Intralesional rituximab for cutaneous manifestations of systemic B-cell lymphoma

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INTRODUCTION

Cutaneous B-cell lymphomas (CBCL) are a heterogeneous group of lymphoproliferative diseases[1] that can be classified in 2 broad categories: primary and secondary.[2] The latter implies a systemic lymphoproliferative disease that causes visible cutaneous lesions.[2] Numerous articles regarding the diagnosis and treatment of primary CBCL have been published. However, there is a paucity of literature on local therapeutic options for secondary CBCLs. Therefore, we report a case of successful treatment of secondary CBCL with intralesional rituximab.

Abbreviation used:

CBCL: cutaneous B-cell lymphoma

CASE REPORT

In August 2014, a 79-year-old man was sent to the dermatology department for evaluation of erythematous, infiltrated plaques on the scalp and frontotemporal regions evolving over a 6-month period. His medical history included a squamous cell carcinoma of the left scalp in 1990 treated by localized excision, left cervical lymph node dissection, and radiotherapy. In 2009, the patient presented to the dermatology department with an erythematous nodule on his forehead. Cutaneous biopsy found follicle center cutaneous B-cell lymphoma with immunohistochemistry profile positivity for CD20, CD79, Bcl-2, and Bcl-6. He had positive translocation (t[14:18]) on the cutaneous biopsy specimen. He then underwent systemic workup. The computed tomography scan found lymph nodes in the paravertebral area, around the aorta, and at the base of the mesenteric vessels. His bone marrow biopsy found the presence of lymphoma cells. Therefore, systemic follicle center non-Hodgkin B-cell lymphoma was diagnosed and successfully treated with 5 courses of R-CVP chemotherapy (rituximab, cyclophosphamide, vincristine, and prednisone). He remained clinically stable on follow-up with complete regression of the cutaneous lesions until August 2014 when the new cutaneous lesions were reported. Cutaneous lesions resulting from his systemic lymphoma was the primary working diagnosis. The patient was otherwise asymptomatic with no general symptoms of fever, weight loss, or night sweats. His positron emission tomography scan, complete blood count, liver function tests, creatinine, and electrolytes were normal. He, therefore, had a quiescent systemic disease and no indication for chemotherapy.

On physical examination, there was an erythematous infiltrated 4.2- × 3-cm plaque on the left scalp and 4 erythematous coalescent nodules on the left and right frontotemporal regions. There were no enlarged lymph nodes. We proceeded with a skin biopsy of the largest plaque. Histopathology found a dermal lymphocytic nodular infiltrate made of small to intermediate size cells with notched nucleus and the presence of dispersed large size cells. Immunohistochemistry profile showed positivity for CD79 and Bcl-2. A pathologist confirmed that the cellular architecture was of follicle center origin. Therefore, this information confirms the recurrence of cutaneous lesions of the patient's secondary follicle center B-cell lymphoma even though his systemic workup found no current active disease.

After literature review and discussion with the patient and his hematologist-oncologist, we decided

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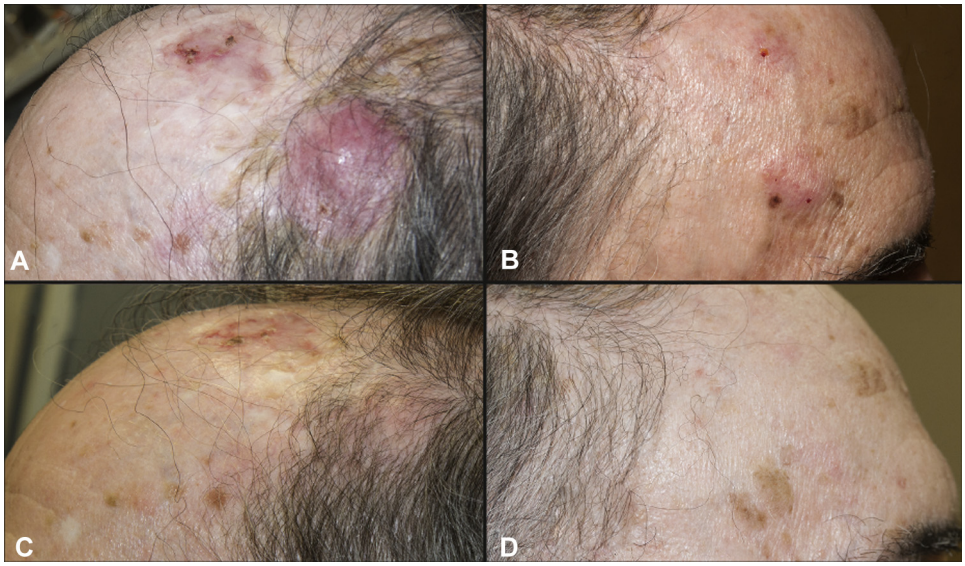

Fig 1. **A** and **B,** Cutaneous lesions before intralesional rituximab. **C** and **D,** The result after the last treatment cycle.

to treat the secondary CBCL with intralesional rituximab at a concentration of 10 mg/mL. Our treatment regimen was based on the study for intralesional rituximab in primary cutaneous B-cell lymphomas by Gamo et al.[1] We followed their treatment protocol, and each cutaneous lesion was injected with 10 to 30 mg (10 mg in the small nodules and 30 mg in the large infiltrated plaque), 3 times a week every 4 weeks until resolution. One treatment cycle corresponds to 3 intralesional injections on week 1 and 3 weeks without treatment. After the first treatment cycle, all lesions had responded. Complete regression of the right frontotemporal lesions was noted after the first treatment cycle, the left frontotemporal lesions after the second, and the left scalp after the third cycle (Fig 1). We recorded no recurrence during treatment or during follow-up, which is currently at 12 months posttreatment. A total cumulative dose of 185 mg of rituximab was used. The treatment was well tolerated with only mild pain of short duration at the injection sites. Complete blood count, liver function tests, creatinine, and electrolytes remained normal during treatment and at follow-up.

DISCUSSION

Rituximab is a monoclonal antibody composed of a murine anti-CD20 variable region and a human IgG1 constant region. Rituximab binds to anti-CD20 antigens on malignant and benign B cells. Once bound to anti-CD20 antigens, it signals for cell cycle arrest and apoptosis.[3] It is a well-documented therapeutic approach for primary cutaneous B-cell lymphomas and systemic B-cell lymphomas. This case report also shows its usefulness for local treatment of secondary cutaneous follicle center B-cell lymphoma with quiescent systemic disease.

The downfall with intralesional rituximab in secondary CBCL is the risk of relapse by not treating the systemic disease. However, rituximab is found to deplete peripheral circulating CD20 and CD19 B lymphocytes for up to 6 months after intralesional injection without causing side effects.[3] We hypothesize that this small systemic effect could possibly have been sufficient to maintain an otherwise inactive systemic disease, as we presented in this article, while not causing disagreeable symptoms.

Advantages to intralesional rituximab are its tolerability, with brief pain at injection sites,[4] the need for minimal amounts to achieve clinical response compared with the doses needed in systemic treatments, and the quick administration time. It had no systemic effects on blood and chemistry profile and was, therefore, well tolerated systemically. It also had no adverse effect on treated skin. We noted no cutaneous atrophy and no scars.

Limitation to our treatment protocol could be the lack of initial therapy with intralesional corticosteroids. This treatment option was initially considered for our patient; however, the fact that rituximab is a well-known useful treatment in primary cutaneous B-cell lymphomas and has a tolerable side effect profile, we chose to treat our patient with intralesional rituximab before a trial of steroids.

CONCLUSION

Intralesional rituximab was a successful choice for our patient. A gradual but complete response was documented over the course of 3 months and 3 treatment cycles, without relapse during 12 months of follow-up. This case shows the usefulness for local treatment of secondary CBCL with otherwise quiescent systemic disease. It will be interesting to see how long the remission period will last, for both skin lesions and systemic disease. Although rituximab may not be a first-line therapeutic approach, we showed its usefulness and effectiveness in this select case.

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