

Case Report

Successful Treatment of Erythrodermic Mycosis Fungoides with Mogamulizumab Followed by Etoposide Monotherapy

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Keywords

Erythrodermic mycosis fungoides · Mogamulizumab · Etoposide

Abstract

Mogamulizumab induces cytotoxicity against CCR4+ lymphoma cells by antibody-dependent cell-mediated cytotoxicity in advanced cutaneous T-cell lymphoma patients. Since the efficacy of mogamulizumab in mycosis fungoides (28.6%) is lower than that in Sézary syndrome (47.1%), reagents that enhance the antitumor immune response induced by mogamulizumab are needed to further optimize its use for the treatment of erythrodermic mycosis fungoides. In this report, we present a case of erythrodermic mycosis fungoides successfully treated with mogamulizumab followed by etoposide monotherapy.

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Introduction

Mogamulizumab is a humanized anti-CCR4 antibody that shows cytotoxicity against CCR4+ lymphoma cells by antibody-dependent cell-mediated cytotoxicity in advanced cutaneous T-cell lymphoma (CTCL) patients [1]. For the treatment of CTCL, the efficacy of mogamulizumab in mycosis fungoides (28.6%) is lower than that in Sézary syndrome

(47.1%) [2]. Since mogamulizumab exhibits clinically meaningful antitumor activity even in patients with relapsed CTCL [3], reagents that enhance the antitumor immune response induced by mogamulizumab are needed to further optimize its use for the treatment of erythrodermic mycosis fungoides [2]. In this report, we present a case of erythrodermic mycosis fungoides successfully treated with mogamulizumab followed by etoposide monotherapy.

Case Report

A 42-year-old Japanese man visited our outpatient clinic with systemic pruritic erythema. He had been diagnosed with erythrodermic mycosis fungoides and administered bexarotene for 3 months without any improvement. On his initial visit, physical examination revealed extensive dark erythema (Fig. 1a). A biopsy specimen from the left abdomen revealed a band-like infiltration of atypical lymphocytes with epidermotropism in the superficial dermis (Fig. 1b, c). Immunohistochemical staining revealed that these atypical lymphocytes were positive for CD2, CD3, CD4, CD30, CD45, and CCR4 and negative for CD5, CD7, and CD8. We screened for possible metastatic lesions with CT scan and found no evidence of lymph node swelling or visceral lesions. From the above findings, we diagnosed this patient with bexarotene-resistant erythrodermic mycosis fungoides. We treated the patient with mogamulizumab 1 mg/kg/week for 4 weeks, which improved the mSWAT score from 104 to 40 (Fig. 1d). Because of grade 3 lymphopenia, we changed mogamulizumab to bexarotene (300 mg/m²/day) for 4 weeks and infiltrated plaque recurred on the trunk and extremities (Fig. 2a) together with an elastic nodule on the tongue (Fig. 2b). We re-administered mogamulizumab 1 mg/kg/week for three weeks with radiotherapy (30 G in 15 fractions) without any improvement of the mSWAT score (101.4–105.1). Then, we administered etoposide 50 mg/day for 3 weeks. The infiltrated plaque and nodule on the tongue diminished 4 weeks after the administration of etoposide (Fig. 2c, d). Six months after remission, erythroderma was still under remission.

Discussion

Mogamulizumab is a humanized anti-CCR4 antibody that shows cytotoxicity against CCR4+ lymphoma cells by antibody-dependent cell-mediated cytotoxicity in advanced CTCL patients [1]. Since CCR4 is also expressed on regulatory T cells (Tregs) and Th2 cells [4], both of which contribute to cancer progression, mogamulizumab might improve the immunosuppressive tumor microenvironment in CTCL. Indeed, as we previously reported, similar to the administration of ipilimumab, mogamulizumab induced abscopal effects with intensity-modulated radiotherapy in a patient with follicular mycosis fungoides [5]. Since the abrogation of Tregs function by a monoclonal antibody, such as anti-CTLA4 antibody and anti-CCR4 antibody, augment the systemic anti-tumor immune response, the administration of these antibodies might affect other immune cells at the tumor site. For example, several chemokines from CD163+ tumor-associated macrophages (TAMs) are needed for tumor formation in the early stage of mycosis fungoides [6], which could be modified by anti-CTCL drugs (e.g., IFN α and IFN γ) [7, 8], leading to a therapeutic effect. Interestingly, etoposide also possesses immunomodulatory effects that re-polarized M2 into M1 macrophages [9]. In

aggregate, these reports suggested that etoposide might improve the tumor immunomicroenvironment through TAMs.

In this report, we present a case of erythrodermic mycosis fungoides successfully treated with mogamulizumab followed by etoposide monotherapy. Notably, etoposide was administered immediately after mogamulizumab was tolerated. Since mogamulizumab consists of IgG1 antibodies, which have a half-life of 3 weeks in the blood, this sequential therapy was effective not only on CTCL cells but also on both Tregs and TAMs, leading to the induction of additional anti-immune response like nivolumab/ipilimumab combination therapy for melanomas. Since this report presents only a single case, further cases may provide fundamental insights into the mechanisms of the anti-CTCL response of mogamulizumab followed by etoposide.

Statement of Ethics

The patient gave written informed consent.

Disclosure Statement

The authors have no conflicting interests to declare.

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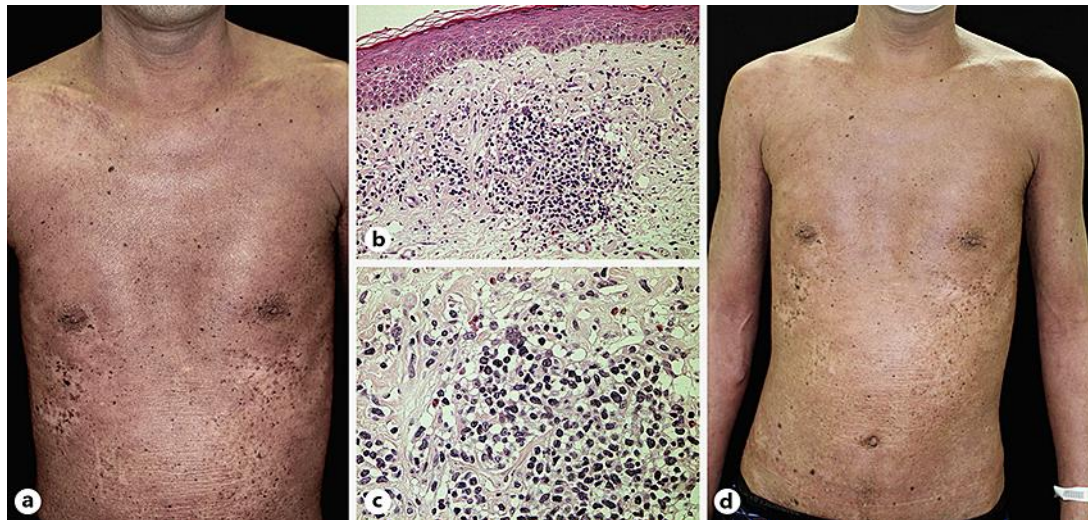


Fig. 1. **a** Extensive dark erythema on the trunk and extremities. **b, c** Band-like infiltration of atypical lymphocytes with epidermotropism in the superficial dermis. **d** The administration of mogamulizumab improved the mSWAT score from 104 to 40.

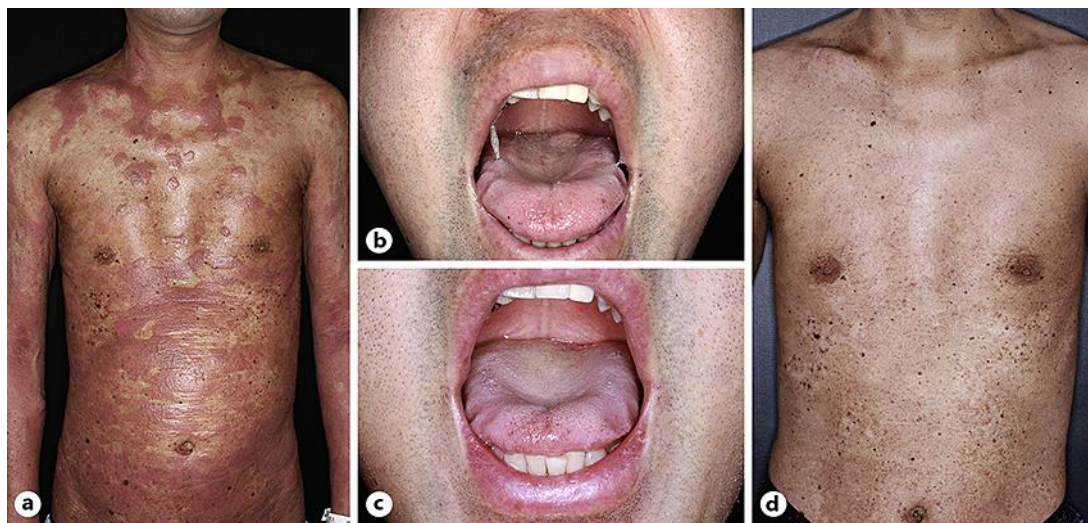


Fig. 2. An infiltrated plaque recurred on the trunk and extremities (**a**) together with an elastic nodule on the tongue (**b**). **c, d** The infiltrated plaques and nodule on the tongue diminished 4 weeks after the administration of etoposide.