Case Report

Mycophenolate Mofetil for the Treatment of Subcutaneous Panniculitis-Like T-Cell Lymphoma: Case Report and Review of the Literature

Benjamin Heyman, Anne Beaven

Clinical Practice Points

- Subcutaneous panniculitis-like T-cell lymphoma (SPLTCL) is a rare cutaneous T-cell lymphoma originating from αβ T cells.
- Although initially thought to be an aggressive disease, it has now been shown to follow an indolent clinical course, typically responding to immunosuppression.
- We present a case of successful treatment of SPLTCL with mycophenolate mofetil.
- Mycophenolate mofetil deserves further investigation as a steroid-sparing agent for patients with SPLTCL.

Clinical Lymphoma, Myeloma & Leukemia, Vol. ■, No. ■, ■-■
Keywords: Cutaneous T-cell lymphoma, Immunosuppression, Relapsed, Steroid-sparing, αβ T-cell

Introduction

Subcutaneous panniculitis-like T-cell lymphoma (SPLTCL) is a rare cutaneous T-cell lymphoma that has undergone changes in its classification and treatment over the past decade. What was once thought to be an aggressive cutaneous lymphoma and treated with combination cytotoxic chemotherapy is now recognized to follow a more indolent course with improved survival when treated with immunosuppression. In this report we present a patient with SPLTCL, who has been successfully treated with mycophenolate mofetil (MMF).

T-cell non-Hodgkin lymphomas (NHLs) are a heterogeneous group of hematologic malignancies with diverse biology and clinical presentations. Notably, many T-cell NHLs have tropism for the dermis and epidermis. SPLTCL is a rare cutaneous T-cell NHL that was first described by Gonzalez et al as a T-cell lymphoma simulating a panniculitis associated with hemophagocytic syndrome (HPS).[1] Initially SPLTCL was thought to be an aggressive cutaneous T-cell lymphoma. This view changed after investigators from the European Organization for Research and Treatment of Cancer (EORTC) cutaneous lymphoma group analyzed clinical, histological, and immunophenotypic behavior of 83 patients with SPLTCL.[2] Cases were subdivided according to the T-cell receptor (TCR). An αβ T-cell subtype consisted of an immunophenotype that was $CD4^-$, $CD8^+$, $CD56^-$, and T-cell receptor β+ (βF1). Alternatively, a γδ T-cell subtype consisted an immunophenotype that was $CD4^-$, $CD8^-$, $CD56^+$, and $\beta F1^-$. Through analysis of specific TCR subtypes, they discovered that SPLTCL was in fact 2 distinct disease entities with different clinical behaviors.

Patients with the αβ subtype presented with nodular skin lesions that were limited to the subcutaneous tissues with adipotropism and lobular panniculitis. The median age of diagnosis was 36 years, often with known autoimmune disorders, and were unlikely to be diagnosed with concurrent HPS. Patients tended to have an indolent course with a 5-year overall survival (OS) of 82%. In contrast, patients with the γδ subtype presented with nodular lesions that infiltrated the subcutaneous tissues, the dermis, and the epidermis, with ulcerations, angioinvasion, and angiodestruction. These patients were older at diagnosis, with a median age of 56 years, often having systemic B symptoms, with concurrent lymphadenopathy, splenomegaly, cytopenias, and frequently had concurrent HPS. In addition, patients with the γδ subtype had a dismal prognosis, with a 5-year OS of 11%. The investigators also determined that the αβ subtype could be treated successfully with immunosuppression, rather than conventional chemotherapy.[2] This work and the work

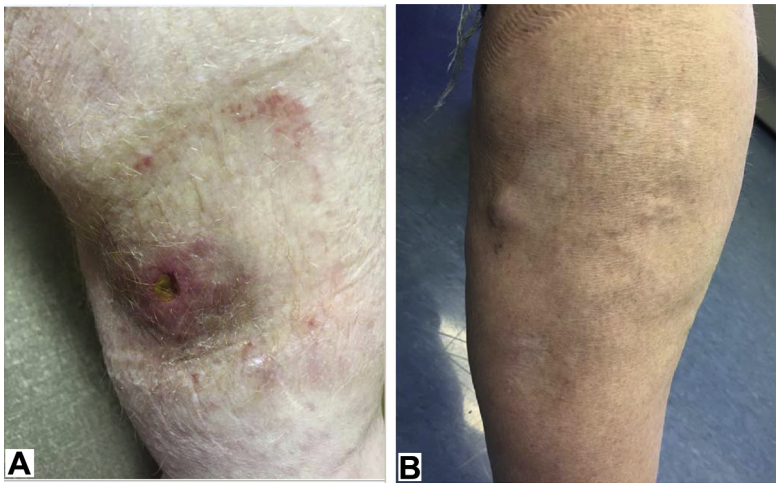
Division of Hematology/Oncology, Department of Medicine, Duke University, Durham, NC

Submitted: May 15, 2018; Revised: Jun 26, 2018; Accepted: Jul 9, 2018

Address for correspondence: Benjamin Heyman, MD, Division of Hematology/Oncology, Duke University Medical Center, 2301 Erwin Rd, Durham, NC27710 Fax: 919-684-3309; e-mail contact: Benjamin.Heyman@duke.edu

2152-2650/$ - see frontmatter
https://doi.org/10.1016/j.clml.2018.07.283

Figure 1 Patient's Right Lower Extremity (A) Before Initiation and (B) After 12 Months of Treatment With Mycophenolate Mofetil (MMF). The Size, Induration, and Erythema of the Subcutaneous Nodule Has Significantly Reduced After Treatment With MMF



of others ultimately lead to the recent World Health Organization reclassification of SPLTCL, in which SPLTCL now only reflects patients with the αβ subtype, and a new diagnosis of primary cutaneous γδ T-cell lymphoma has been created to encompass patients previously classified as γδ SPLTCL.[3-5] In this case report, we present, to our knowledge, the first known case of a patient with SPLTCL successfully treated with MMF.

Case Report

A 53-year-old woman with a medical history significant for obesity, type 2 diabetes mellitus, and asthma presented with fatigue, fever, nausea, bilateral pedal edema, and new lesions on her bilateral lower extremities and low back. The lesions were described as erythematous nodules, macules, and plaques without epidermal changes. The largest measured 11 × 7 cm and was located on her right thigh with minimal induration at the border (Figure 1A). There was no evidence of lymphadenopathy or splenomegaly on physical examination. She was treated with a 7-day course of trimethoprim and sulfamethoxazole for presumed cellulitis without any significant improvement in her lesions.

An incisional biopsy of a lesion on the right anterior thigh was performed and revealed an atypical lymphocytic infiltrate in the subcutaneous tissue. The lobules of the subcutaneous tissue exhibited necrosis with numerous foamy macrophages as well as numerous atypical lymphocytes. CD3 decorated the lymphocytic portion of the infiltrate and highlighted focal rimming of adipocytes. CD4 stained the macrophages as well as the T cells. CD8 highlighted the T-cell population and rimming of the adipocytes. The T cells were positive for TCR α/β and were found to be $\beta F1^+$; there was no discrete population of TCR γ/δ-positive T cells. The dermis exhibited perivascular chronic inflammation associated with dermal mucin, but no evidence of an atypical lymphocytic infiltrate. T-cell clonality studies were indeterminate for T-cell receptor β and γ chain rearrangements. The pathology report was most consistent with a diagnosis of SPLTCL.

Consequently, treatment with 40 mg oral prednisone daily was started, with improvement in her fevers, nausea, and the size of her established lesions. However, during prednisone treatment, she developed new lesions on her right lower extremity. A complete blood count after initiating steroids showed a white blood cell count (WBC) of 11.0 × 10^9/L, hemoglobin (Hgb) of 8.6 g/dL, and platelets of 280 × 10^9/L. A basic metabolic panel was significant for a newly elevated creatinine (Cr) of 2.3 mg/dL. A positron emission tomography/computed tomography (PET/CT) scan was ordered, which showed numerous hypermetabolic lesions in the subcutaneous tissues of the bilateral lower extremities (Figure 2A). She was subsequently referred to a tertiary care medical center for further management. At her initial visit with dermato-oncology, laboratory analysis revealed a WBC of 12.7 × 10^9/L with a differential of 93.6% neutrophils and 4% lymphocytes, Hgb of 9.3 g/dL, and platelets of 289 × 10^9/L. A comprehensive metabolic panel was significant for a Cr of 2.1 mg/dL, ferritin was 71 ng/mL, an antinuclear antibody screen was positive with a titer of 1:160, and lactate dehydrogenase was 162 U/L. She was also found to have normal thyroid-stimulating hormone, and negative anti-smooth muscle, anti-ribonucleoprotein, and anti-sjogren's-syndrome-related antigen A and B antibodies.

She was referred to hematology for further management and consideration of systemic therapy for treatment of her lymphoma. The decision was made to start treatment with bexarotene as a steroid-sparing agent. The starting dose of bexarotene was 75 mg/m^2 and was titrated to a dose of 200 mg/m^2, as the steroids were tapered off. Unfortunately, after 6 months of therapy with bexarotene and weaning completely off steroids, she began to suffer from increased nausea, fatigue, and developed new painful bilateral lower extremity subcutaneous nodules. Because of her history of kidney