ORIGINAL RESEARCH

Intralesional Corticosteroid as a Treatment Option for Primary Cutaneous B-Cell Lymphomas: A Case Series and Literature Review

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Introduction

Primary cutaneous B-cell lymphomas (PCBCL) represent a class of mostly indolent malignancies which by definition are confined to the skin. They represent about 20-25% of all cutaneous lymphomas,[1,2] and usually affect middle-aged adults, more commonly men than women.[3]

The PCBCLs were re-classified in 2008 by the World Health Organization (WHO), and these guidelines were updated in 2016,[4] with the following subtypes currently recognized: primary cutaneous follicle center lymphoma (PCFCL); extra-nodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT), or primary cutaneous marginal zone lymphoma (PCMZL); primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT); and intravascular diffuse large B cell lymphoma (IDLBCL). PCFCL is the most common with about 55% of diagnoses.[3] PCMZL is the second most common (10-40%) and PCDLBCL the third most common (15%). While 5-year survival rates for PCFCL and PCMZL are above 95%, PCDLBCL-LT is the more aggressive subtype, with a tendency to spread to extracutaneous sites and a 5-year survival rate of only 50%.[3] About 20% of cases of PCDLBCL arise on sites other than the lower extremities, known as PCDLBCL, non-leg type, and are more indolent.[5] IDLBCL is extremely rare and aggressive, with most cases disseminated at the time of diagnosis.[6]

There are multiple treatment options available to patients, although some of these non-aggressive tumors may be conservatively observed. Excision and/or radiation therapy are most commonly utilized for localized disease.[1,2,7] One retrospective study of 50 patients with PCMZL reported 17 were treated with radiotherapy, and 10 underwent excision.[2] These patients had either single lesions or localized multifocal involvement. All except one of these patients had complete remission with the initial treatment, while one that was refractory to radiotherapy later underwent excision with good response.[2] Radiotherapy doses ranged from 12-40Grays (Gy). Nine patients experienced relapses, but outside the radiation field. Patients with extensive multifocal disease were treated with chemotherapy, including chlorambucil (11 patients), the CHOP regimen consisting of cyclophosphamide, doxorubicin, vincristine, and prednisone (three patients), or a variant (two patients). Of the patients treated with chlorambucil, 10 experienced a full or partial remission. Four of five patients who received CHOP regimens had complete remissions, however all four relapsed. None of these patients received intralesional corticosteroids (ILCS).

Rituximab, either intravenously or intralesional, and intralesional interferon-alpha have also been utilized.[1] In addition, some cases that are associated with *Borrelia burgdorferi* infection have been successfully treated with antibiotics, however this link has mostly been reported in European studies, and not in North America.[8,9]

The use of ILCS has been documented as a primary method of treatment, but its use is not well-defined. It was included as a non-first-line therapeutic option in the 2008 consensus guidelines for treatment of PCBCL published by the World Health Organization-European Organization for Research and Treatment of Cancer (EORTC), however they did not include any cases describing its use in their literature review.[1] Several cases have been reported, mostly of patients with PCMZL who relapsed after an initial therapy.[10–13] One woman had been treated with radiation for PCMZL with two relapses, had subsequent resolution with ILCS, through follow-up duration was not specified.[10] She received nine courses of injections with 5 milliliters (mL) of triamcinolone to seven lesions, although the concentration of the injections was not specified. A pediatric patient with PCMZL and suspected *B. burgdorferi* co-infection who failed a four-week antibiotic course achieved subsequent resolution with 64mg total of intralesional triamcinolone to eight lesions.[11] No relapse was reported within 20 months of follow-up. A review of 13 additional pediatric cases of PCMZL found only one additional case treated with ILCS, with complete remission after relapse from initial electron beam therapy.[11] A single-institution retrospective review of nine patients treated with ILCS, including two with PCFCL, three with PCMZL, three with unspecified PCBCL, and one with PCDLBCL, non-leg type, demonstrated complete response in four patients (with median follow-up time of 47 months) and partial response in five patients.[12]

The present study aims to characterize the various methods used to treat PCBCLs at an academic medical center, with the specific goal of describing patients treated with intralesional

corticosteroids, particularly for conditions other than PCMZL, which has not been widely reported in the literature.

Methods

We performed a retrospective analysis of patients aged 18 or older who had a diagnosis of extranodal marginal zone lymphoma, extranodal mantle cell lymphoma, extranodal follicular lymphoma, or extranodal diffuse large B cell lymphoma as well as documented administration of intralesional triamcinolone at the University of California Los Angeles (UCLA) Health center as of 2016. Data was extracted from the UCReX database. Patient charts were then manually reviewed to assess for proper inclusion of patients and determine their clinical course. Patients were manually excluded if they did not have a diagnosis of primary cutaneous lymphoma, including nodal lymphomas, extranodal mucosal-associated lymphoid tissue (MALT) lymphomas in sites other than the skin, soft tissue lymphomas including bone; and cases where the primary diagnosis was not clear. Patients with a primary cutaneous lymphoma that had not been treated with intralesional triamcinolone were not included in the primary sample, but those cases were still reviewed to assess their treatment course. The study was approved by the UCLA Institutional Review Board # 16-001446-CR00002.

Results

The study sample consisted of 220 patients who met the inclusion criteria. After manual review of patient charts, eight patients with primary cutaneous B-cell lymphomas were included in the study. Several other patients were identified with other types of cutaneous lymphomas, whose cases were also analyzed.

Of the eight patients included, five had a diagnosis of primary cutaneous marginal zone lymphoma (PCMZL); two had a diagnosis of primary cutaneous diffuse large B cell lymphoma (PCDLBCL), subtype not specified; and one had a diagnosis of primary cutaneous follicle center lymphoma (PCFCL).

Of the five patients with PCMZL, three were treated with intralesional triamcinolone injections with resolution of their lesions reported. One patient with lesions on the bilateral forearms had received a combination of intralesional triamcinolone, oral and topical corticosteroids, and doxycycline approximately ten years prior to presenting to our clinic. At UCLA he was treated with four rounds of injection with intralesional triamcinolone at a dose of 10 milligrams per milliliter (mg/mL) for a total of 14.5 milligrams (mg) injected. Complete resolution was noted two months after the last injection. Another patient had a lesion on the right upper back, which resolved after three rounds of injection with intralesional triamcinolone at a dose of 40mg/mL for a total of 48mg injected. The final patient had a lesion on the right thigh which responded to one injection of intralesional triamcinolone at a dose of 10mg/mL for a total of 5mg with subsequent application of topical triamcinolone 0.1% cream. These three patients received an average of 22.5mg of triamcinolone over an average of 2.7 visits. No side effects were reported. The remaining two patients with PCMZL were both treated with radiation at a total dose of 30Gy with subsequent resolution.

Patients with other subtypes of PCBCL were also identified in the manual chart review, however none received intralesional corticosteroid treatment. The patient with PCFCL was treated with excision on the scalp with subsequent resolution. The two patients with PCDLBCL both received radiation; one with subsequent resolution after 30Gy, but the other developed satellite lesions with extension into bone only five weeks into the course of radiation so was then treated with chemotherapy with subsequent resolution.

Discussion

In our study, PCMZL was most commonly treated with intralesional triamcinolone, with three of five patients receiving this treatment. All three received ILCS as their only treatment. Two other patients with PCMZL were treated with radiation therapy. Patients with other subtypes of PCBCL were also identified, including PCFCL and PCDLBCL, unspecified type, however they did not receive any intralesional steroid injections. Our experience aligns with previous reports. Indolent types of PCBCL, specifically PCMZL, which have a localized presentation may be well-suited to skin-directed therapy with intralesional triamcinolone. Especially given the high degree of relapse reported in patients treated with radiation, intralesional triamcinolone represents an effective, non-surgical alternative with few side effects. However, it may not be appropriate for patients with multifocal or widespread disease.

This study is limited by a small sample size. Further, the large proportion of cases that were excluded after manual chart review indicates that the search terms for initial patient abstraction from the database were either too broad or not representative of our desired sample. It suggests that our sample may not have captured additional patients with these conditions that could have met inclusion criteria. Follow up was limited to information available in the chart as this was a retrospective study. A prospective study would be better suited to track outcomes including rates of remission and recurrence.

Conclusion

Intralesional triamcinolone represents a viable treatment option for primary cutaneous lymphomas which are localized to the skin, and should be considered in patients for whom radiation or excision are less-desirable alternatives.

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