Cutaneous B-cell pseudolymphoma treated with rituximab and methotrexate

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Abstract

Cutaneous B-cell pseudolymphoma (CBPL), or cutaneous lymphoid hyperplasia, is the most common pseudolymphoma. It typically responds well to local treatment and follows a benign course. Herein, we describe the unique case of a patient with CBPL that was refractory to a variety of treatments, with subsequent response to rituximab followed by methotrexate. This case explores the complex interplay of T and B lymphocytes, and the potential role of perifollicular T cells in treatment resistant CBPL. Further, it describes the additive therapeutic effect of rituximab and methotrexate to target both B cell and T cell populations in CBPL, a strategy already employed in a number of other conditions.

Keywords: B-cell disorders, methotrexate, pseudolymphoma, rituximab

Introduction

Primary cutaneous B-cell disorders encompass a spectrum of disorders from cutaneous B-cell pseudolymphomas (CBPL) to primary cutaneous B-cell lymphoma (PCBCL). Cutaneous B-cell pseudolymphoma has a number of etiologies, including trauma, *Borrelia burgdorferi* infection, and contact allergy [1,2]. Cutaneous lymphoid hyperplasia, or lymphocytoma cutis, is the most common pseudolymphoma and is most frequently localized to the face. Cutaneous B-cell pseudolymphoma usually follows a benign course and responds well to local treatment [1]. General treatment strategies are varied, but include identification and removal of a causative agent, topical or intralesional corticosteroids, surgical excision if isolated, and radiation therapy [2]. Herein, we present a unique patient with CBPL that was refractory to treatment, including strict allergen avoidance, oral and topical corticosteroids, hydroxychloroquine, methotrexate, and narrowband ultraviolet B (nbUVB) therapy, who was subsequently responsive to infusions of rituximab followed by methotrexate.

Case Synopsis

A 72-year-old man presented with a year-long history of infiltrative, purple-brown plaques along the cheeks, temples, and bilateral ears (**Figure 1A**). He previously had extensive evaluation, including skin and bone marrow biopsies, PET-CT scans, patch testing, and extensive evaluation for infection and autoimmune diseases. Initial skin biopsies showed an atypical lymphoid infiltrate favoring cutaneous lymphoid hyperplasia. Prior interventions, including two courses of oral prednisone, doxycycline and niacinamide, oral methotrexate, hydroxychloroquine, topical corticosteroids, and strict allergen avoidance, were all unsuccessful. Repeat biopsy revealed a deep, B cell-predominant, dermal infiltrate with polytypic expression of kappa and lambda light

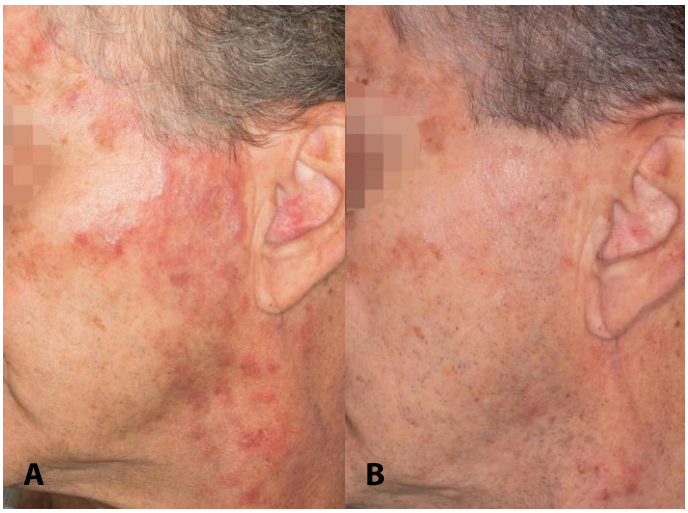

Figure 1. ***A)*** *Cutaneous B cell pseudolymphoma. Initial presentation demonstrating infiltrative, purple-brown plaques along the cheeks, temples, and bilateral ears.* ***B)*** *Resolution of cutaneous B-cell pseudolymphoma. After treatment with rituximab and methotrexate.*

chains and no clonal rearrangement of the immunoglobulin gene, consistent with follicular lymphoid hyperplasia. BCL6 and Ki67 were positive within follicle centers and BCL6 was positive in marginal zone cells. Additionally, a small number of T cells were noted at the periphery of the infiltrate (**Figure 2**). He completed four months of nbUVB therapy and oral prednisone without improvement. Because of the disfiguring nature of his disease, he started four weekly infusions of rituximab 375mg/m^2 with moderate improvement of his skin lesions. Approximately 2.5 months after the final rituximab infusion, methotrexate 20mg weekly led to dramatic improvement with complete resolution of the plaques by 8 months of therapy (**Figure 1B**). At follow-up, four months after discontinuing all medications, the patient remained clear.

Case Discussion

We present an interesting patient with CBPL that was refractory to multiple treatment modalities and partially responsive to rituximab infusions, with subsequent complete clearance following addition of methotrexate. Rituximab is an anti-CD20 antibody and is well-documented as effective treatment for CBPL and PCBCL [3-5]. Our patient experienced partial response to rituximab infusions, which targeted the majority, B cell component of his pseudolymphoma. Methotrexate was added to target both the T cells observed at the periphery of the infiltrates, as well as the atypical B cell population. With this additive combination, the patient experienced complete resolution.

Pseudolymphomas, lymphoproliferative and autoimmune disorders, involve a complex interplay of immune cells which are influenced by treatment. For example, a T cell-rich recurrence of PCBCL after rituximab treatment has been reported, suggesting that initial B cell depletion may allow proliferation of surrounding, reactive T cells [6]. Previous studies have suggested expanded T cell populations result from the disrupted B cell/T cell interactions following rituximab therapy for systemic lymphoma [7]. The dual targeting of B cells and T cells using rituximab combined with methotrexate is a principle already employed in the treatment of a number of other disorders, including rheumatoid arthritis, graft-versus-host disease, and primary central nervous system lymphoma [8-10]. Of note, methotrexate has been reported to induce immunosuppression-related CD30-positive lymphoproliferative disorders and thus should be initiated with caution in patients with CBPL [11].

Conclusion

The partial response after B cell depletion with rituximab alone in our case suggested that there was either a persistent, CD20-negative B cell population or possible expansion of the peri-lymphoid T cells following B cell depletion. This case demonstrates the potential additive effect that rituximab and methotrexate treatment can have by dual targeting of the B cell and T cell component of CBPL.

Potential conflicts of interest

Dr. Mangold reports personal fees from Kirin, grants from Elorac, MiRagen, Solagenix, DUSA/Sun Pharma, and Acetilion, outside the submitted work. All other authors have nothing to disclose.

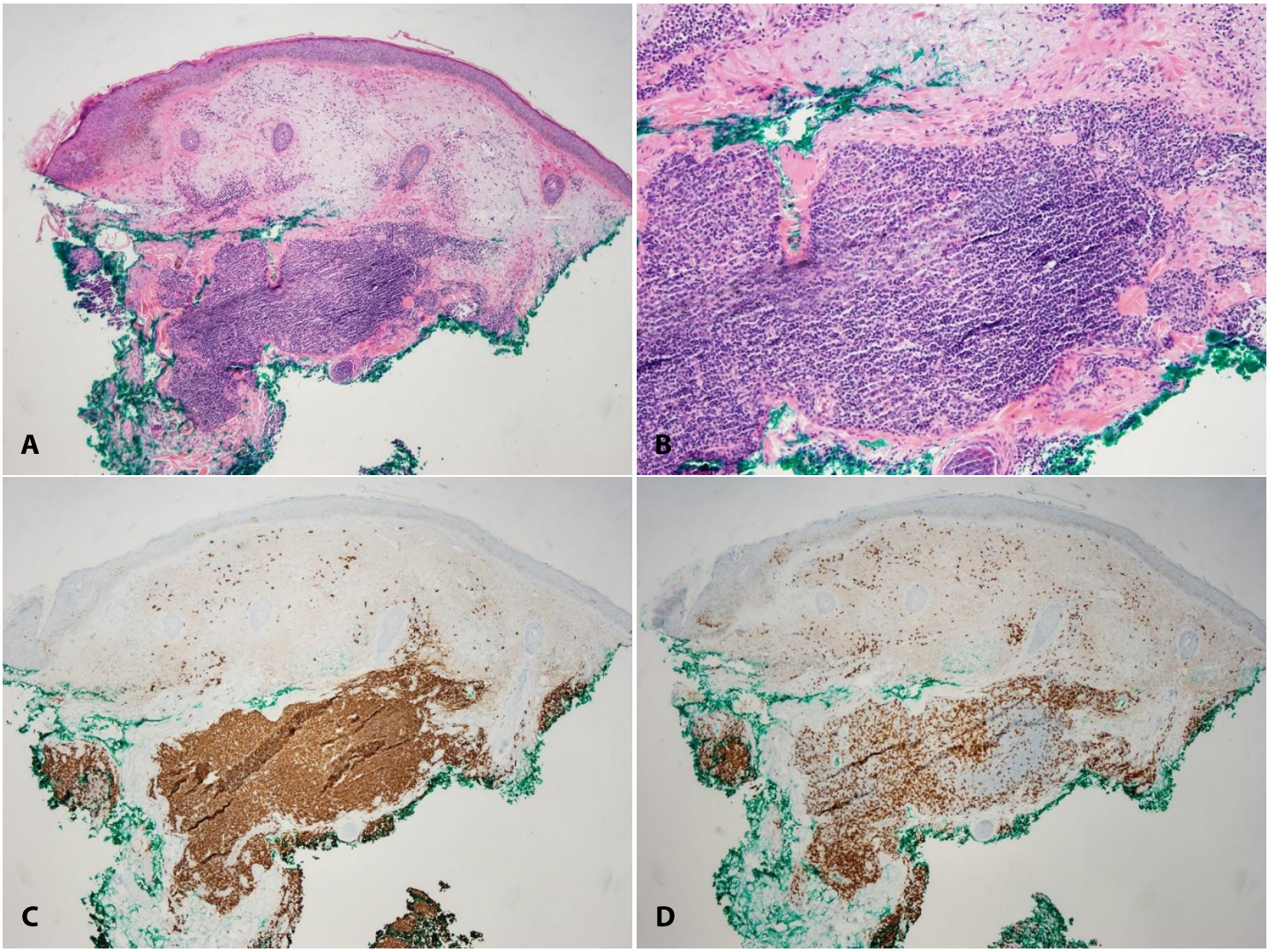

Figure 2. ***A, B)*** *Lymphocytic infiltrate with reactive follicular hyperplasia involving the dermis. H&E,* ***A)*** *40×;* ***B)*** *100×.* ***C)*** *CD20-positive B cells form lymphoid follicles, 40×.* ***D)*** *CD3-positive T cells are admixed with the predominant B cells, 40×.*

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