

Idiopathic Cutaneous Pseudolymphoma Treated Successfully with Hydroxychloroquine: A Case Report and Literature Review

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Cutaneous pseudolymphoma (CPL) is a reactive polyclonal lymphoproliferative disorder that develops in association with known and unknown aetiologies (1). It can be localized or disseminated in the skin, and be transient or persistent for years. Although topical application and local injection of corticosteroids are the most common treatments for idiopathic CPL, there has been no established treatment for cases that are intractable to these treatments. We report here a case of idiopathic CPL disseminated on the face, which was refractory to local application of corticosteroids but responded well to hydroxychloroquine (HCQ).

CASE REPORT

A 58-year-old Japanese man presented with a 5-year history of erythema with induration over the face, mainly on the forehead and bilateral cheeks. He was treated with topical nadifloxacin, dexamethasone propionate, local injection of triamcinolone acetonide, and oral minocycline, but with no effect. No aetiology was detected for the lesions. A biopsy specimen from an erythematous plaque on the left cheek revealed distinct lymphoid follicle structures in the entire dermis without infiltration of atypical lymphocytes (Fig. 1a). Follicle-forming lymphocytes were positive for CD20 (Fig. 1b), but negative for Bcl-2 in the follicular centre. Tingible body macrophage were also observed in the follicles. No kappa or lambda light chain restriction was detected. Immunoglobulin heavy chain gene rearrangement was not found in the skin sample. The clinical and histological findings were consistent with a diagnosis of idiopathic B-cell-CPL. Oral prednisolone (30 mg) resolved the indurative erythema on the face, which flared when the dose was tapered to 12.5 mg (Fig. 1c). The addition of etretinate to prednisolone was attempted, but, due to paronychia, was not tolerated. The patient was started on

treatment with HCQ as a single daily dose of 200 mg and 400 mg, alternately. Four months later, the lesion was markedly reduced, and the prednisolone dose was gradually reduced to 3 mg without recurrence (Fig. 1d). He had no recurrence for 6 months on HCQ without any side-effects related to HCQ.

DISCUSSION

CPL is classified into B-cell or T-cell types, as well as a mixture type. It is induced by drugs, tattooing, tick

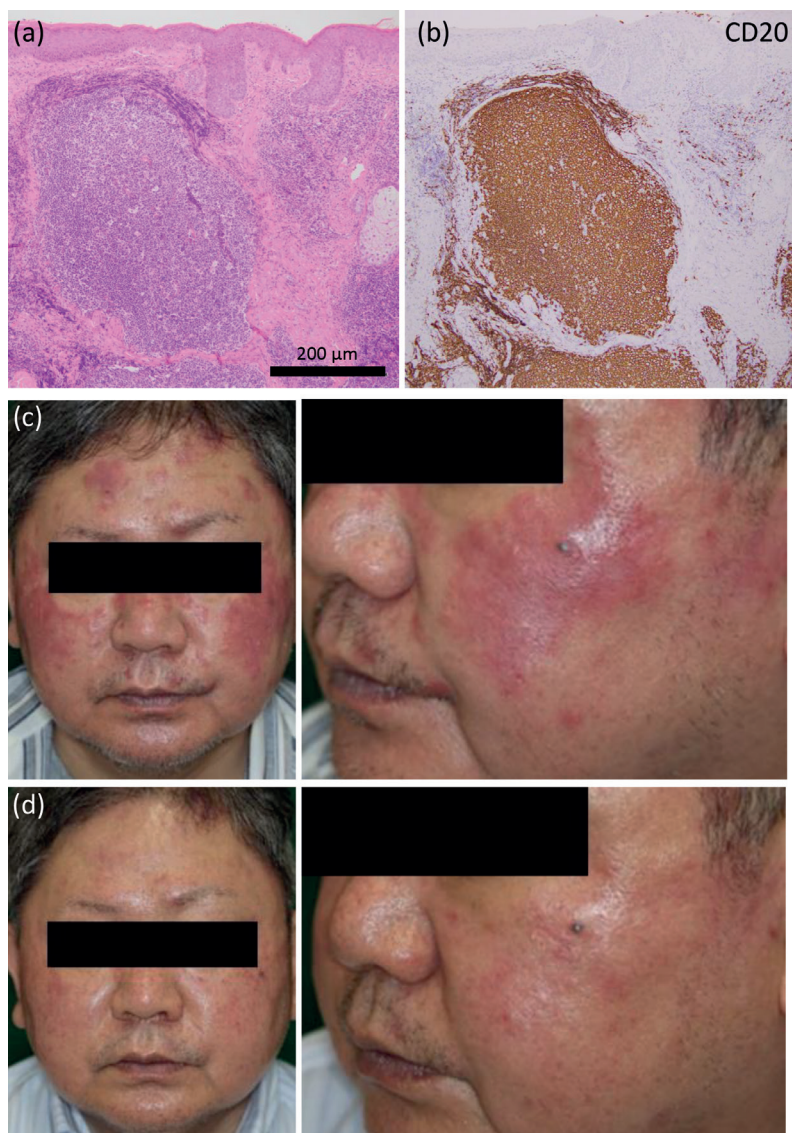


Fig. 1. (a) Histopathological examination of a biopsy specimen demonstrating lymphoid follicle structures in the entire dermis without atypia of lymphocytes (haematoxylin and eosin staining). (b) Follicle-forming lymphocytes are positive for CD20. (c) The patient shows erythema with induration on the forehead and bilateral cheeks when on oral prednisolone (12.5 mg), before the administration of hydroxychloroquine (HCQ). (d) The lesion is markedly reduced 4 months after starting treatment with HCQ as a single daily dose of 200 mg and 400 mg, alternately.

Table I. Literature review of cases of cutaneous pseudolymphoma (CPL) treated effectively with hydroxychloroquine (HCQ)

References	Clinical forms	Causes	Lesions	Dose of HCQ	Efficacy	Concurrent treatments
Stoll DM (1983) (2)	CPL	Unknown	Face, trunk, extremities	200 mg/day for a month, followed by 400 mg/day	Effective (disappearance of the lesions)	None
Dragonetti E et al. (2004) (3)	B-cell-CPL	Idiopathic	Neck (single lesion)	400 mg/day	Effective (disease-free and no recurrence for 1 year)	None
Moulounguet I et al. (2012) (4)	B-cell-CPL	Tick bites	Forehead, bilateral cheeks, mandible, neck	400 mg/day	Effective (gradual regression and no recurrence for 6 months)	None
Ye CH et al. (2021) (5)	B-cell/T-cell-CPL	Unknown	Face, scalp	200 mg/day	Effective (gradual regression and no recurrence for 10 months)	Methyl PSL (4 mg), clobetasol propionate cream
Current case	B-cell-CPL	Idiopathic	Forehead, bilateral cheeks	200 mg and 400 mg/day alternately	Effective (with a dose reduction of systemic corticosteroid)	PSL (3–12.5 mg), topical tacrolimus, betamethasone butyrate cream

PSL: prednisolone; HCQ: hydroxychloroquine.

bites, or trauma; however, most cases are idiopathic. In addition to the topical application and local injection of corticosteroids, various treatments, including systemic corticosteroids, surgical excision, ultraviolet light therapy, and radiotherapy, have been reported for CPL (1). In the current case, a high dose of systemic corticosteroid was required to control the CPL lesion on the face; however, HCQ added to corticosteroid markedly reduced the lesion, leading to a reduction in corticosteroid dose.

The efficacy of HCQ for the treatment of CPL has been reported in only a few cases (Table I) (2–5). In addition to the current case of idiopathic B-cell-CPL, Dragonetti et al. (3) described the beneficial effect of 400 mg HCQ for idiopathic B-cell-CPL. The effectiveness of 400 mg HCQ was also reported for B-cell-CPL caused by tick bites (4), suggesting that HCQ is effective for the idiopathic CPL as well as secondary cases. HCQ was effective in the presence and absence of concurrent treatments, such as topical and systemic corticosteroids (2–5). However, not all cases of pseudolymphoma respond to HCQ. Joshi TP et al. (6) recently reported a patient who was treated successfully with dupilumab.

The mechanism of action of HCQ on CPL is associated with an increase in the intracellular pH of antigen-presenting cells, thereby decreasing their antigen-presenting ability and exerting immunomodulatory properties (7). It has been reported that plasmacytoid dendritic cells are involved in the pathogenesis of pseudolymphoma (8), and we speculate that HCQ exerts its therapeutic effect by inhibiting their activation. In addition, HCQ inhibits TNF- α and IL-1 production, which may be also possible mechanism contributing regression of CPL lesions (9).

In this case, multiple lesions of idiopathic CPL on the face responded well to HCQ along with dose reduction of concurrent prednisolone. This result suggests that HCQ may be a treatment option for a certain population

of patients with multiple CPL lesions that are difficult to surgically resect or are refractory to conservative local therapies.

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REFERENCES

- Miguel D, Peckruhn M, Elsner P. Treatment of cutaneous pseudolymphoma: a systematic review. *Acta Derm Venereol* 2018; 98: 310–317.
- Stoll DM. Treatment of cutaneous pseudolymphoma with hydroxychloroquine. *J Am Acad Dermatol* 1983; 8: 696–699.
- Dragonetti E, Cianchini G, Mastrangelo L, Mellone P, Baldi A. Cutaneous pseudolymphoma: a case report. *In Vivo* 2004; 18: 549–551.
- Moulounguet I, Ghnassia M, Molina T, Fraïtag S. Miliarial-type perifollicular B-cell pseudolymphoma (lymphocytoma cutis): a misleading eruption in two women. *J Cutan Pathol* 2012; 39: 1016–1021.
- Ye CH, Chen CJ, Chang KC, Wu YH, Chen ML, Chiu TM. Cutaneous pseudolymphoma with Langerhans cell hyperplasia – a rare case with clinical presentation mimicking malignancy and potential diagnostic pitfall. *Am J Dermatopathol* 2021; 43: e280–e284.
- Joshi TP, Duvic M, Torres-Cabala CA, Tschen J. Treatment with dupilumab for refractory cutaneous B-cell pseudolymphoma. *JAMA Dermatol* 2022; 158: 697–699.
- Sardana K, Sinha S, Sachdeva S. Hydroxychloroquine in dermatology and beyond: recent update. *Indian Dermatol Online J* 2020; 11: 453–464.
- Kutzner H, Kerl H, Pfaltz MC, Kempf W. CD123-positive plasmacytoid dendritic cells in primary cutaneous marginal zone B-cell lymphoma: diagnostic and pathogenetic implications. *Am J Surg Pathol* 2009; 33: 1307–1313.
- Müller-Calleja N, Manukyan D, Canisius A, Strand D, Lackner KJ. Hydroxychloroquine inhibits proinflammatory signalling pathways by targeting endosomal NADPH oxidase. *Ann Rheum Dis* 2017; 76: 891–897.