〈Case Report〉

Folliculotropic mycosis fungoides treated with electron beam therapy that evolved into fatal, tumor-stage mycosis fungoides and erythroderma with multiple ulcerations

Ryo TANAKA[1)], Takenobu YAMAMOTO[1)], Daigo OKA[1, 2)], Junichi HIRATSUKA[3)], Takuya MORIYA[2)], Yumi AOYAMA[1)], Wataru FUJIMOTO[1)], Hideho WADA[4)]

1) Department of Dermatology, Kawasaki Medical School,
2) Department of Pathology, Kawasaki Medical School,
3) Department of Radiation Oncology, Kawasaki Medical School,
4) Department of Hematology, Kawasaki Medical School

ABSTRACT A 71-year-old woman diagnosed with mycosis fungoides with multiple erythematous plaques and follicular papules on the scalp, trunk, and thigh was referred to our institution. Folliculotropic mycosis fungoides was histologically diagnosed, and the erythematous papules and plaques regressed temporarily after total-skin electron beam therapy. The patient then developed tumors and erythroderma. The area of painful erosion spread, and her condition rapidly worsened. The patient died 3 years and 4 months after the first examination due to multiple organ failure caused by sepsis. The cause of rapid evolution into erythroderma remains elusive and requires further investigation in similar cases.

doi：10.11482/KMJ-E202046073 *(Accepted on June 15, 2020)*

Key words：Folliculotropic mycosis fungoides, Erythroderma, Ulceration, TSEBT, LEBT

INTRODUCTION

Mycosis fungoides (MF) is the most common form of primary cutaneous T cell lymphoma, and is clinically characterized by skin patches that subsequently evolve into plaques and tumors[1)]. Histologically, MF is defined by the proliferation of small- to medium-sized T lymphocytes with cerebriform nuclei[1)]. Folliculotropic MF (FMF) is an uncommon variant of MF that is characterized by acneiform and follicular papules and plaques[2-6)]. The grouped follicular papules are often associated with alopecia. In FMF, follicular infiltrates of atypical T lymphocytes are present, occasionally with epidermotropism. MF generally progress slowly through several stages. However, the prognosis of FMF is significantly worse than the classic type of MF[1)], with reported disease-free survival rates of 68% at 5 years and 26% at 10 years[2)]. Herein, we report an unusual case of FMF that evolved into fatal, tumor-stage MF and erythroderma with multiple ulcerations.

CASE REPORT

A 71-year-old woman diagnosed with MF was

Corresponding author
Ryo Tanaka
Department of Dermatology, Kawasaki Medical School,
577 Matsushima, Kurashiki, 701-0192, Japan
Phone : 81 86 462 1111
Fax : 81 86 462 1199
E-mail: ryot@med.kawasaki-m.ac.jp

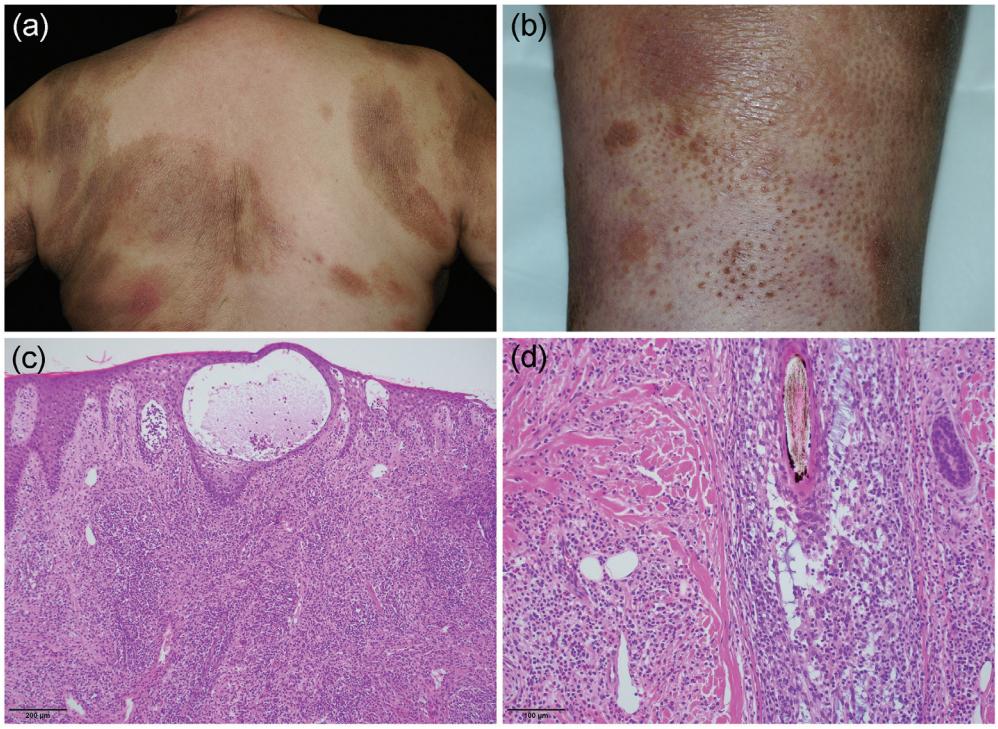

Fig. 1. Clinical and histopathological features at the initial presentation
(a) Brownish-colored erythematous plaques on the back. (b) Multiple follicular papules on the thigh. (c) Abundant infiltration of lymphoid cells and eosinophils in the dermis with an intraepidermal vesicle and Pautrier's microabscess (hematoxylin-eosin [HE], original magnification ×100). (d) Intensive lymphoid infiltration in the hair follicle (HE, ×200).

referred to our institution due to a 3-year history of intensely pruritic skin lesions that were resistant to the treatments of psoralen phototherapy, interferon γ, and etoposide. Physical examination revealed multiple erythematous plaques and follicular papules on the scalp, trunk, and thigh (Fig. 1a, 1b). The patient had no systemic symptoms or lymphadenopathy. A biopsy taken from a follicular papule on her scalp showed epidermotropism with Pautrier's microabscess in the epidermis and diffuse infiltration of lymphocytes and eosinophils in the dermis (Fig. 1c). An intensive folliculotropic lymphoid infiltration was detected in the dermis (Fig. 1d). Mucin deposition within the follicular epithelium was present. The lymphocytes were positive for CD3, but negative for CD20, CD56, and CD79a. The predominance of CD4+ cells was evident, but scattered CD8+ cells were also detected. Additionally, these infiltrated cells included cells positive for cytotoxic marker T-cell intracellular antigen (TIA)-1 and granzyme B (GrB). Programmed death-1 receptor was barely detectable in infiltrated lymphocytes. T-cell receptor Cβ1 gene rearrangement was detected in the skin biopsy specimen. Serological tests were negative for human T-cell leukemia virus 1 (HTLV-1). The patient was diagnosed with FMF, stage IB (T2b, N0, M0, B0).

The erythematous papules and plaques regressed temporarily after total-skin electron beam therapy (TSEBT) (cumulative dose, 16 Gy). However, 10 months later, new plaques developed, and so additional TSEBT (12 Gy), and localized electron beam therapy (LEBT) (10 Gy) were conducted. Ten months later, 4 months of combination

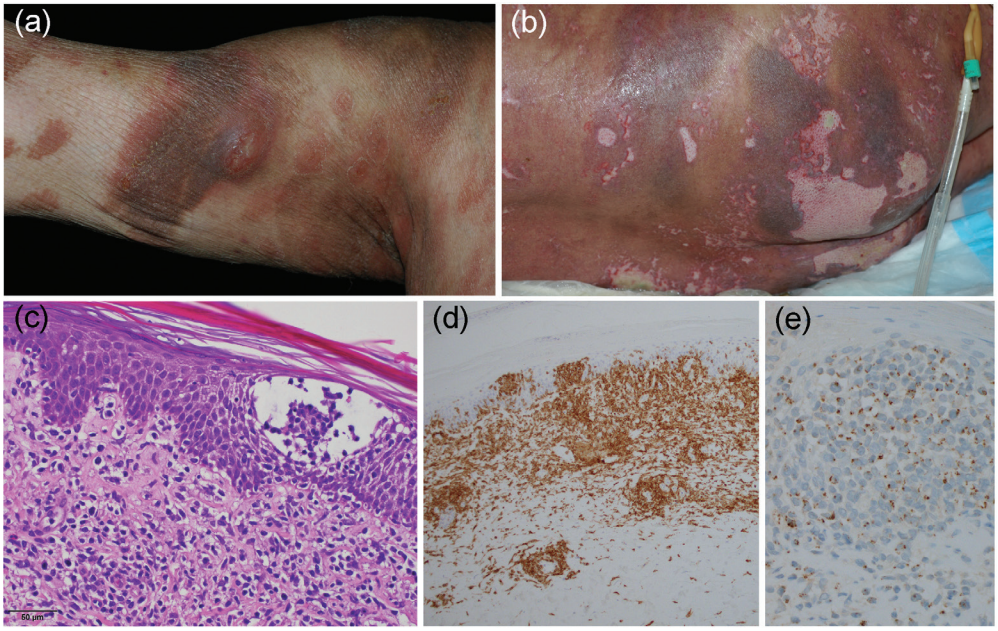

Fig. 2. Clinical, histopathological, and immunohistopathological features in the advanced stage
(a) Nodules and erythematous plaques on the arm. (b) Painful ulcerations and erosions on the buttocks. (c) Dense lymphoid infiltration in the superficial dermis with epidermotropism (HE, ×400) (d) Immunostaining for CD4 (x100). (e) Immunostaining for T-cell intracellular antigen-1 (TIA-1, x400).

chemotherapy was administered (oral etoposide 25 mg/day on days 1-3, q7, with oral sobuzoxane 400 mg/day on day 1, q7). However, 5 months later, new nodules, erosions, and ulcers developed on the trunk and extremities (Fig. 2a). Although additional LEBT (20 Gy) was performed, the erythematous skin lesions evolved into erythroderma with multiple ulcerative lesions (Fig. 2b). A skin biopsy from the abdomen showed a dense lymphoid infiltrate in the superficial dermis with epidermotropism (Fig. 2c). The CD4+ neoplastic cells still outnumbered the CD8+ cells (Fig. 2d). TIA-1- and GrB-positive cells were also seen (Fig. 2e). The area of painful erosion spread, and her condition rapidly worsened. Giant cells associated with herpes simplex virus or varicella zoster virus were not detected, and polymerase chain reaction studies of cutaneous ulcerations were negative for varicella zoster virus and herpes simplex virus. Cytomegalovirus (CMV) was not detected by immunohistochemical staining. It was difficult to resume chemotherapy because of poor general condition, therefore only continuous symptomatic treatment could be provided. During the course, CMV antigenemia was detected using the C7HRP method and was treated with ganciclovir. However, skin-related symptoms persisted without obvious improvement. Despite Sezary cells not being detected in the peripheral blood and there being no evidence of organ infiltration upon imaging diagnostic tests, blood soluble interleukin-2 receptor (sIL-2R) levels gradually increased throughout the clinical course, with the final value being 10, 100 U / mL. The patient died at 3 years and 4 months after the first examination due to multiple organ failure caused by sepsis.

DISCUSSION

The most common findings in FMF are grouped follicular papules and patch or plaque lesions, while erythroderma is observed in only 6-18% of patients

with FMF[3-5]. Although TSEBT is considered an effective therapy for FMF[3], a recent review of 24 patients with FMF treated with TSEBT showed that only 33.3% and 20.5% had a complete and partial response, respectively[6]. The skin lesions in the current case recurred after a clinical remission of only 5-6 months after TSEBT, and evolved into erythroderma with multiple ulcerations. In a previously reported case of MF presenting with multiple ulcerations due to disseminated cutaneous CMV infection, the TSEBT was thought to be a possible inciting factor that reactivated a latent CMV infection[7]. Such viral infections were not demonstrated in the current case. Abundant eosinophilic infiltration in skin lesions might be associated with resistance to TSEBT[8]. Correlation analysis between GrB/TIA-1 expression in first diagnostic biopsies from patches or plaques from 40 patients with T2N0M0-stage MF and clinical follow-up data did not reveal differences in clinical behavior and survival[9]. It is unlikely that these lesions developed as acute complications of TSEBT, as they appeared 10 months after the completion of TSEBT and LEBT[10, 11]. The cause of the rapid evolution into erythroderma remains elusive and requires further investigation in similar cases of FMF.

ACKNOWLEDGMENT

We thank Kelly Zammit, BVSc, from Edanz Editing (www.edanzediting.com/ac), for editing a draft of this manuscript.

CONFLICTS OF INTEREST

Not declared

FINANCIAL DISCLOSURE

Not declared

REFERENCES

1) Willemze R, Jaffe ES, Burg G, *et al.*: WHO-EORTC Classification for Cutaneous Lymphomas. Blood 2005; 105(10): 3768-85. doi: 10.1182/blood-2004-09-3502

2) van Doorn R, Scheffer E, Willemze R: Follicular Mycosis Fungoides, a Distinct Disease Entity With or Without Associated Follicular Mucinosis: A Clinicopathologic and Follow-Up Study of 51 Patients. Arch Dermatol 2002; 138(2): 191-8. doi: 10.1001/archderm.138.2.191

3) Muniesa C, Estrach T, Pujol RM, Gallardo F, Garcia-Muret P, Climent J, Servitje O: Folliculotropic Mycosis Fungoides: Clinicopathological Features and Outcome in a Series of 20 Cases. J Am Acad Dermatol 2010; 62(3): 418-26. doi: 10.1016/j.jaad.2009.03.014

4) Gerami P, Guitart J: The Spectrum of Histopathologic and Immunohistochemical Findings in Folliculotropic Mycosis Fungoides. Am J Surg Pathol 2007; 31(9): 1430-8. doi: 10.1097/PAS.0b013e3180439bdc

5) Lehman JS, Cook-Norris RH, Weed BR, Weenig RH, Gibson LE, Weaver AL, Pittelkow MR: Folliculotropic Mycosis Fungoides: Single-Center Study and Systematic Review. Arch Dermatol 2010; 146(6): 607-13. doi: 10.1001/archdermatol.2010.101

6) Wieser I, Wang C, Alberti-Violetti S, Lyons G, Tran C, Talpur R, Duvic M: Clinical Characteristics, Risk Factors and Long-Term Outcome of 114 Patients With Folliculotropic Mycosis Fungoides. Arch Dermatol Res 2017; 309(6): 453-459. doi: 10.1007/s00403-017-1744-1

7) Kim JK, Ahmad A, Selim MA, Olsen EA, Cardones AR: Disseminated Cutaneous Cytomegalovirus Infection Following Total Body Electron Beam Irradiation for Mycosis Fungoides. JAMA Dermatol 2015; 151(12): 1380-1. doi: 10.1001/jamadermatol.2015.2233.

8) Ionescu MA, Rivet J, Daneshpouy M, Briere J, Morel P, Janin A: In Situ Eosinophil Activation in 26 Primary Cutaneous T-cell Lymphomas With Blood Eosinophilia. J Am Acad Dermatol 2005; 52(1):32-9. doi: 10.1016/j.jaad.2004.03.003

9) Vermeer MH, Geelen FA, Kummer JA, Meijer CJ, Willemze R: Expression of Cytotoxic Proteins by Neoplastic T Cells in Mycosis Fungoides Increases With Progression From Plaque Stage to Tumor Stage Disease. Am J Pathol 1999; 154(4): 1203-10. doi: 10.1016/S0002-9440(10)65372-2

10) Elsayad K, Kriz J, Moustakis C, *et al.*: Total Skin Electron Beam for Primary Cutaneous T-cell Lymphoma. Int J Radiat Oncol Biol Phys 2015; 93(5): 1077-86. doi: 10.1016/j.ijrobp.2015.08.041

11) Hoppe RT: Mycosis Fungoides: Radiation Therapy. Dermatol Ther 2003; 16(4): 347-354. doi: 10.1111/j.1396-0296.2003.01647.x