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Case Report

Bexarotene monotherapy for patient with refractory early stage mycosis fungoides

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Abstract Mycosis fungoides (MF) is a subtype of cutaneous T-Cell lymphoma and oftenly difficult to treat. We report a case of mycosis fungoides in which several lines of therapy were employed including both skin-directed and systemic treatment strategies with no clinical remission. This case highlights MF's insidious onset. In this patient, the early stage of disease was marked by erythematous plaque and misdiagnosed as tinea corporis. The lack of symptomatic control led to biopsy of the lesion, which in turn precipitated the accurate diagnosis of MF. Several lines of treatment were initiated with unsatisfactory outcomes. Bexarotene therapy was started and good clinical and histological response was observed. We conclude bexarotene as salvage therapy is an efficacious therapeutic option for this patient with plaque mycosis fungoides and its safety profile is favorable for long-term use.

Key words
Mycosis fungoides, bexarotene, treatment, diagnosis.

Introduction

Mycosis fungoides (MF) is a subtype of cutaneous T cell lymphoma and often difficult to treat. We report a case of mycosis fungoides in which several lines of therapy were employed including both skin-directed and systemic treatment strategies with no clinical remission. Clinical response was achieved with oral bexarotene therapy.

Case Report

A 47-year-old man presented complaining of an itchy plaque on the left leg with 2 years of evolution. Clinical examination revealed a 7-10 cm diameter, infiltrated, erythematous-scaling plaque on the left thigh (**Figure 1**). Lymph nodes were unremarkable. The first diagnosis was tinea corporis. The patient was treated for two months with antifungal drugs and no response was observed. The lesion increased progressively in the following months to 18 cm diameter. A skin biopsy was performed revealing extensive cutaneous T-cell infiltration and the presence of Pautrier's microabscesses (**Figure 2**). Blood tests were normal, revealing a leukocyte count of 10,000/mm^3, platelet count of 250,000/mm^3, hemoglobin of 16 g/dl, C-reactive protein level of 145 mg/l and no circulating Sézary cells. Computed tomography scans indicated neither adenopathy nor visceral involvement. The diagnosis was stage IA mycosis fungoides. T1 N0 M0. First-line therapy for this patient consisted of systemic PUVA for one month and had a complete response. Upon suffering a relapse after 2 months, a second course with systemic PUVA therapy was performed. Treatment continued for 3 months and for second time, the patient achieved a complete response. The third attempt to control disease was with PUVA plus acitretin 30 mg, but the

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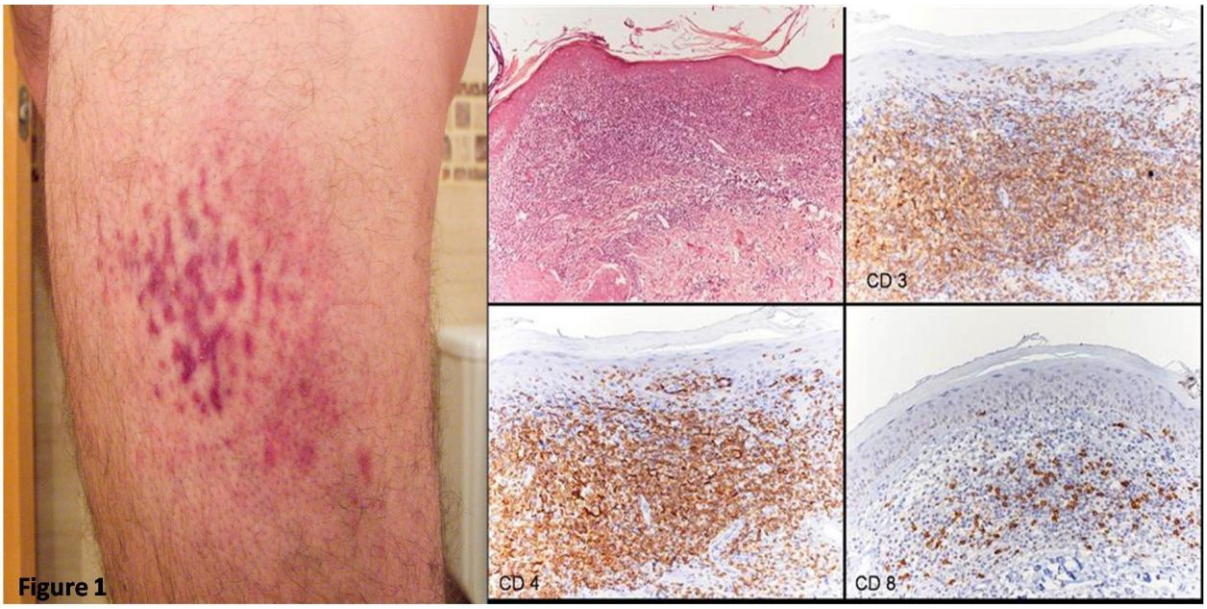

Figure 1 An infiltrated, erythematous-scaling plaque of mycosis fungoides is observed on the left thigh. Histological studies show extensive cutaneous infiltration of CD4 lymphocytes and the presence of Pautrier's microabscesses. There is a low infiltration of CD8 lymphocytes.

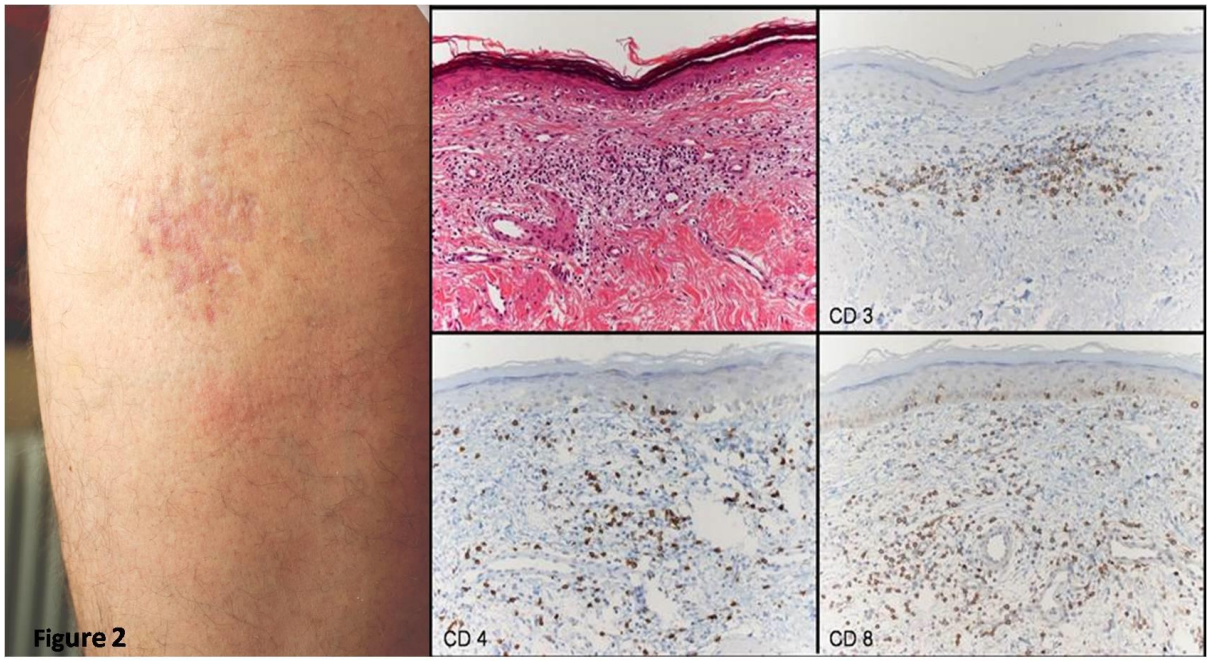

Figure 2 A dramatic improvement of the plaque was observed after 4 months of treatment. The skin biopsy confirmed this improvement with absence of CD4 cells on dermis.

patient did no experience a complete response. Methotrexate (15 mg/week) was initiated and a disease control was achieved. The treatment was continued and tolerated well until the recurrence of erythrodermic plaques. Prior to initiating bexarotene therapy, lab values were again examined. Routine lab values were unremarkable. Lymph nodes and bone marrow were confirmed normal. The CD4/CD8 blood ratio increased slightly compared to those previously documented. The patient began bexarotene therapy at the dose of 300 mg/m^2/day. After 4 months of treatment, the patient exhibited marked improvement in

pruritus and a 50% reduction of cutaneous lesion. The dose of bexarotene was adjusted to 200 mg/m^2/day due to severe bexarotene-associated hyperlipidemia. Triglyceride levels were 399 mg/dl and cholesterol levels were 253 mg/dl. Management of hyperlipidemia included treatment with simvastatin (40 mgr/day). Lab values also indicated hypothyroidism with TSH levels of 0.02 mU/L and a hormone replacement therapy was initiated. Tumor regression continued and the bexarotene dose was reduced to 150 mg/m^2/day. The patient went on to achieve full clinical regression while taking this dose. Lipid status improved to normal levels. Clinical remission has been maintained for over one year with bexarotene monotherapy. Hormone replacement therapy continues.

Discussion

This case highlights MF's insidious onset. In this patient, the early stage of disease was marked by erythematous plaque and misdiagnosed as tinea corporis. The lack of symptomatic control led to biopsy of the lesion, which in turn confirmed the diagnosis of MF. Due to the staging of the tumor as IA, which carries an expected 5-year survival of 96%,[1] and also in an attempt to minimize the need for systemic intervention, the patient was treated consecutively with conservative skin-directed therapy (PUVA). No clinical remission was achieved neither with PUVA or PUVA associated to acitretin. The choice of low-dose methotrexate as a second-line therapy was supported by study results reported by Zackheim,[2] but this therapy brought no symptomatic control. The emergence of bexarotene as an active agent in the treatment of MF has brought therapeutic options for patients with advanced/refractory disease[3] and we decided to initiate it in our patient. Bexarotene-induced hypothyroidism and hyperlipidemia were persistent side effects. Although asymptomatic in this patient, hypertriglyceridemia and hypercholesterolemia can be problematic but clinically managed with thyroxine and simvastatin. A reduction in dose of bexarotene from 300 mg/m^2/day to 200 mg/m^2/day aided in reducing tryglicerides and cholesterol and recuperating thyroid function, demonstrating that reduction of dose can both maintain remission and manage hyperlipidemia.

We conclude bexarotene as salvage therapy is an efficacious therapeutic option for this patient with plaque mycosis fungoides and its safety profile is favorable for long-term use.

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