Oral Isotretinoin for Refractory Cutaneous Pseudolymphoma: A Case Report

Natsinee Tangkijngamvong MD, Marisa Pongprutthipan MD.
Division of Dermatology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

ABSTRACT:
Cutaneous pseudolymphoma is a benign lymphoproliferative disorder that can mimic cutaneous lymphoma's clinical and histological features. While spontaneous resolution is observed in some cases, others may exhibit a persistent or recalcitrant clinical course. In such instances, alternative therapeutic options become imperative. Here, we present a case of an 83-year-old female with erythematous plaques on the right cheek. The pathological examination confirmed the diagnosis of cutaneous pseudolymphoma, with a history of recalcitrant to various treatment modalities. Oral isotretinoin was initiated as a monotherapy, and skin lesions were resolved within a few weeks without significant adverse events. This case report aims to provide additional evidence supporting the efficacy of isotretinoin as a viable treatment option for refractory cutaneous pseudolymphoma.
Key words: Cutaneous pseudolymphoma, Refractory, Isotretinoin, Oral retinoids, Treatment

Introduction

Cutaneous pseudolymphoma (CPL) poses challenges in diagnosis and management due to its variable clinical course and triggering factors. While some cases may undergo spontaneous resolution, some are recalcitrant[1-3]. Various treatment modalities have been reported, but the outcomes remain inconsistent[4]. Several case reports on treatment options are successful for refractory cases. This report presents a case of refractory CPL successfully treated with oral isotretinoin as a monotherapy, highlighting the potential of oral retinoids as a treatment option for refractory CPL.

Case Presentation

An 83-year-old female presented with progressively enlarging red plaques on her right cheek over the past 2 years. The patient occasionally experienced mild pruritus associated with the lesions and denied any pain or other symptoms. Her medical history was notable for ischemic heart disease, status post percutaneous coronary intervention, hypertension, and paroxysmal atrial fibrillation. Her current medications included clopidogrel, apixaban, amiodarone, losartan, and bisoprolol.

Physical examination showed erythematous, infiltrative, non-ulcerated plaques on the right cheek (Figure 1A). Lymph nodes were non-palpable. The differential diagnosis included chronic infection and non-infectious causes such as lymphoma, pseudolymphoma, Jesser lymphocytic infiltration of the skin and lupus tumidus.

Corresponding author: Marisa Pongprutthipan MD., email: dr_marisa@yahoo.com

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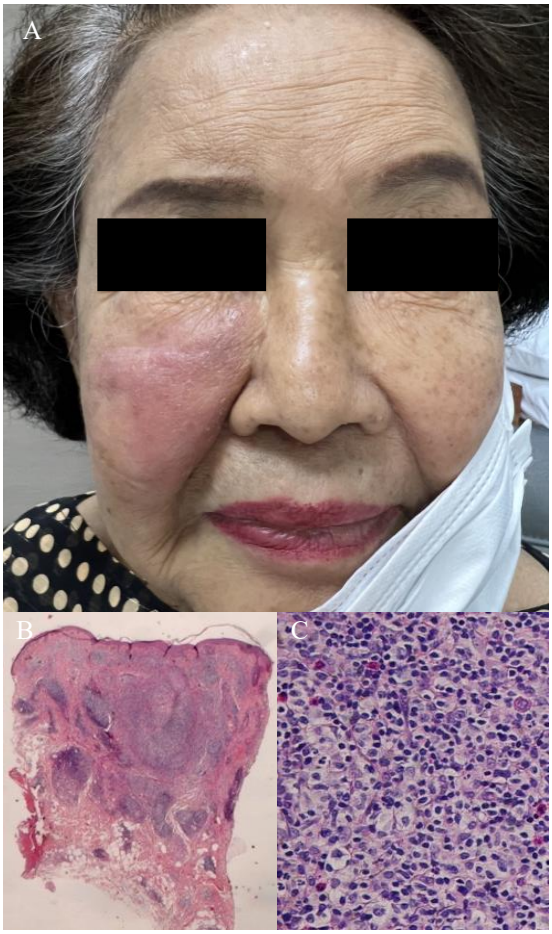

Figure 1
A) Erythematous infiltrative plaque on the right cheek.
B) and C) Lymphoid follicles with a mixed inflammatory cell infiltrate in the entire dermis, comprising of lymphohistiocytes and eosinophils

Histopathology examination showed lymphoid follicles with a mixed inflammatory cell infiltrate, consisting of lymphohistiocytes and eosinophils, throughout the dermis (Figure 1B, 1C). Periodic Acid-Schiff, acid-fast bacilli, and modified acid-fast staining were negative for organisms. Alcian blue staining failed to reveal mucin deposition. Immunohistopathological findings demonstrated CD20+ B-cell infiltrates in the follicles with intermixed CD3-positive cells. Germinal centers were highlighted by BCL6 staining, while BCL2 showed no aberrant expression. Kappa/lambda staining was polytypic. The presence of mixed inflammatory infiltrates, and immunohistochemical findings revealed polyclonality of lymphocytes, polytypic kappa/lambda light chain, BLC6 and BLC2 results suggested reactive lymphoid hyperplasia, and there was no evidence of lymphoma. Based on the clinical, histological findings and immunohistochemical staining, the diagnosis was cutaneous pseudolymphoma (CPL)[1,2].

The patient received several treatment modalities, including intralesional steroid injections (7 times), systemic corticosteroid, cryotherapy (2 times), and surgical removal, but still showed no significant improvement over one year.

Oral isotretinoin was initiated as a monotherapy at a dosage of 10 mg daily. After three months, improvements in the lesion were observed, including decreased size and flattening (Figure 2A). Isotretinoin was discontinued over one year, with a total cumulative dose of 40 mg/kg, until lesions were resolved. Following treatment discontinuation, no recurrence was observed after four months of evaluation (Figure 2B).

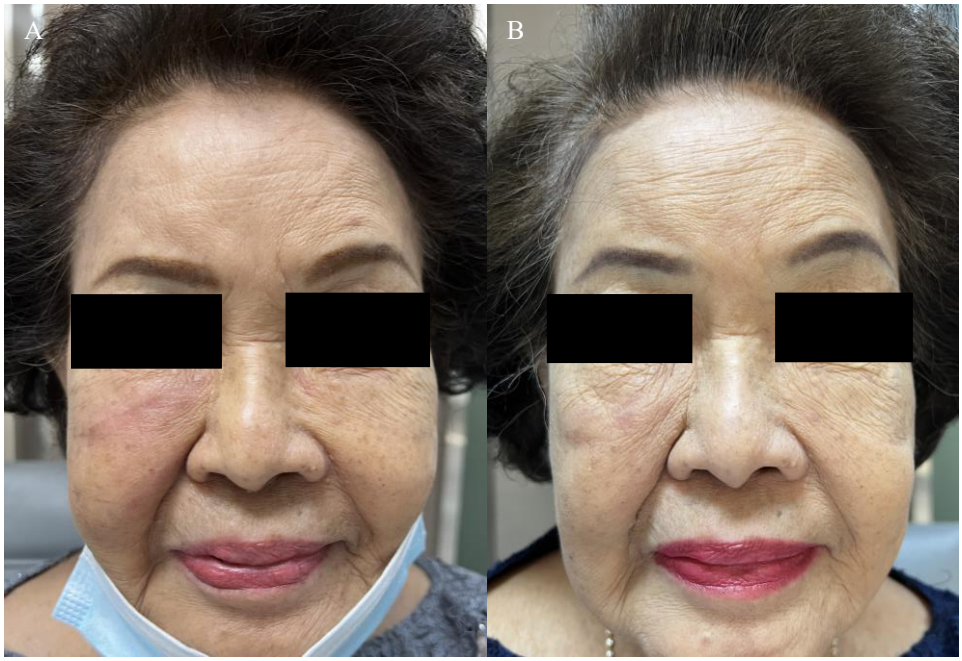

Figure 2 A) At 3 months of oral isotretinoin treatment. **B)** At 4 months after discontinuation of oral isotretinoin

Discussion

Cutaneous pseudolymphoma (CPL) is a benign reactive lymphoproliferative disorder closely resembles cutaneous lymphoma clinically and histologically[1, 2]. Although most of CPL are idiopathic, various factors, including contact dermatitis, infection, and drug, must be excluded[1-3]. In cases where the etiology can be identified, the primary approach is to address and manage the underlying cause. The clinical course of CPL varies from spontaneous resolution to challenging to treat[3]. Several treatment modalities have been reported, but the individual response is unpredictable[4].

Well-documented causes of CPL are infections, photosensitivity, foreign agents, and drugs such as beta-blockers, antiarrhythmics, and angiotensin-converting enzyme inhibitors[2]. In this case, the potential trigger could be drug-induced CPL. The cutaneous presentation of drug-induced CPL may consist of solitary or a few plaques that cannot be distinguished from other causes or idiopathic CPL. Establishing a temporal relationship between the drug and cutaneous onset is difficult due to the cumulative effect of drugs on immune regulation[5]. However, given the significant underlying condition that requires medications, it was not possible to discontinue the medication. Regular follow-up to reassess the nature of the lesion may aid in determining its etiology. The potential treatment, including intralesional steroid injections, systemic corticosteroid, cryotherapy, and surgical excision, have been tried with the recurrence of the lesions in the adjacent and original sites.

Case reports of the successful treatment with etretinate, as monotherapy and adjunctive therapy, have been documented in several small case series, and it has also appeared to be effective even in cases of cutaneous T-cell lymphoma (CTCL)[6-9]. From the literature review, response rates have shown considerable variation, ranging from 40% to 100%, with a median response duration ranging from 3 to 13 months for CTCL[10] and clearance observed by

11 months for CPL[6]. The precise mechanism of action for oral retinoids in CPL and CTCL remains unclear; however, it is hypothesized that their immunomodulatory actions contribute to the resolution of the lymphoproliferative process[10].

The response observed in this report was encouraging. The resolution of the lesions was observed as early as the third month after initiating oral isotretinoin treatment. These findings were consistent with the previous report that treated with etretinate[6], suggesting oral isotretinoin's effectiveness in treating CPL. The patient also reported significantly reduced discomfort and improved quality of life. Regarding safety, the patient did not experience any serious adverse effects, and blood test results were normal. Only mild eyes, lips, and skin dryness were reported during isotretinoin treatment.

Since most of the available data on the use of oral retinoids were case reports and small series, there is a pressing need for further research to establish the efficacy, tolerability, and long-term outcome of isotretinoin in CPL management.

In conclusion, this case highlights the challenges in managing refractory CPL with the limited evidence-based data regarding available treatment options. Our case report contributes to the growing body of evidence suggesting the effectiveness of isotretinoin as a treatment option for refractory CPL. The improvement in the lesion supports the potential role of isotretinoin in managing refractory cases. However, larger studies are needed to validate these findings and elucidate the optimal dosage, duration, and long-term outcomes of isotretinoin therapy in CPL.

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