International Journal of Research in Dermatology
Jairath R et al. Int J Res Dermatol. 2021 Jan;7(1):126-128
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20205608

Case Report

Persistence pays: a case of primary cutaneous B-cell lymphoma masked by granulomas

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Received: 22 October 2020
Accepted: 27 November 2020

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ABSTRACT

Primary cutaneous diffuse large B cell lymphoma is a form of cutaneous lymphoma characterized by a clonal proliferation of B cells that is often presents with a delayed diagnosis, and therefore often carries poor prognosis. We report a 77-year-old female presenting with a shin lesion resembling a deep dermal or fungal process. Initial biopsy revealed superficial and deep mixed granulomatous inflammatory infiltrate, which suggested an initial diagnosis of Majocchi's granuloma, despite negative fungal cultures. Despite treatment, the progressive worsening of the skin lesions prompted multiple repeat biopsies, which eventually revealed CD20, Bcl-2, and Bcl-6 staining, loss of CD3 and CD30, and high Ki67, compatible with a cutaneous high-grade B-cell lymphoma. Clinical presentations of primary cutaneous diffuse large B cell lymphoma can mimic several different clinical entities, rarely including granulomatous disease, such as a fungal pathology. This report highlights the importance of persistence and a multimodal approach to the diagnosis of unidentified skin lesions, especially in the setting of failure to respond to standard therapies.

Keywords: Primary cutaneous B cell lymphoma, Leg type, Cutaneous oncology, Lymphoma, Metastasis, Fungal, Granulomatous

INTRODUCTION

Primary cutaneous lymphomas are a rare group of disorders, representing 19% of extranodal non-Hodgkin lymphomas (NHLs) and comprise a diverse array of clinical, immunologic, cytogenetic, histologic, and molecular features.[1] Although the majority of cutaneous lymphomas are T-cell lymphomas (65%), other groups of lymphomas include the B-cell lymphomas (25%) and the natural killer-cell lymphomas (10%).[1] Given their low incidence in the general population, cutaneous B-cell lymphomas present unique, yet critically important diagnostic challenges. The world health organization-European organization for Research and Treatment of Cancer (WHO-EORTC) group defines four separate subtypes of cutaneous B-cell lymphomas, including primary cutaneous follicle center lymphoma (PCFCL), primary cutaneous marginal zone B-cell lymphoma (PCMZL), primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT), and PCDLBCL-other.[2] Here, we report a case of PCDLBCL-LT, which presented very similarly to a fungal lesion. PCDLBCL-LT carries a 5-year disease-specific survival rate of 55%, so it is paramount that clinical suspicion for these cases exists where appropriate, as advanced stages carry poor prognosis and require early initiation of treatment.[2]

CASE REPORT

A 77-year-old female with past medical history significant for multiple blistering sunburns before and after age 10 presented with an erythematous and swollen lower leg. Her primary care provider treated this with two weeks of cephalexin, neomycin ointment, and white petrolatum

given concern for cellulitis, which worsened the lesion. The patient reported the appearance of this lesion after bruising her leg upon impact with furniture. The lesion was non-pruritic but occasionally caused warmth and a burning sensation. She denied fevers, chills, weight loss, weight gain or any tobacco use. On physical exam, the lesion appeared to be a 9.0 cm area of erythema with early vesiculation. A diagnosis of stasis dermatitis with contact dermatitis to neomycin ointment was made, and she was prescribed halobetasol propionate.

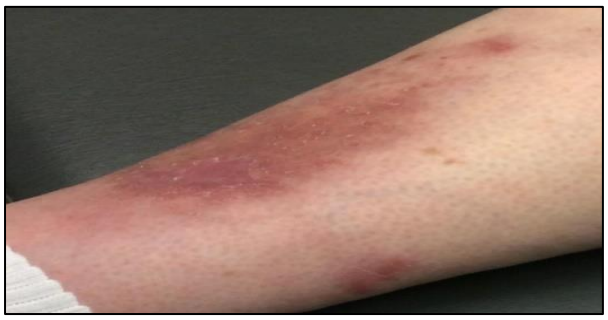

Figure 1: Clinical images of the patient's right leg lesion at the time of presentation prior to the first biopsy.

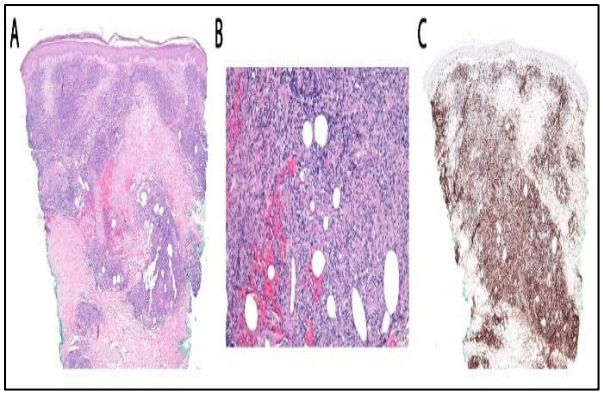

Figure 2: Granulomatous dermatitis suggestive of Majocchi's granuloma. (A) low power view (4x) showing a superficial and deep mixed inflammatory infiltrate. (B) medium power view (20x) highlighting the granulomatous component. (C) CD20 immunostain highlighting B-cells.

On follow up one month later, the patient reported improvement of her lesion with application of dish soap and topical lidocaine. However, upon inspection, the right pretibial area demonstrated worsened erythema and slight scaling measuring 17×10 cm with scattered dermal papules, raising concern for a dermal process (Figure 1). The differential diagnosis included deep dermal stasis dermatitis, contact dermatitis with dish soap or lidocaine, and Majocchi's granuloma. She was prescribed triamcinolone 0.1% cream for two weeks. A full-thickness punch biopsy displayed a superficial and deep mixed granulomatous inflammatory infiltrate composed of a mixture of CD163 positive histiocytes, CD20 positive B-cells, and scattered CD3 positive T-cells (Figure 2). While PAS and AFB stains were negative, the clinical findings remained suspicious for an infectious process such as Majocchi's granuloma. Pathologist recommended tissue cultures for fungus, bacteria, and AFB.

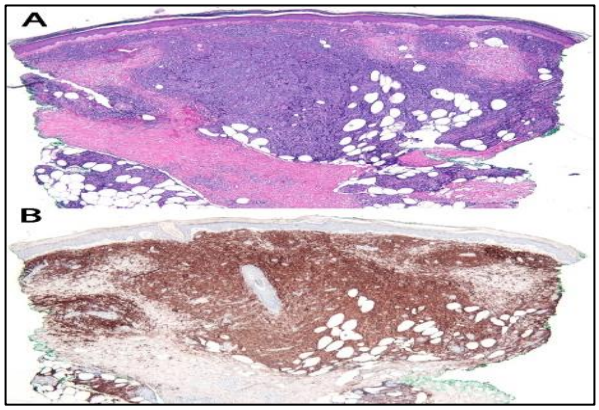

Figure 3: High grade B-cell lymphoma. (A) low power view (4x) of a dense lymphoid proliferation. (B) CD20 immunostain confirming B-cell lineage.

Due to the coronavirus 2019 (COVID-19) pandemic, patient was delayed and returned in two weeks for tissue culture. Examination demonstrated lesion enlargement to 18×10 cm in size with few scattered thickened, erythematous, dermal lesions and new satellite lesions. At this point, the patient was noted to have onycholysis, tenderness, and dystrophy of the distal toenails with presumed onychomycosis and surrounding tinea pedis, offering a potential source of infection. Therefore, the patient was started on ciclopirox cream twice daily and biopsy was obtained. Gram stain, Grocott-Gomori's methenamine silver (GMS) stain, acid-fast bacilli (AFB) stain and all cultures were negative. Terbinafine was later started given improvement on ciclopirox, and although onycholysis and tinea pedis improved, the presenting rash did not, raising concern for two separate disease processes.

At 4 months from initial presentation, the patient presented with 3 new asymptomatic 1 cm satellite lesions. The larger lesion had become an atrophic, hyperpigmented 9×2 cm post-inflammatory lesion. A full-thickness punch biopsy of one of the new satellite lesions showed a dense sheet-like growth composed of highly atypical lymphocytes with vesicular chromatin, prominent nucleoli, and scattered mitotic figures. The atypical infiltrate was positive for MUM1, CD20, Bcl-2, and Bcl-6, negative for CD3 and CD30, and Ki67 showed a high proliferative index (Figure 3), compatible with a cutaneous high-grade B-cell lymphoma. She was referred to medical oncology for further management of her newly diagnosed primary cutaneous B-cell lymphoma, leg type. Positron emission tomography (PET) scan revealed no evidence of disseminated disease, confirming the diagnosis of primary cutaneous B cell lymphoma. The patient underwent treatment with rituximab and radiation therapy, with complete response.

DISCUSSION

Primary cutaneous B-cell lymphomas are defined as lymphoproliferative neoplasms that present with a primary cutaneous manifestation, with no extracutaneous involvement.[3] The patient in our case presented with PCDLBCL-LT, a specific subtype of cutaneous B-cell lymphoma that presents histologically with a predominance or confluent sheets of Centro blasts and immunoblasts, usually arising on the lower legs in elderly women.[2-6] Generally, these lymphomas are diagnosed at a stage in which they are rapidly growing, and in contrast to the other subtypes, PCDLBCL-LT is more likely to disseminate to extracutaneous sites, with poor prognosis.[5,6] Clinically, the presence of multiple skin lesions at diagnosis is a poor prognosticator. Whereas a single skin tumor on one leg demonstrates disease-specific survival of 85% at 5 years, patients with multiple skin lesions on one or both legs have a 5-year disease specific survival rate of 45% and 36% respectively.[6]

A prominent granulomatous reaction in the setting of cutaneous lymphoma has been described. With the exception of the granulomatous variant of mycosis fungoides, these cases are quite rare. In one retrospective study, only 22 (1.8%) patients with cutaneous lymphoma demonstrated a prominent granulomatous reaction, defined as granulomatous reaction exceeding 25% of the dermal infiltrate, delaying diagnosis for up to 216 months.[7] Of these, only one case was classified as a large B-cell lymphoma. In some cases, the granulomatous component of a cutaneous lymphoma is prominent enough to mask the lymphomatous features.[7] These case reports serve to emphasize the fact that in atypical presentations, and in the absence of complete therapeutic response to granulomatous disease, a diagnosis of cutaneous lymphoma should be considered. It may be beneficial to perform sequential biopsies, as well as complete phenotypic and molecular genetic analyses, to accurately rule out or confirm this diagnosis.

CONCLUSION

In conclusion, we present a rare case of PCDLBCL-LT that displayed prominent granulomatous features on initial biopsy, requiring sequential biopsies spread over several months to obtain a diagnosis. This case also touches on the difficulty in managing diagnostically challenging cases through the era of COVID-19, especially those requiring thorough physical exams and histologic examinations. Most importantly, this case highlights the needs for clinicians to keep a clinical suspicion for the diagnosis of cutaneous lymphoma in cases of atypical or unusual granulomatous disease, to facilitate early diagnosis and prompt treatment initiation.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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Cite this article as: Jairath R, Jairath NK, Vandenboom T, Goldfarb MT. Persistence pays: a case of primary cutaneous B-cell lymphoma masked by granulomas. Int J Res Dermatol 2021;7:126-8.