

Case Report

Large Cell Transformation of Mycosis Fungoides Unresponsive to Skin Directed Therapies: A Case Report

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ABSTRACT

Mycosis fungoides (MF) is the most common cutaneous T-cell lymphoma. Large cell transformation (LCT) is a rare but aggressive evolution occurring in a subset of MF patients and is associated with poor prognosis, especially when CD30 expression and nodal involvement are present. Early recognition and prompt initiation of systemic therapy are crucial. We report a case of a 38-year-old female who presented with widespread hyperpigmented, scaly plaques and systemic symptoms such as fever and weight loss. Clinical evaluation revealed multiple lymphadenopathies. Histopathological analysis of skin biopsy showed large atypical lymphocytes ($\geq 4\times$ size of small lymphocytes), with CD3, CD4 and CD30 positivity, confirming LCT of MF. The patient was staged as IIA (T2N1MOBO). Initial treatment with steroids and narrowband ultraviolet B was ineffective. CHOP chemotherapy was initiated, leading to partial clinical improvement. However, the patient succumbed to sepsis 3 months post-therapy. This case highlights the aggressive nature and poor prognosis of LCT-MF, particularly in young patients with nodal involvement and systemic symptoms. Comparison with similar cases in literature reinforces the need for early systemic therapy and multidisciplinary management to improve outcomes in this challenging variant of cutaneous lymphoma

Keywords: Cutaneous T-cell lymphoma, Fungoides, Large cell transformation, Large cell transformed-mycosis fungoides, Mycosis fungoides, Unresponsive mycosis

INTRODUCTION

Primary cutaneous lymphomas are the second most common extranodal non-Hodgkin Lymphomas. They may be of either T-cell, B-cell or NK cell origin. Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma (CTCL). Large cell transformation (LCT) of MF represents a rare but clinically significant event in the disease course, characterised by the transition of the typical small lymphocytes of MF into larger, more aggressive cells resembling Hodgkin's or non-Hodgkin's lymphoma.^[1]

CASE REPORT

We report a case of LCT of MF nonresponsive to skin directed therapies. A 38-year-old female presented with hyperpigmented, scaly lesions associated with itching all over the body since one year. Lesions were initially small red, and flat on right thigh which gradually increased in size, encircling the thigh, became pigmented and raised over a period of one year with associated itching. Subsequently lesions developed over breast, back and arms. There was a history of fever,

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weight loss and reduced appetite. She was also a known case of hepatitis B.

Cutaneous examination revealed large, hyperpigmented, indurated, scaly plaque almost involving the entire right thigh, extending from inguinal region to knee on the anterolateral aspect [Figure 1a] multiple (12–15), erythematous to pigmented, ill-defined patches of varying sizes (3 × 3 to 5 × 7 cm) with fine scaling over the breasts, back, arms and shoulders with relative sparing of midline [Figure 1b and c].

Lymph node examination revealed Inguinal lymphadenopathy – four in number on the right side and three on the left side, non-tender, discrete, mobile, of varying sizes from 2 × 2 to 3 × 3 cm. Bilateral axillary lymphadenopathy – three on the right and two on the left side, non-tender, discrete, mobile, of varying sizes from 2 × 1 to 3 × 2 cm. Few cervical and jugulodigastric nodes were palpable on right side.

Hair, nails, mucosae, palms and soles were normal.

General and systemic examination was unremarkable.

Differential diagnosis considered were psoriasis, large plaque parapsoriasis and MF.



Figure 1: (a) Large, hyperpigmented, indurated, scaly plaque almost involving the entire right thigh, extending from inguinal region to knee on the anterolateral aspect. (b and c) Multiple (12–15), erythematous to pigmented, ill-defined patches of varying sizes (3 × 3 to 5 × 7 cm) with fine scaling over back, arms and shoulders with relative sparing of midline.

Routine investigations such as complete blood count, liver and renal function test, erythrocyte sedimentation rate, chest X-ray and ultrasonography abdomen were within normal limits. Contrast-enhanced computed tomography chest and abdomen revealed axillary lymphadenopathy and multiple right inguinal nodes (largest measuring 2.6 × 3.7 × 2.3 cm).

Skin biopsy showed lymphocyte exocytosis with moderate, diffuse infiltrate of small lymphocytes in superficial and mid dermis admixed with large cells and plasma cells [Figure 2a].

Lymph node section showed preserved lymphoid follicles with prominent germinal centres, there is expansion of paracortical areas with lymphocytes, histiocytes and plasma cells, some of the histiocyte nuclei show nuclear grooves, focal pigmented cells suggestive of dermatopathic lymphadenopathy. Immunohistochemistry of MF panel consisting of CD3, 4, 5, 7, 8 and 30 was performed over skin biopsy which showed CD3+, CD 4+ and CD 30+ [Figure 2b-d].

A diagnosis of cutaneous T-cell lymphoma CD 30+ LCT MF stage IIA (T2 N1 M0 B0) was made and patient was started

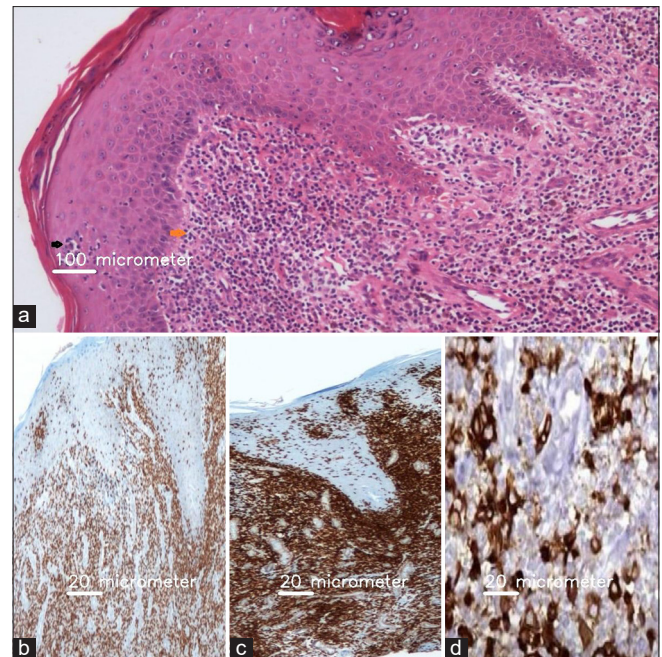


Figure 2: (a) Haematoxylin and eosin-stained section (10× magnification) showing lymphocyte exocytosis with a moderate (black arrow), diffuse infiltrate of small lymphocytes admixed with large atypical cells and plasma cells in the superficial and mid dermis (orange arrow). (b) Immunohistochemistry demonstrating CD3 positivity in approximately 80% of the infiltrating lymphocytes 40×. (c) Immunohistochemistry showing strong CD4 positivity in approximately 70% of the neoplastic T-cell population 40×. (d) CD30 positivity observed in approximately 30–40% of the large transformed cells on immunohistochemistry, consistent with large cell transformation HPE 40×.

on steroids with narrowband ultraviolet B therapy. Steroids were given to manage inflammation and for symptomatic relief. Patient showed no response and was shifted to CHOP regimen consisting of cyclophosphamide, doxorubicin, vincristine and prednisone after the oncologist consultation. After three cycles, there was reduction in scaling and itching [Figure 3]. Three months after the last cycle, she succumbed due to sepsis.

DISCUSSION

MF typically presents with patch, plaque, tumour and erythrodermic stage. MF tends to be an indolent disease, where

serial biopsies are required for the diagnosis.^[2] LCT within skin or lymph node biopsies is defined as large cells ≥ 4 times the size of a small lymphocyte, which are CD30+ or CD30- in $\geq 25\%$ of the dermal infiltration. Incidence of LCT vary between 8% and 55%, more common in advanced disease.^[3,4]

Campo *et al.* proposed that genetic alterations and dysregulation of signalling pathways may contribute to this phenomenon. Talpur *et al.* further suggested that alterations in cytokine expression and immune dysregulation may drive the transformation process.^[5,6]

Patients with LCT-MF present with rapidly enlarging skin tumours, nodal involvement and systemic symptoms such as

Table 1: Comparison of reported cases of LCT of MF.

Parameter	Vergier <i>et al.</i> ^[3]	Talpur <i>et al.</i> ^[6]	Diamandidou <i>et al.</i> ^[7]	Cappelli <i>et al.</i> ^[8]	Benner <i>et al.</i> ^[4]	Jawed <i>et al.</i> ^[2]
Study type	Retrospective, multicentre	Retrospective	Retrospective	Retrospective, single-institution	Retrospective	Review article
No. of patients	45	187	Not specified	46 (18 with LCT)	100	Not applicable
Key clinical findings	Median time to transformation: 6.5 years; most patients t3 stage at transformation	LCT at diagnosis and age >60 associated with poor prognosis	Poor prognosis with early transformation and advanced disease	LCT patients had better initial response to LD-TSEBT but shorter duration of response	25% CD30+; median survival significantly lower in transformed MF	LCT noted as adverse prognostic factor in MF and SS
Immunohistochemistry	31% CD30+; CD4 predominant; CD68 used to exclude histiocyte-rich MF	Not specified	Not specified	Not detailed for LCT cohort	CD30+ and CD20+ assessed; transformation linked to CD30 positivity	Overview of diagnostic markers including CD30
Treatment modalities	Topicals, methotrexate, chemotherapy, radiotherapy, SCT	Varied including systemic therapies	Systemic chemotherapy	LD-TSEBT (12 Gy in 6 fractions)	Combination approaches	Summarises therapeutic approaches
Prognostic indicators	Extracutaneous involvement and age ≥ 60 linked to poor outcome	Advanced stage, LCT at diagnosis, older age	Early transformation and advanced stage	LCT associated with shorter PFS and duration of response	Transformed MF has lower median survival	LCT associated with worse prognosis
Treatment response	Median survival 22 months; 5-year survival 20.8%; 31% CD30+ cases	LCT associated with poor prognosis; shorter survival with CD30+, advanced age	Poor survival with early transformation; median survival not stated	Overall response 91.3%; LCT group had shorter duration of response (7.4 months) and PFS (9.8 months)	CD30+ transformation associated with worse survival	Not applicable
Comparison with present case	Similar stage (IIA) at diagnosis; patient had nodal involvement and died within 3 months post-CHOP	Current case fits profile of poor prognosis due to nodal involvement and rapid progression	Aggressive course aligns with literature findings of poor survival in early transformation	Response pattern matches: initial partial response but early mortality	CD30+ case with poor outcome—mirrors findings in current case	Presents typical markers and progression of LCT-MF as seen in this case

LCT: Large cell transformation, MF: Mycosis fungoides, PFS: Progression-free survival, LD-TSEBT: Low dose total skin electron beam therapy; CHOP: Cyclophosphamide, doxorubicin, vincristine and prednisone



Figure 3: Significant reduction in scaling and improvement in plaque thickness over the right thigh after three cycles of CHOP chemotherapy.

fever, weight loss and night sweats indicating an aggressive disease course. Treatment options include multi-agent chemotherapy, targeted therapies such as brentuximab vedotin, radiation therapy and hematopoietic stem cell transplantation. The prognosis for patients with LCT-MF is generally poor compared to those with early-stage MF. The median survival after transformation is significantly reduced between 1 and 3 years. Talpur *et al.*^[6] and Diamandidou *et al.*^[7] found that early transformation and advanced stages were associated with poor prognosis. Talpur *et al.*^[6] reported poor prognosis in combination with advanced age, LCT at the time of initial diagnosis of MF.^[6,7]

Similarly, the recent study by Cappelli *et al.* reported improved initial responses in LCT patients treated with low-dose total skin electron beam therapy (TSEBT), but their duration of response and progression-free survival were significantly shorter—mirroring the aggressive nature seen in this case. CD30 positivity, as noted in the current patient, has also been associated with transformation and poor outcomes in multiple studies.^[8]

A comparison of the present case with the existing literature is summarised in Table 1.^[2-4,6-8]

CONCLUSION

We conclude that LCT-MF represents a complex clinical entity requiring initiation of systemic therapies at the earliest. A multidisciplinary approach involving dermatologists, oncologists and pathologists is essential for accurate diagnosis and appropriate management which could impact the prognosis of the patient.

Ethical approval: Institutional Review Board approval is not required.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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REFERENCES

1. Willemze R, Cerroni L, Kempf W, Berti E, Facchetti F, Swerdlow SH, *et al.* The 2018 Update of the WHO-EORTC Classification for Primary Cutaneous Lymphomas. *Blood* 2019;133:1703-14.
2. Jawed SI, Myskowski PL, Horwitz S, Moskowitz A, Querfeld C. Primary Cutaneous T-cell Lymphoma (Mycosis Fungoides and Sézary Syndrome): Part I. Diagnosis: Clinical and Histopathologic Features and New Molecular and Biologic Markers. *J Am Acad Dermatol* 2014;70:205.e1-16; quiz 221-2.
3. Vergier B, De Muret A, Beylot-Barry M, Vaillant L, Ekouevi D, Chene G, *et al.* Transformation of Mycosis Fungoides: Clinicopathological and Prognostic Features of 45 Cases. *French Study Group of Cutaneous Lymphomas. Blood* 2000;95:2212-8.
4. Benner MF, Jansen PM, Vermeer MH, Willemze R. Prognostic Factors in Transformed Mycosis Fungoides: A Retrospective Analysis of 100 Cases. *Blood* 2012;119:1643-9.
5. Campo E, Swerdlow SH, Harris NL, Pileri S, Stein H, Jaffe ES. The 2008 WHO Classification of Lymphoid Neoplasms and Beyond: Evolving Concepts and Practical Applications. *Blood* 2011;117:5019-32.
6. Talpur R, Sui D, Gangar P, Dabaja BS, Duvic M. Retrospective Analysis of Prognostic Factors in 187 Cases of Transformed Mycosis Fungoides. *Clin Lymphoma Myeloma Leuk* 2016;16:49-56.
7. Diamandidou E, Colome-Grimmer M, Fayad L, Duvic M, Kurzrock R. Transformation of Mycosis Fungoides/Sézary Syndrome: Clinical Characteristics and Prognosis. *Blood* 1998;92:1150-9.
8. Cappelli L, Cappelli M, Haldar N, Paul T, Mandel J, Zhan T, *et al.* Condensed Low-Dose Total Skin Electron Beam Therapy for Mycosis Fungoides: An Institutional Retrospective Review and Subgroup Analysis of Patients with Large Cell Transformation. *Arch Dermatol Res* 2025;317:531.

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