemotaxis. The Mucin 1 C-terminal component regulates cell division, regeneration, apoptosis, and invasion, all of which are significant oncogenesis pathways. Cells are protected from reactive oxygen species induced demise by this heterodimeric protein. This protein has been observed to be overexpressed in CTCL cell culture lines [40]. The preservation of redox equilibrium has been indicated as a key element in preventing apoptosis in tumor cells in CTCLs [40].

Cancer stem cells are known to have several attributes similar to normal stem cells, such as less division, strong self regeneration capability, apoptotic resilience, and the capability to remain immature, resist cell aging, and specialize into all cell types. Chemotherapeutic drugs are resilient to them due to their few mitotic divisions. Furthermore, these cells are responsible for tumor metastatic disease. In CTCL lesions,

the activation of embryonic stem cell genes such Nanog homeobox (NANOG), OCT4 (POU class 5 homeobox [POU5F]-1) and SRY (sex determin- ing region Y)-box (SOX)-2, as well as their downstream and upstream signaling members was seen [2]. The growth of blood and lymphatic vessels is thought to be implicated in the advancement of CTCL. Angiogenic substances synthesized by neoplastic T cells include podoplanin (PDPN), vascular endothelial growth factor-C (VEGF-C), lymphatic vessel hyaluronan receptor-1 (LYVE-1), VEGF-R3, and lympho-toxin alpha (LT), all of which are involved in neoangiogenesis and neo-lymphangiogenesis. Angiogenesis is induced by the interplay of LT, IL-6, and VEGF, which promotes endothelial cell budding and colony formation [3]. Chronic skin inflammation and the eventual genesis of CTCL have been linked in several studies [9]. Long-term psoriasis, urticaria, and chronic or occupational exposure of skin to chemical substances have all been cited as risk factors [21]. T cells that have been stimulated for a long time may ultimately form an unusual T cell clone [9]. For example, it seems that granulomatous inflammation precedes lymphoma in granulomatous MF, leading to T cell proliferation by macrophage produced IL-6 [41].

It has been claimed that MF and microbial colonization/infection have a link [9,42]. Bacterial cultures harboring staphylococcal enterotoxin-A (SEA) have been demonstrated to increase disease development in cancerous T cells by promoting STAT3 activation and IL-17 expression42. Loss of the normal TCR repertoire, on the other hand, leads to immunodeficiency and increased infections, which may lead to mortality in CTCLs [12]. The relevance of viral infection in CTCL development is still debatable. Lately, the pathophysiology of these illnesses has been linked to herpesvirus family members like Epstein-Barr virus, human herpesvirus 8, and cytomegalovirus, and retroviruses like human T cell leukemia virus type 1 (HTLV-1) and HTLV-2, as well as human immunodeficiency virus. By stimulating the secretion of tumor necrosis factor-alpha (TNF-), interleukin-6 (IL-6), and interleukin-1a (IL-1a), viral infection may enhance tumoral infiltration. Furthermore, these organisms act as a persistent chronic antigen in the skin, causing T cells to clonally proliferate, resulting in CTCLs [4].

### *3.2 Diagnosis*

The existence of diverse clinical manifestations [1], [43], [44] and the absence of definite diagnostic criteria [1], [45] make early detection of CTCLs problematic. As a result, it requires an average of six years from the commencement of the illness to the affirmation of the disease [1], [44]. There have been recent advancements in CTCL diagnostic accuracy. The National Comprehensive Cancer Network's recommendations advocate sampling of questionable skin locations and further examination in terms of histopathology, immunohistochemical, and genetic analysis of TCR gene alterations to identify CTCLs [14]. The cornerstones in suspecting CTCLs are examination of the skin. The usual method for staging these illnesses is to palpate lymph nodes [14], [45], [46]. Because the clinicopathologic features of CTCLs are diverse, details acquired from just one biopsy sample may result in wrong diagnosis [18], [19], [45], 46] numerous samples are often necessary to establish the final diagnosis. Detecting abnormal cells in the peripheral blood of CTCL patients is crucial for early detection of SS and evaluating prognosis [47,48]. Blood analysis, on the other hand, is of restricted use because it lacks a precise marker for detecting CTCLs in a sensitive process [9], [14]. LDH can measure tumor load non-specifically and has been associated with poor outcome in CTCLs [9], 14]. These findings offer a reliable method for determining gene alterations in CTCLs [3], [35].

The presence of a neoplastic T cell clone is a crucial sign for CTCL confirmation. TCRγ PCR analysis finds malignant T cells in only a portion of patients, while high end TCR sequencing detects malignant T cells with greater specificity and sensitivity than TCRγ PCR. Indeed, high end TCR sequencing is beneficial for determining the source and localization of malignant CTCL cells, as well as for accurately diagnosing all

phases of CTCLs, differentiating these illnesses from benign inflammatory diseases [14], [44]. Flow cytometry detection of cancerous cells in SS patients is a significant diagnostic for SS diagnosis. [14], [39], [45]. Biopsies of the lymph nodes and bone marrow are essential diagnostic tools in advanced patients [14]. The absence of T cell surface markers including CD7, CD26, and CD27 on neoplastic T cells may help with CTCL diagnosis. On the contrary, CD164 upregulation has been seen in helper T cells from SS patients. Detecting more than 20% CD164 on helper T cells in the peripheral blood of erythema patients in flow cytometric investigations is strongly suggestive for SS. These tests' specificity and sensitivity should, however, be taken with care [48]. PCTCL-NOS is related to the lack of practically all T cell surface antigens, CD56 expression, and limited or no CD30 expression, among other things [8]. Ki67, AgNORs, and CD34 are well-known indicators for CTCL development since they represent cell proliferation and angiogenesis characteristics. They are overexpressed in late stages of MF and have been linked to a reduced life expectancy [10].

T-cell-specific soluble IL-2 receptor (sIL-2r) is possibly diagnostic of CTCL activity, severity, and prognosis, however it is not specific for CTCL diagnosis [9]. There has been a link found between elevated sIL-2r and either adnexal pathology or late stage MF. As a prognostic indicator, this factor is more precise than LDH [9]. New studies have verified the TOX gene's relevance as a CTCL marker. Furthermore, this gene is a chemotherapeutic option [22]. EPHA4 has been identified as a diagnostic and prognostic marker for SS in studies [13]. CTCLs may be diagnosed via miRNA profiling. Minimal miRNA detectors have been found in studies to be capable of detecting cancerous skin lesions [25]. In advanced situations, HTLV serology must be examined [14]. Nodal and systemic spread are investigated using magnetic resonance imaging (MRI) or computed tomography (CT) scans [9], [46]. The fluorine-18 fluorodeoxyglucose positron emission tomography-CT (18F-FDG PET-CT) may be used to diagnose skin and extracutaneous CTCL lesions, as well as assess treatment response and disease recurrence. This technique is more specific and sensitive than a CT scan in identifying both skin and extracutaneous involvement, especially lymph node involvement [46].

### *3.3 Management*

Because there is no absolute cure for MF and SS, therapy choices are primarily palliative [1], [49]. Treatment aims include symptom relief, inducing remission, and postponement of disease progress while minimizing major adverse effects induced by therapeutic methods [12]. Due to the significant risk of infection in individuals with a weak skin barrier, multi-drug treatment techniques are not recommended for CTCLs [50]. Accurate staging is required before deciding on the optimal treatment strategy for this aggressive illness [1], [46], [51]. In general, treatment choices are divided into two categories. Skin-directed treatments [1], [11], [45], [52], [53] are the first line of defense against illness in the initial stages (IA to IIA) when it affects less than 20% of the areas of the body [1]. For instances like resistance cases in the initial stages and those with late stage disease, systemic treatments are employed [1], [6], [11], [45], [52], [53]. Topical and systemic steroids are beneficial in the treatment of CTCLs [9], [54], [55]. Topical steroids may be used to treat resistant patients in both early and late stages of illness. Relapse of illness is one of the issues with corticosteroid treatment [1]. The anti-proliferative and apoptotic signal initiation pathways of retinoids are useful in the treatment of CTCLs [56], [57]. The retinoic acid receptor beta2 gene functions as a tumor suppressor gene [56]. The US FDA has authorized bexarotene, for treating stage I MF [1], [58], [59] and relapsed resistant CTCLs [58]. Dose-dependent and reversible adverse reactions of bexarotene include severe hypercholesterolemia with a considerable drop in HDL levels and hypothyroidism [60]. Another topical retinoid, Tazarotene, has been reported to be effective as a single drug therapy in the management of early stage CTCLs [61]. CTCLs have been effectively treated with systemic retinoids like acitretin, bexarotene and isotretinoin [9].

Anti-neoplastic drugs which are histone deacetylase inhibitors (HDACI) are new treatment possibilities for CTCLs [1], [9], [62]. Their mode of action include (a) enhancing the activity of gene that control cell division and promote apoptosis, (b) promoting changes to the internal structure of chromatin, (c) controlling miR-22 activity, and (d) boosting reactive oxygen species production while reducing mitochondrial membrane [63]. Transformed cancer cells are more vulnerable to these chemicals than normal cells [11]. Vorinostat and romidepsin are approved by FDA for treatment of progressive, chronic, or relapsing CTCLs in this treatment program [11], [50], [58]. When administered as single agents, these agents may cause a 30 to 35 % overall treatment response rate, although only 2 to 6% of patients have a full response rate [11]. Other HDACIs under investigation include entinostat, panobinostat, belinostat, AN-711 and quisinostat [1], [64]. HDACIs are generally well tolerated. Weakness, stomach discomfort, decreased blood cells, and dehydration have all been documented as minor adverse effects of these drugs [1].

A toll-like receptor 7 (TLR7) agonist, named imiquimod, is found to be efficacious in the management of MF. It acts by causing plasmacytoid dendritic cells that are found in inflammatory and cancerous cutaneous lesions, to produce TNF, IFN-α, IL-8, IL-6, and IL-1. Topical application of resiquimod, an imidazo-quinoline with TLR8- and TLR7-stimulating action, was reported to be effective in the treatment of initial stage CTCLs. Its ability to induce the reduction of untreated lesions has been described, and it is thought to be facilitated by an increase in overall anti-tumor immunity. Resiquimod seems to work by boosting the activities of cutaneous T cell activator and natural killer cells by gathering and growing normal clones of T cells [54].

Denileukin diftitox is an FDA-approved recombinant protein complex [9], [50] that combines diphtheria toxin with IL-2 to cure CTCLs [51]. It has been revealed that alemtuzumab and zanolimumab are effective in treating CTCLs. Zanolimumab is less likely to cause infection than alemtuzumab [50]. IFN-, for example, is beneficial in treating MF and SS, although it may worsen PCTCL-NOS [8]. As a first-line systemic treatment for MF, IFN-2b is still the best choice [51]. By activating cellular immunity and cytotoxic T cell reactions in the host, recombinant IL-12 is effective for managing CTCLs [54]. Chemotherapeutic drugs are used to treat CTCLs, however significant side effects have been documented [11]. Topical chemotherapeutic treatments such mechlorethamine and carmustine are beneficial in treating early-stage diseases for the most part, but their efficacy in managing advanced diseases is debatable [1], [11]. The FDA has authorized methlorethamine for the management of stage Ia and Ib MF. It's an alkylating drug that works by suppressing proliferative cells and changing the relationships between keratinocytes, Langerhans cells, and T lymphocytes. Patients getting this drug in combination with phototherapy, radiotherapy, and immunotherapy have developed non-melanotic skin malignancies [11]. Methotrexate, gemcitabine, chlorambucil, and pegylated doxorubicin are among the additional systemic chemotherapeutic drugs that have been utilized to treat CTCLs. Pralatrexate is a methotrexate analogue that has been licensed by the FDA for the treatment of refractory or relapsed CTCLs [50]. Cyclophosphamide, vincristine, doxorubicin, and prednisone (CHOP) have demonstrated varying success in the management of severe CTCLs [9], [50].

The most popular therapies for attaining remission or preventing progression in MF are psoralen plus ultraviolet A (PUVA), ultraviolet B (UVB), UVA, and excimer laser [9], [1], [65]. UVB is less efficient than PUVA in addressing invasive lesions, and the length of remission is shorter with UVB [9]. For the treatment of CTCLs, radiation is an efficient skin focused therapy [66], [67]. Radiotherapy has been very effective on lymphocytes. Radiotherapy to isolated lesions or the whole skin helps manage illness in more severe cases. This method may be effective in instances with a single lesion [66]. CTCLs in stages I to III are successfully treated with electron beam radiotherapy [49], [50], [68], [69]. For more advanced diseases,

a Full body skin electron beam is an acceptable approach [1], [50]. In tumor-stage illness, the full recovery rate is lower than in plaque-stage disease (36 vs 98.3%) [49]. Traditional photodynamic treatment with aminolevulinic acid (ALA-PDT) is successful in a fraction of CTCLs since it induces programmed cell death, which is facilitated by the low activity of cell death receptors such as FAS in neoplastic T cells. Methotrexate combined with ALA-PDT improves photodynamic treatment effectiveness by upregulating FAS and blocking of its promoter methylation [70]. Extracorporeal photopheresis is an immunomodulatory procedure that results in a rise in the circulating dendritic cells and a boost in the immune response of T helper cells [71]. It's an effective treatment for unresponsive, early stage MF [71] and SS [50], [71]. A partial response rate of 30 to 80 percent and a full remission rate of 14 to 25% are anticipated with this technique [50]. Late stages of MF, SS, and PCTCL-NOS are treated with allogeneic blood stem cell transplants [7], [53], [54], [72], [73]. This treatment strategy has been proven in studies to be suitable for young patients with recurrent disorders that develop despite many lines of chemotherapy [7], [50], [72]. Tazarotene, forodesine, lenalidomide, synthetic oligonucleotides, temozolomide, everolimus, C-beta kinase inhibitors, mucin 1C inhibitors, PD1/PD-L1 inhibitors, brentuximab vedotin, and mogamulizumab are among the medicines whose effectiveness is being investigated [40], [50], [74], [75]. Treatments that target mucin1 are efficient in controlling CTCLs because mucin1 is overexpressed in CTCL cells. Mucin1C inhibitors (such as GO-203) might theoretically be an effective therapy since they raise the quantity of reactive oxygen species and cause oxidative stress causing late cell death [40]. Everolimus, which inhibits cancerous T cell growth by targeting the mTOR pathway, seems to be beneficial in managing T cell neoplasm [74].

### *3.4 Prognosis*

CTCLs are chronic illnesses that reoccur when treatment is stopped, even if the condition does not worsen [54]. Despite the emergence of various treatment alternatives for CTCLs, the neoplastic cells have a tendency to involve lymph nodes and circulating blood as they grow and become resistant to therapy, resulting in distressing symptoms. CTCL has been found to progress to tumor stage, when the malignant cells have migrated to the lymph nodes and other internal organs, in fewer than 5% of instances. CTCL prognostic factors include clinical factors such as age, stage and morphologic and genetic features of the tumor cells [76]. Cutaneous lesions are severe in CTCL instances with organ involvement, and the risk of dermatitis is significant. Autopsy investigations, on the contrary, have revealed that 70 to 90% of individuals with MF die with multi-organ dissemination [5]. Furthermore, primary CTCLs differ from systemic lymphomas with skin involvement in terms of clinical behavior [77]. Early on, there is no substantial difference in life longevity between CTCL patients and healthy persons, but as the disease progresses, survival rate drops to 3.2 to 9.9 years [1], [5]. Individuals with MF have a long-term course that may last years or even decades; a large number of them expire of unconnected causes, while roughly a quarter of them die of lymphoma [9]. The most prevalent causes of disease-related mortality are immunodeficiency and secondary infection [11]. SS has a bad prognosis. Its average life expectancy is between 2 and 4 years, and its 5-year survival rate is around 18-20% [1], [7]. The 5-year survival rate for PCTCL-NOSs would be less than 20% [8].

## 4. Conclusion

Despite the fact that several research studies have been conducted on the pathophysiology and treatment of CTCLs, many concerns concerning this complex group of disorders remain unresolved.

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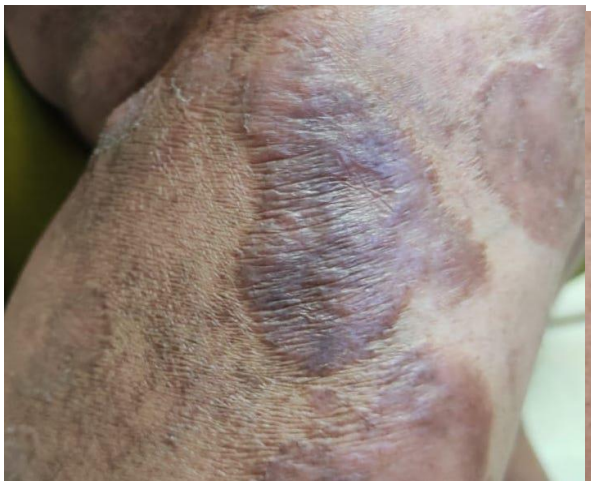


**Fig1**_Leg lesions

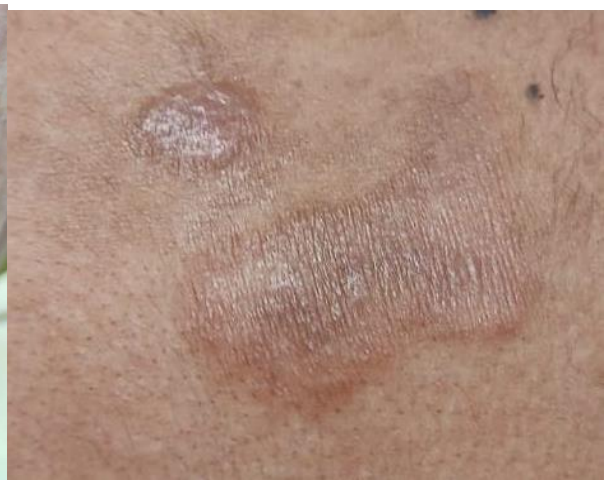
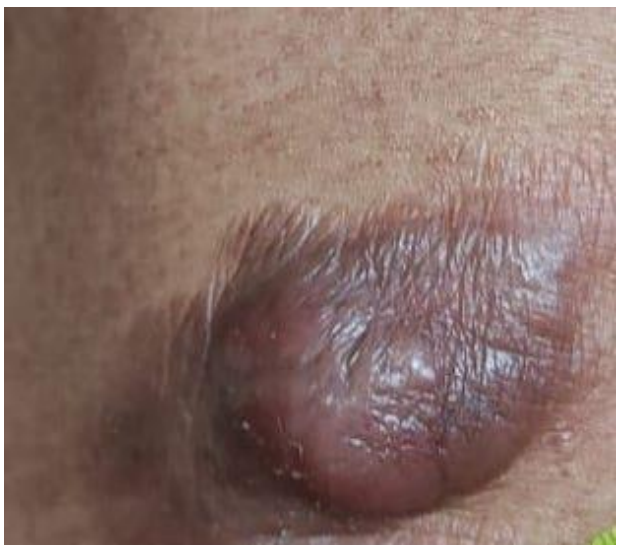


**Fig2**_Lesions in the back



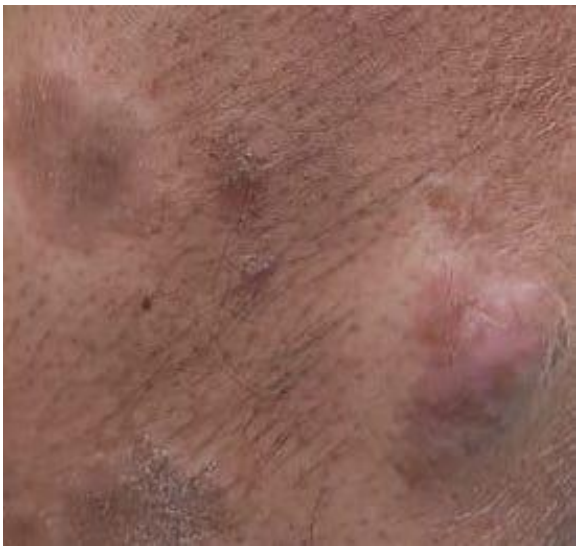


**Fig3**_Shoulder lesions **Fig4**_Forearm lesions

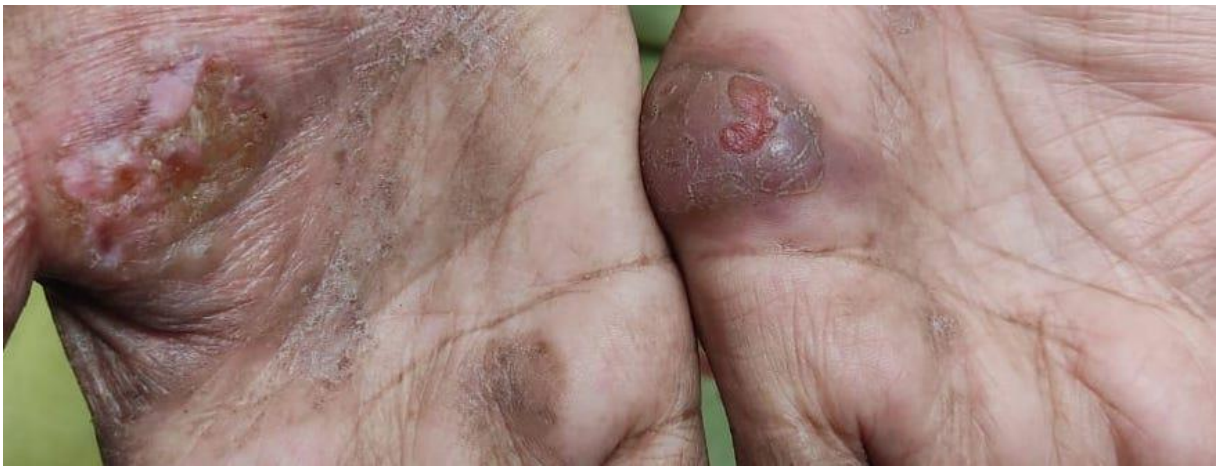


**Fig5**_Hand lesions

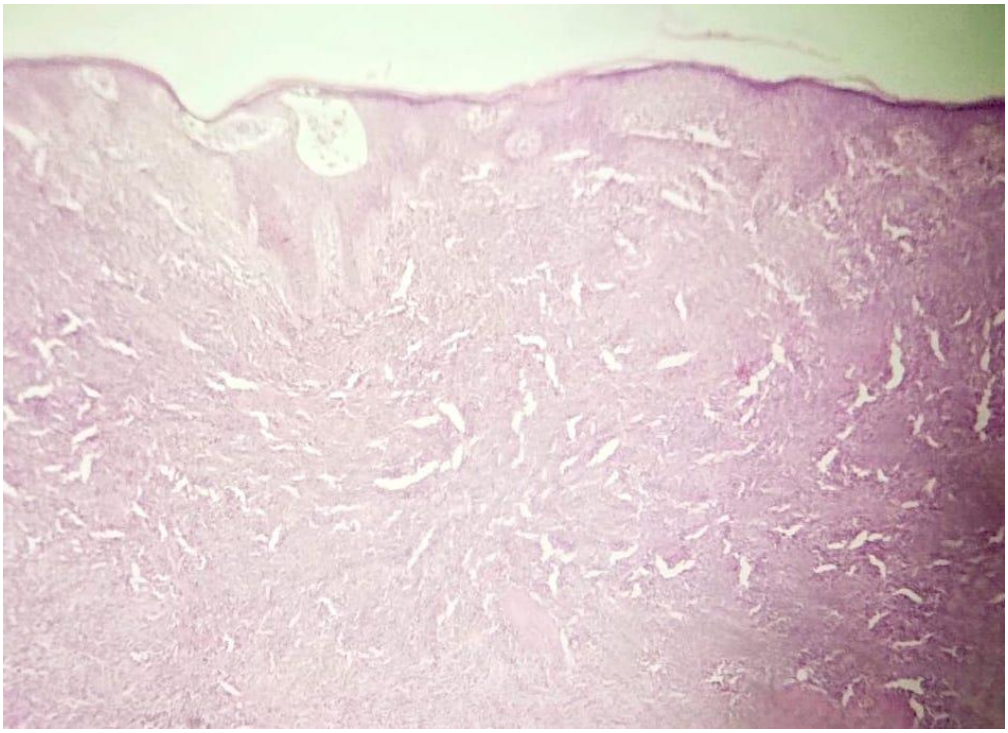


**Fig6**_H&E, 4X, lesion infiltrating epidermis and dermis

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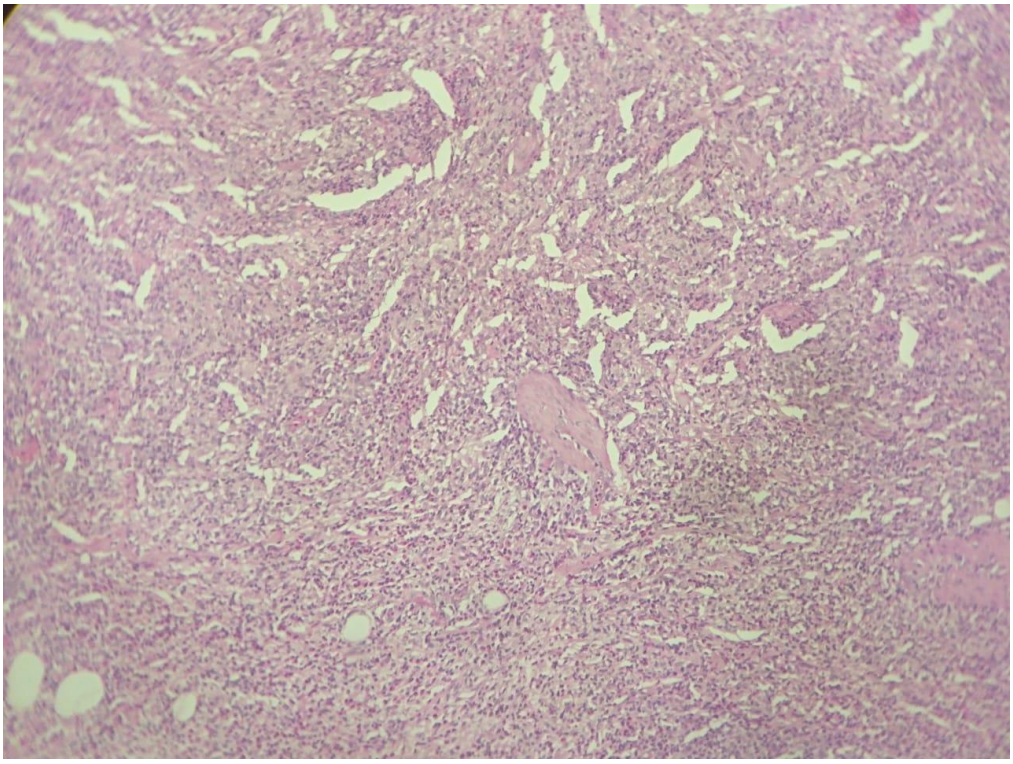

**Fig7**_H&E, 10X,Tumourous cells

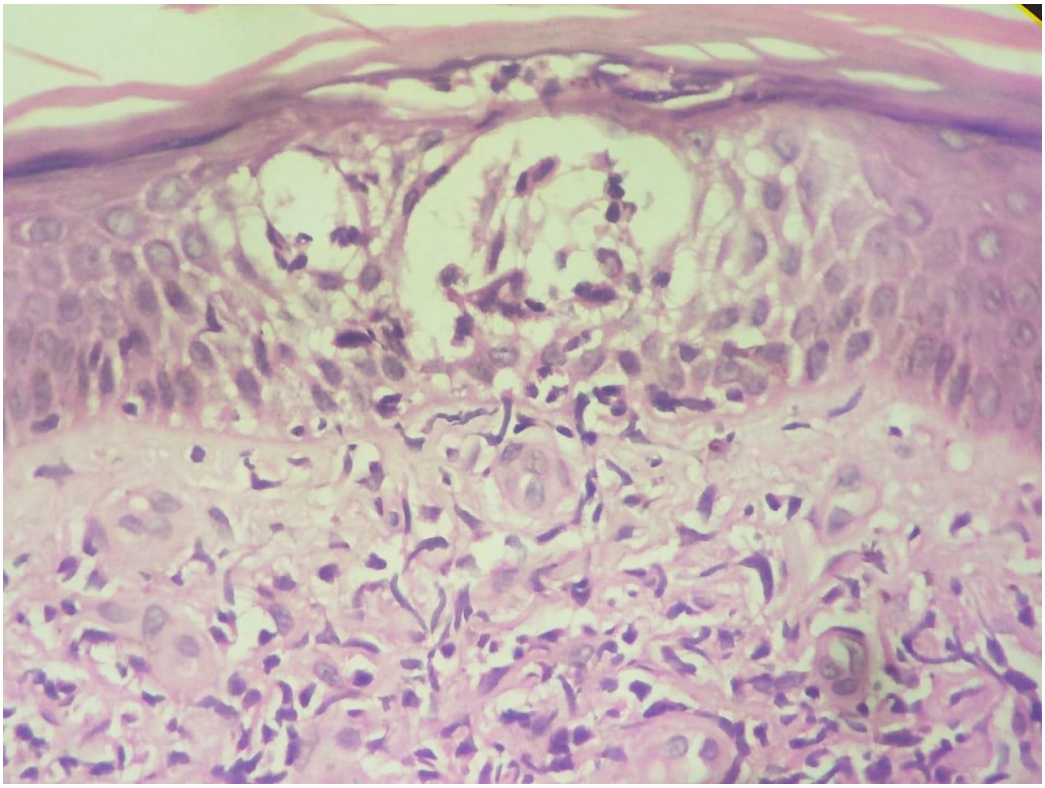

**Fig8**_H&E, 40X, Tumourous cells

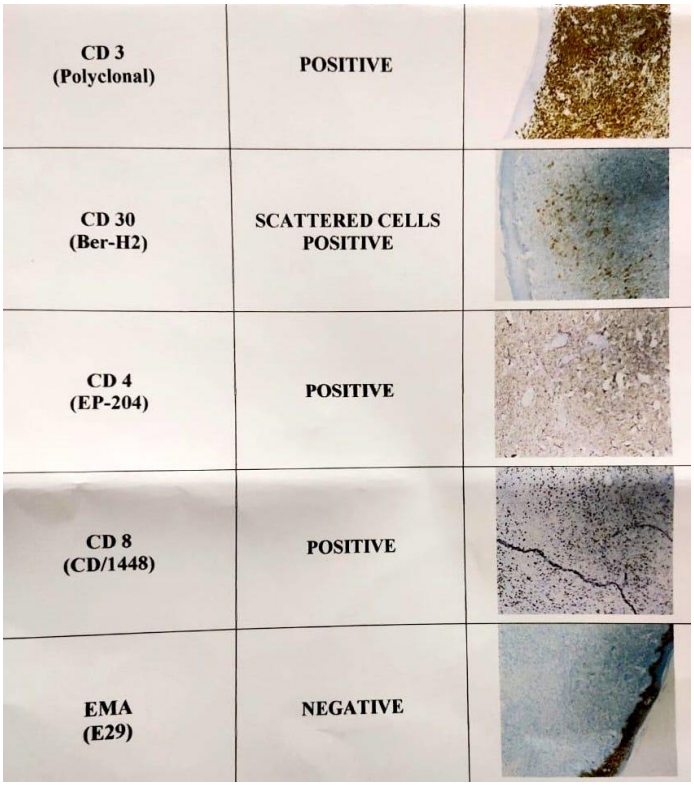


**Fig9**_Immunohistochemical characteristics of the tumour cells