Dermatology Case Reports

OPEN ACCESS Freely available online

Case Report

# A Rare Case of Primary Cutaneous Marginal Zone B-cell Lymphoma

**Michelle D. Sim*, Claribel L. Jimenez**

*Department of Dermatology, Southern Philippines Medical Center, Philippines*

## ABSTRACT

Primary Cutaneous B-cell lymphomas represent 20%-30% of all cutaneous neoplasm. It has an estimated incidence of 10 case per 1,000,000 persons per year based on surveillance epidemiology. Primary Cutaneous Marginal Zone Lymphoma (PCMZL) is a rare and indolent type of cutaneous B-cell lymphoma which accounts for 10% of cases, with an excellent survival rate in 5 years exceeding 95%. It is composed of mixed infiltrates of marginal zone B-cells, lymphoplasmacytic cells, plasma cells, and reactive T-cells. We report a case of PCMZL in a 39 year old female who presented with generalized erythema, multiple violaceous plaques and nodules, located on the face, trunk and extremities. Definitive diagnosis based on clinicopathologic correlation as well as confirmation by immunohistochemical staining, is critical in distinguishing PCMZL from other types of lymphomas so that patients are properly evaluated and treatment management can be correctly instituted.

**Keywords:** Cutaneous lymphoma; B-cell lymphoma; Marginal zone lymphoma

## INTRODUCTION

Primary Cutaneous Lymphomas (PCL) are the most frequent extra-nodal lymphomas, with an incidence of around 10 cases per million per year, from which 20%-30% are Primary Cutaneous B-Cell Lymphomas (PCBCL) [1]. Like other cutaneous lymphomas, PCBCL are categorized according to the classification of the consensus between the World Health Organization (WHO) and the European Organization for Research and Treatment of Cancer (EORTC) [1,2].

One of the most indolent forms of PCBCL includes the Primary Cutaneous Marginal Zone B-Cell Lymphoma (PCMZL). It is a very indolent type of lymphoma that is restricted to the skin at the time of diagnosis. However, despite the excellent prognosis, still have cutaneous recurrences. It comprises about 7% of all primary cutaneous B-cell lymphomas [3]. Definitive diagnosis requires a multi-parameter approach with the incorporation of clinical features, histopathologic findings, immunophenotypic features and adequate clinical staging [1-4].

PCMZL usually occurs in adults in the 5$^{th}$ or 6$^{th}$ decade, non-Hispanic whites, with a male predominance [4-7]. Onset in childhood, although rare, also has been observed [6]. Extracutaneous involvement and dissemination to extracutaneous sites are uncommon at the time of diagnosis. Associations with infectious agents, such as Borrelia burgdorferi, and autoimmune diseases have been reported [4].

Patients with PCMZL frequently present with multifocal erythematous to violaceous patches, plaques, nodules or tumors that may be solitary, localized or multifocal. This may occur in any part of the body but is more commonly seen on the trunk and arms, less commonly the face [5-8]. Histopathologic findings may be composed of varying proportions of mixed infiltrates such as small B-lymphocytes, lymphoplasmacytoid cells, plasma cells, marginal zone B-cells and reactive T-cells [3-5]. Marginal zone B-cells characteristically express BCL-2, but lack BCL-6 or CD10 expression [7].

The diagnosis of PCMZL may be particularly challenging in many cases mainly because it requires the correlations of immunophenotypic and detailed clinical information. Moreover, there are limited number of neoplastic cells as well as having a broad spectrum of reactive disorders that can mimic cutaneous lymphomas clinically and histologically [8]. In this case report, we will discuss the clinicopathologic features of PCMZL and emphasize the diagnostic workup of this lymphoma.

## CASE REPORT

We present a case of R.M.B, a 39-year old female, married, who previously worked as banana plantation worker in Davao City who sought consult due to generalized desquamation, with multiple plaques, nodules and tumors seen mainly over the trunk and extremities.

History started three years prior to consult (PTC), when the patient noted multiple erythematous plaques with scales on the trunk and extremities, associated with pruritus. The patient sought

**Correspondence to:** Michelle D. Sim, Department of Dermatology, Southern Philippines Medical Center, Philippines, Telephone: +639778119688; E-mail: mdsim821@yahoo.com

**Received:** January 23, 2021; **Accepted:** February 06, 2021; **Published:** February 20, 2021

**Citation:** Sim MD, Jimenez CL (2021) A Rare Case of Primary Cutaneous Marginal Zone B-cell Lymphoma. Dermatol Case Rep 6:174.

consult with a private physician and was diagnosed as a case of psoriasis vulgaris. No skin punch biopsy was done. Patient was given unrecalled topical medications which provided partial relief. However, recurrences of lesions with increase in the number of lesions were noted.

Two years PTC, still with the persistence of said lesions, patient now observed multiple nodules and tumors on her back. No consult was done nor medications taken and applied.

In the interim, patient noted spread of lesions and increase in the number of nodules and tumors now involving the posterior axillary area and thighs. She self-medicated with herbal ampalaya capsules twice a day for 1 month.

One month PTC, Patient noted severe pruritus and progression of plaques and tumors now involving her face. She applied boiled guava leaves concoction as well as herbal oil all over her body every day.

Ten days PTC, patient noted exfoliation all over her body, associated with 1 episode of undocumented fever, chills and body malaise. Hence, prompted consult at our institution.

There was no previous history of weight loss, oral ulcers. Past medical history was unremarkable. Family history was negative for malignancy. Patient was a non-smoker and non-alcoholic beverage drinker. Obstetrics and Gynecological History was also unremarkable.

Upon physical examination, patient was generally well, ambulatory and slightly tachycardic with heart rate of 102 bpm. Patient was noted to have poor temperature body hemostasis.

Upon dermatologic examination, patient presented with generalized erythema with multiple erythematous, violaceous plaques topped with course scales over the face, trunk and extremities. There was also note of multiple firm nodules and tumors over the axilla, back and both lower extremities with inguinal lymphadenopathy and bipedal edema, non-pitting. Hair and nail findings were unremarkable. No mucosal lesions were noted (Figures 1-3).

Dermoscopic examination showed presence of salmon colored background, scales, polymorphous vessels and white areas (Figure 4). Laboratory workup were requested and only showed albuminemia with elevated LDH levels. 12L ECG showed sinus tachycardia. Liver enzymes and Hepatitis profile showed normal results. Peripheral blood smear revealed normal blood cell morphology. Chest x-ray and PPD test was done which were also unremarkable. Whole abdominal ultrasound showed normal results.

Skin punch biopsy was done on a tumor. Histomorphological findings of which are consistent with Cutaneous B-cell lymphoma, showing a diffuse pattern with presence of large cleaved cells.

There are noted inflammatory infiltrates in the dermis composed predominantly of lymphocytes and presence of large pale-staining population of medium-sized cells with abundant cytoplasm (Figure 5).

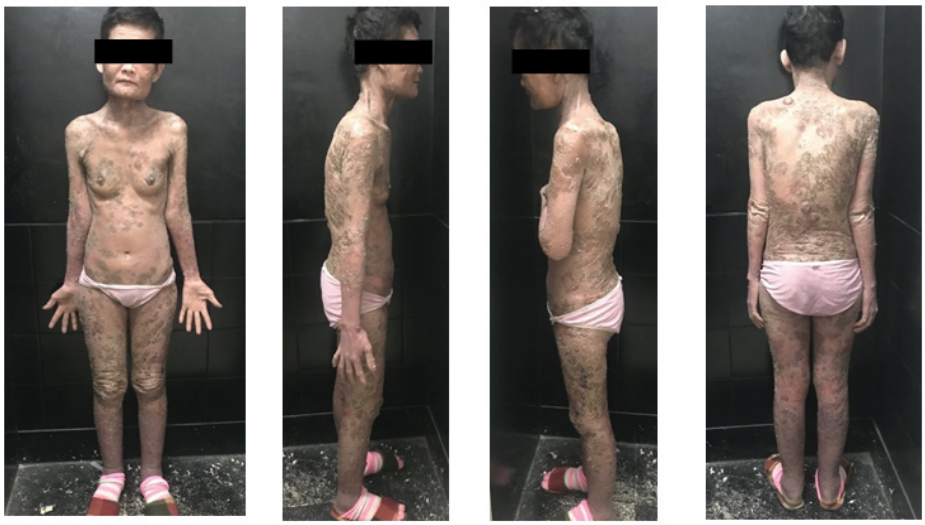

**Figure 1:** (+) generalized erythema and scaling.

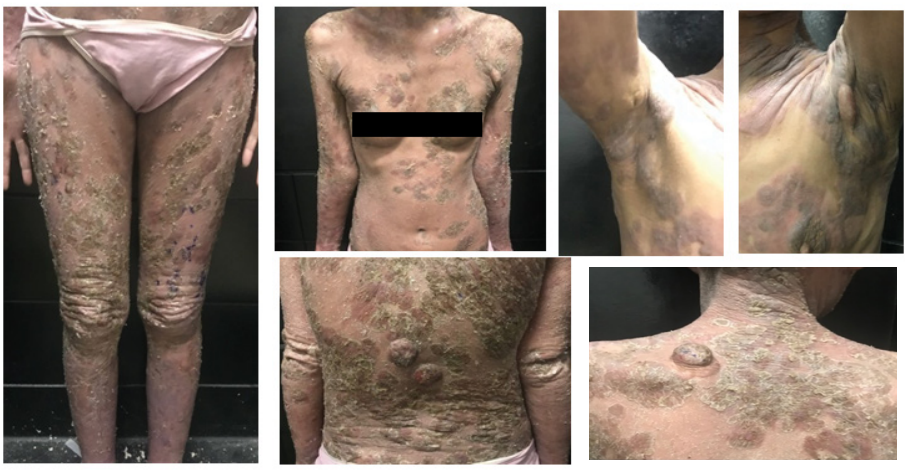

**Figure 2:** (+) plaques with scales, nodules and tumors on the trunk, axilla and extremities.

Immunohistochemical staining was done and was reported as CD3-, CD20+, CD79a+, Bcl2+, and Bcl6-. Hence, the diagnosis of Primary Cutaneous Marginal Zone Lymphoma (PCMZL) was made on the basis of the clinicopathological and immunohistochemical analysis (Figure 6).

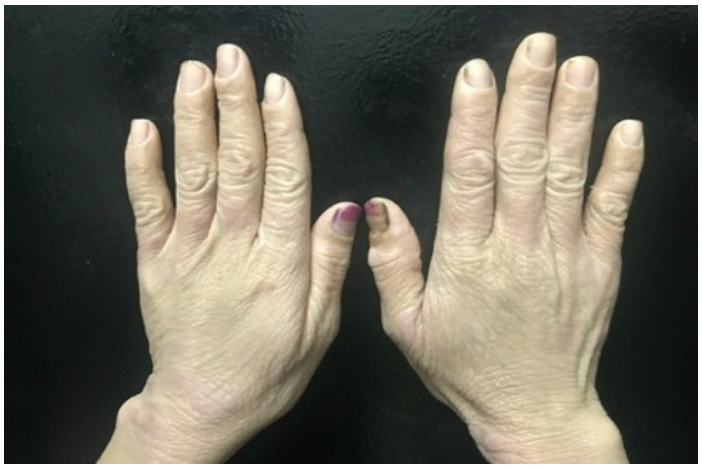

**Figure 3:** Non-pitting edema.

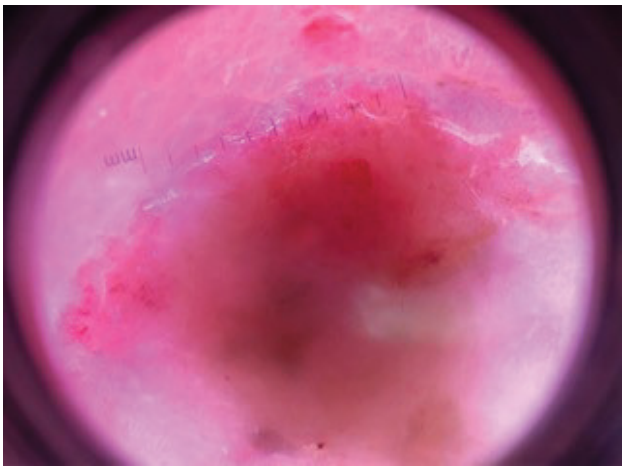

**Figure 4:** Dermoscopic examination showing presence of salmon colored background, scales, polymorphous vessels and white areas.

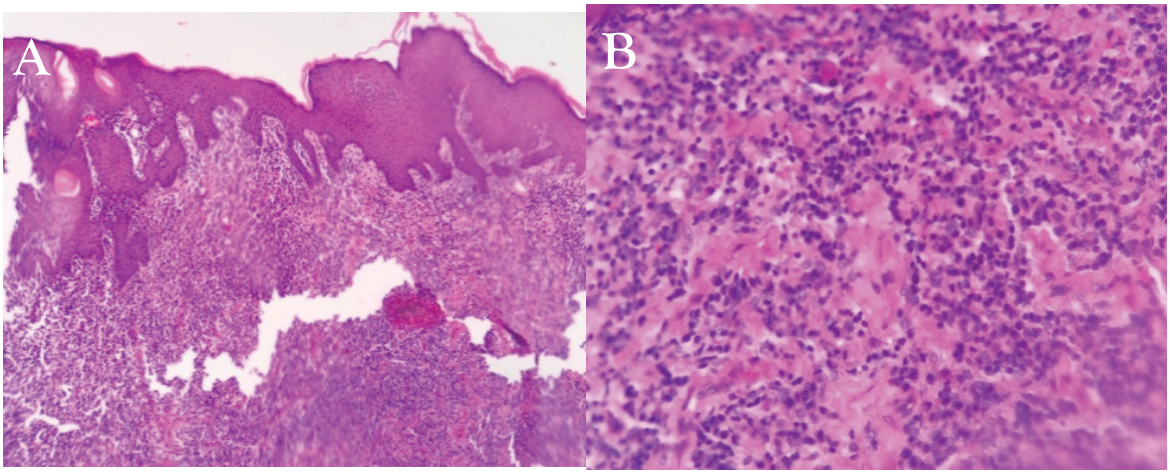


**Figure 5:** (a): (+) diffuse pattern; (b): (+) pale staining population of medium sized cells with abundant cytoplasm; (+) lymphocytic infiltrates; (+) large cleaved cells.

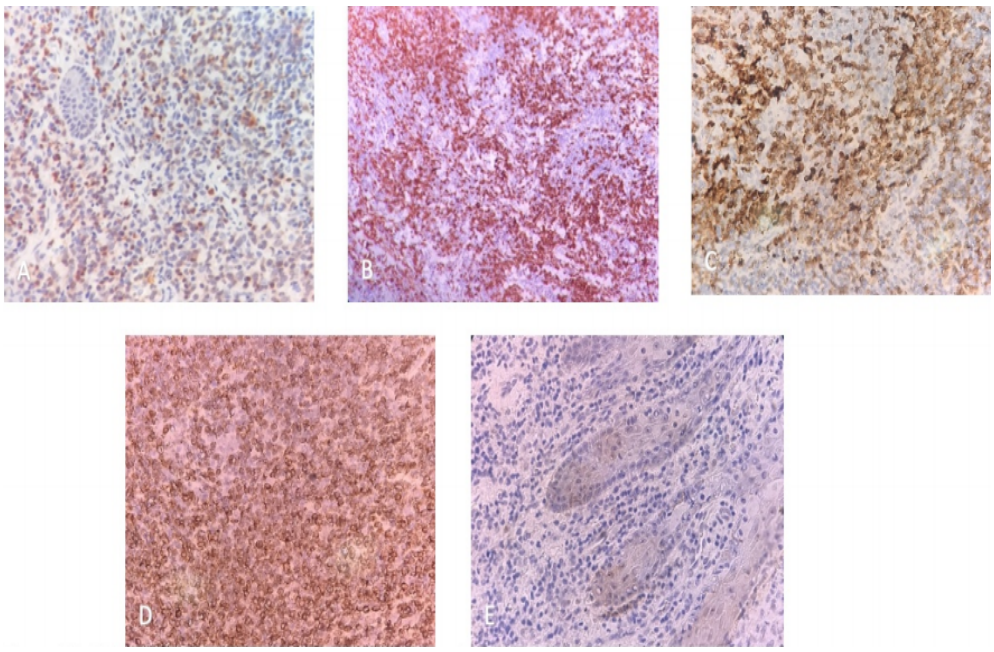


**Figure 6:** (a): CD3 negative; (b): CD20 positive; (c): CD79a positive; (d): Bcl2 positive; (e): Bcl6 negative.

Patient was advised referral to a medical oncologist to start treatment with IV Rituximab or chemotherapy with CHOP or R-CHOP. However, patient did not consent and opted not to continue with the treatment. Patient was given Clobetasol propionate +PJ (1:1) dilution, emollients and Hydroxyzine as symptomatic treatment.

## DISCUSSION

Primary cutaneous B-cell lymphoma is a heterogeneous group of diseases consisting of different B-cell lymphomas with distinct treatment and prognosis. Their clinical presentation is relatively uniform, mostly manifested by nodules. One of the indolent types of B-cell lymphoma is Primary Cutaneous Marginal Zone B-Cell Lymphoma (PCMZL). It is more common in adults with male predominance. Dermatologic manifestations include solitary or multiple erythematous, or violaceous plaques, dome-shaped papules, nodules and tumors with a predilection on the trunk and limbs. Some cases have been associated with *Borrelia burgdorferi* infection and Anetoderma [8]. However, there appears to be a geographic variation, with associations mainly from Europe, but rarely found in Asia and the United States [9].

Histopathologically and cytomorphologically, PCMZL usually presents with dense dermal perivascular nodular or diffuse infiltrates consisting of lymphocytes, with an indented nucleus or abundant, pale-staining cytoplasm [3,8] known as marginal zone B-cells, centrocyte-like cells or monocytoid B-cells [8-10]. They may also present with scattered follicles with germinal centers and a polymorphous proliferation of mostly small to intermediate-sized lymphoid cells, lymphoplasmacytic cells and frequently plasma cells that may exhibit cytoplasmic inclusions and stain positive for Periodic Acid-Schiff (PAS), commonly referred to as "Dutcher bodies" [3,8]. The epidermis is spared with a Grenz zone present [3]

Immunohistochemical studies, includes positivity for CD19, CD20, CD22, CD43, CD79a, BCL2 and KiM1p (monocytoid B-cells), and negativity for CD5, CD10, CD23 and BCL6 [8].

The International Society for Cutaneous Lymphomas (ISCL) and EORTC recently proposed staging recommendations for cutaneous lymphomas other than mycosis fungoides and Sezary syndrome, which include a thorough history, physical examination, appropriate laboratory studies, and imaging of the chest, abdomen, pelvis, and neck with CT, PET or PET/CT [11]. The TNM system addresses the non-MF/SS primary cutaneous lymphomas. The T classification for cutaneous lymphoma reflects the extent/distribution of primary cutaneous involvement. The N classification denotes nodal involvement and M representing extracutaneous manifestations [12]. In contrast, the International Extranodal Lymphoma Study Group identified three independent prognostic factors which includes an elevated LDH, >2 skin lesions, and nodular lesions among patients with PCFCL and PCMZL. Overall survival rate in the absence of any adverse prognostic factors for PCMZL is 91%, with a relatively common extracutaneous dissemination [8-16]. In contrast, the presence of two or three adverse prognostic factors was associated with a 5-year progression-free survival of 48%. Moreover, the presence of multiple skin lesions was also associated with inferior survival [11].

Generally, aggressive treatment of indolent PCBCL such as PCMZL should be avoided, as they have a very good prognosis [8]. However, if patient presents with more lesions and recurrence, radiation treatment for palliative dosing may be warranted. Excision, radiotherapy and intralesional steroids may be done for skin limited localized disease.

Most patients with PCMZL who presents with T1 having solitary skin involvement and T2 disease with a small number of regional skin lesions may be treated with local radiation therapy [12]. The EORTC/ISCL recommends a dose range of 20 Gy to 36 Gy for primary cutaneous marginal zone lymphoma [12].

In our case, patient presented as T3bN0M0, having generalized skin involvement with multiple lesions involving greater than 3 regions, no clinical lymph node involvement and no evidence of extracutaneous disease. Therapeutic options in cases of multifocal/disseminated disease or relapse, include steroids or intravenous Rituximab in monotherapy or in combination with intravenous or oral chemotherapy [14,15]. The dose for IV Rituximab is at 375 mg/m$^2$ per administration, repeated weekly for 4 to 8 weeks [8]. Rituximab is generally well tolerated, mostly with local adverse effects such as pain at injection site, pruritus, and urticaria. Other rare manifestations include lichenoid reactions, epidermal necrolysis and bullous eruptions. Systemic events include anaphylactic reactions and reactivation of viral infections. Polychemotherapy (CHOP, R-CHOP) is reserved for patients with advanced and/or resistant cutaneous disease or extra-cutaneous involvement [8].

Follow-up intervals for patients with indolent CBCL are usually at every 6 months for a complete cutaneous and lymph node exam [13]. CT scans and blood work may again be requested if patient will present "B symptoms" such as weight loss, fever and night sweats or if patient will present with new appearance of lymphadenopathy [13].

## CONCLUSION

PCMZL is an extremely rare and unique form of cutaneous lymphoma. It is one of the indolent types of B-cell lymphoma but it can have a potentially fatal consequence if undiagnosed. Its recognition is important to ensure that the therapeutic approach for these is appropriate and not overly aggressive. Clinicians must take great care to make the correct diagnosis based on a clinicopathologic correlation and immunohistochemical findings, to determine overall treatment strategy, as prognosis may vary.

## REFERENCES

1. Lima M. Cutaneous primary B-cell lymphomas: From diagnosis to treatment. An Bras Dermatol. 2015;90:687-706.
2. Burg G, Kempf W, Cozzio A, Feit J, Willemze R, S Jaffe E, et al. WHO/EORTC classification of cutaneous lymphomas 2005: Histological and molecular aspects. J Cutan Pathol. 2005;32:647-674.
3. Swerdlow SH. Cutaneous marginal zone lymphomas. Semin Diagn Pathol. 2017;34:76-84.
4. Yilmaz F, Soyer N, Vural F. Primary cutaneous B cell lymphoma: Clinical features, diagnosis and treatment. World J Dermatol. 2015;4:50-56.
5. Hoefnagel JJ, Vermeer MH, Jansen PM, Heule F, van Voorst Vader PC, Sanders CJ, et al. Primary cutaneous marginal zone B-cell lymphoma: clinical and therapeutic features in 50 cases. Arch Dermatol. 2005;141:1139-1145.
6. Cho-Vega JH, Vega F, Rassidakis G, Medeiros LJ. Primary cutaneous marginal zone B-cell lymphoma. Am J Clin Pathol. 2006;125:S38-49.
7. Wilcox RA. Cutaneous T-cell lymphoma: 2016 update on diagnosis, risk-stratification, and management. Am J Hematol. 2016;91:151-165.
8. Lima M. Cutaneous primary B-cell lymphomas: From diagnosis to treatment. An Bras Dermatol. 2015;90:687-706.

9. Takino H, Li C, Hu S, Kuo TT, Geissinger E, Muller-Hermelink HK, et al. Primary cutaneous marginal zone B-cell lymphoma: A molecular and clinicopathological study of cases from Asia, Germany, and the United States. Mod Pathol. 2008;21:1517-1526.

10. Lorenzo C, Signoretti S, Höfler G, Annessi G, Pütz B, Lackinger E, et al. Primary cutaneous marginal zone B-cell lymphoma: A recently described entity of low-grade malignant cutaneous b-cell lymphoma. Am J Surg Pathol. 1997;21:1307-1315.

11. Wilcox RA. Cutaneous B-cell lym-phomas: 2019 update on diagnosis, risk stratification, andmanagement. Am J Hematol. 2018;93:1427-1430.

12. Specht L, Dabaja B, Illidge T, Wilson LD, Hoppe RT. Modern radiation therapy for primary cutaneous lymphomas: Field and dose guidelines from the International Lymphoma Radiation Oncology Group. Int J Radiat Oncol Biol Phys. 2015;92:32-39.

13. Chen ST, Barnes J, Duncan L. Primary cutaneous B-cell lymphomas-clinical and histopathologic features, differential diagnosis, and treatment. Semin Cutan Med Surg. 2018;37:49-55.

14. https://www.pathologyoutlines.com/topic/skintumornonmelanocyticMALT.html

15. Domenech ED, Salas Q, Servitje O, Climent F, Pomares H, Lucas A, et al. Treatment of primary cutaneous marginal zone B-cell lymphomas with intralesional rituximab. Blood. 2016;128:1796.

16. Gibson SE, Swerdlow SH. How I diagnose primary cutaneous marginal zone lymphoma. Am J Clin Pathol. 2020;154:428-449.