Trends in Immunotherapy (2017) Volume 1 Issue 3, pp.121–123.
doi: 10.24294/ti.v1.i3.125

CASE REPORT

Hydroxychloroquine enhanced urticarial reaction in a patient

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ABSTRACT

Discoid lupus erythematosus (DLE) is an autoimmune disorder that usually occurs on sun exposed areas. We describe a case of a 31-year-old man with reddish-purple, atrophic plaques on the nose and the bilateral cheeks. Histopathologic and direct immuneofluorescent studies confirmed DLE diagnosis. The skin lesion had been previously resistant to topical clobetasol propionate 0.05% and tacrolimus 0.1% since 2012, and were treated with oral hydroxychloroquine (HCQ) (300 mg daily). Two weeks later, the diarrhea happened frequently as side effects. Then, the decreased HCQ 200 mg daily improved the diarrhea moderately. The patient who had a history of urticaria also complained about urticarial reaction much more frequently 3 weeks later more than the start, which was improved very much by epinastine (10 mg daily) administration. Cutaneous lupus erythematsus disease area and severity index (CLASI) activity score improved from 11 to 5 for 3 months.

***Keywords**: hydroxychloroquine; side effect; urticarial reaction; diarrhea; discoid lupus erythematosus*

ARTICLE INFO
Received: November 13, 2017
Accepted: November 20, 2017
Available online: November 24, 2017

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CITATION
Hirakawa Y, Okuno A, Kimura D, *et al*. Hydroxychloroquine enhanced urticarial reaction in a patient. Trends Immunother 2017; 1(3):121–123. doi: 10.24294/ti.v1.i3.125.

Introduction

Hydroxychloroquine (HCQ) was first used for its anti-malaria activity, but has subsequently been used as an anti-rheumatic drug, and is frequently prescribed for cutaneous and systemic lupus erythematosus (LE) patients[1]. HCQ has a long history of administration to such patients in the world. However, since it is too old drug, there are few scientific evidences and a very small number of mechanisms. A few years ago, we reported a multi-center, double-blind, randomized, parallel-group trial of HCQ in Japanese[2]. Since almost 2 years passed, this case report focused side effects especially urticaria.

Case report

A 31-year-old Japanese man was referred to us in May 2017 with clinical lesions with reddish-purple, atrophic plaques on the nose and the bilateral cheeks. The patient had a history of chronic urticarial and no family history. The patient also had no systemic symptoms of arthralgia, arthropathy, myalgia, fatigue, Raynaud's phenomenon or gastrointestinal complaints. The skin lesions were present on the nose (Figure 1A), and the bilateral cheeks (Figure 1B) with presented as reddish-purple, atrophic plaques. Laboratory data showed a normal complete blood count with differential analysis. Serum electrolytes, blood urea nitrogen, creatinine, and liver function tests were within normal limits.

However, anti-single stranded DNA (ssDNA) revealed a high level of >343 AU/mL, but indirect immunofluorescent antinuclear antibody (ANA) titer was <40 times. Biopsies of the lesions were performed, and were subsequently donated for hematoxylin and eosin (H&E) staining and direct immunofluorescence (DIF) methods.

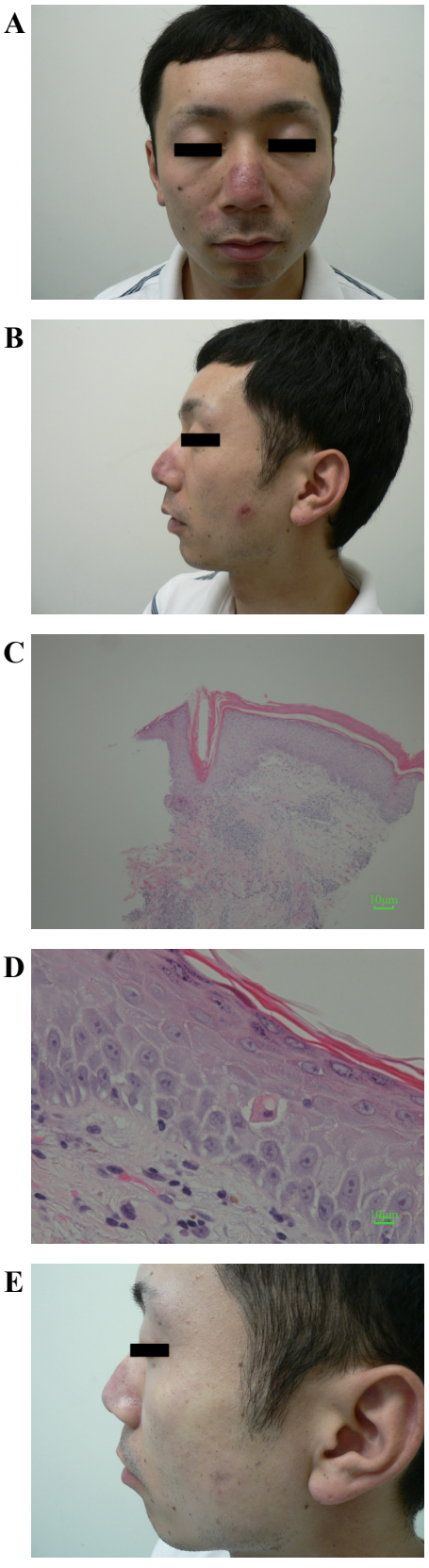

Figure 1. Clinical and histopathological features results. (**A**) Skin lesion on the nose and (**B**) on the left cheek. (**C**, **D**) Histopathological features (H&E). (**E**) Skin lesions after treatment on the left cheek.

Histopathology of a skin biopsy revealed epidermal changes included hyperkeratosis with follicular plugging, basal cell vacuolization, and interface dermatitis (Figure 1C) and atypical epidermal keratinocytes (Figure 1D). DIF studies were negative.

We diagnosed discoid lupus erythematosus (DLE) with unresponsive to topical clobetasol propionate 0.05% and tacrolimus 0.1% for several years. Oral HCQ (300 mg daily) started. However, 2 weeks later as diarrhea appeared frequently as an side effect, decreased HCQ (200 mg daily) provided and the side effect moderately improved. The patient who had a history of chronic urticaria also complained about urticarial reaction more frequently 3 weeks later, which was improved with epinastine (10 mg daily) combination. The primary end point was judged by the change in the cutaneous lupus erythematosus disease area and severity index (CLASI) activity score following of HCQ treatment[2–4]. The CLASI activity score improved from 11 to 5 for 3 months. After 4 months, the patient was improved with a remarkable decrease in the size of the bilateral cheeks (Figure 1E) and the changes of the pigmentation of the nose.

Discussion

The diverse immune modulatory effects of HCQ make it widely used in treatment of autoimmune diseases. In this case, HCQ enhanced urticarial reaction frequently, which represents an unusual, although probably under recognized complication.

The withdrawal of HCQ treatments due to adverse cutaneous eruptions was previously reported in approximately 3% of patients[5]. The Japanese report on side effect of HCQ from September 7, 2015 to April 30, 2017 was 165 cases of 122 patients (unpublished data from the company). The majority of the data comprise skin disorder and gastrointestinal disorders such as diarrhea, and there are 2 cases of urticaria. It is sometimes difficult to establish whether early cutaneous eruptions that appear after the initiation of oral HCQ are due to HCQ or a flare of disease[6].

The patient remarkably responded to anti-histamines, we have hypothesized that the level of urticarial reaction threshold might decrease as HCQ suppresses the activity of the innate immune system. It is hard to answer to this hypothesis. However, our recent experiments of mast cells suggested that mast cells are biphasic-reaction in the skin lesions[7,8]. The HCQ effects on mast cell biology will be expected for better treatment of CLE[9].

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