

Successful Treatment of Psoriasis-like Lesions in HIV Infected Patients in Uganda with Chloroquine

Hasan M. Shihab^{1,4}, Jordan J. Feld^{1,5}, Fred Lutwama¹, Theresa Piloya¹ and Robert Colebunders^{*,1,2,3}

¹Infectious Diseases Institute, Faculty of Medicine, Makerere University, Kampala, Uganda

²Institute of Tropical Medicine, Antwerp, Belgium

³University of Antwerp, Antwerp, Belgium

⁴Division of General Internal Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

⁵Department of Medicine, University Health Network, Toronto Western Hospital, University of Toronto, Toronto, Canada

Abstract: The effect of chloroquine in the treatment of psoriasis remains controversial. Treatment of psoriasis in HIV infection is not well described. Chloroquine has been shown to have direct effects on both the Human Immunodeficiency Virus (HIV) and on the psoriasis disease process. The effect of chloroquine in HIV infected patients with psoriasis has not been well studied.

We report on the effect of chloroquine on psoriasis-like lesions in three HIV infected patients who were not on antiretroviral therapy. Three consecutive HIV positive patients with CD4 cell count below 200cells/mm³ had unequivocal improvement of their psoriasis-like lesions after 2 weeks of a daily dose of 150mg of chloroquine.

In conclusion, chloroquine may be useful in the treatment of psoriasis-like lesions in patients with HIV infection particularly in resource poor settings. Ideally, a controlled clinical trial will be needed to confirm this.

Keywords: Psoriasis, Chloroquine, HIV.

INTRODUCTION

Psoriasis is a common chronic inflammatory skin disease with a world-wide distribution affecting up to 3% of the world's population [1]. A recent report summarized the prevalence estimates of psoriasis world-wide ranging from 0.6% to 4.8% [2]. From a population based study in the United States that involved patient self report of a physician diagnosis of psoriasis, the prevalence was 2.5% in Caucasians and 1.3% in African Americans [3]. More recently, a cross sectional study using the National Health and Nutrition Examination Survey 2003-2004 that involved both patient self report of psoriasis and independent review of standardized clinical photographs by two dermatologists determined the prevalence of diagnosed psoriasis to be 3.15% [2]. Population-based studies from Africa are lacking, however psoriasis was observed to represent less than 1% of all skin diseases in West African countries such as Nigeria, Mali and Senegal and up to 3.2% reported in certain studies done in East Africa [4]. In Human Immunodeficiency Virus (HIV) disease, the prevalence of psoriasis is about the same as in the general population at about 1-2% [5, 6]. A study from Zambia showed a 3.9% prevalence of psoriasis among clinic patients, all but one of whom were HIV positive [7].

HIV infection has however, long been recognized to worsen the course of both psoriasis and psoriatic arthritis [5, 8-13]. Improvement of psoriasis in the setting of HIV infection has been reported with effective antiretroviral therapy [14, 15] however, specific treatment remains elusive. Psoriasis treatment with or without concurrent HIV infection is not curative but only suppressive. Antimalarial drugs are generally considered to be contraindicated in psoriasis [16] but, there still is no strong evidence to refute or support the role of antimalarials in the exacerbation of psoriasis [17].

We report three consecutive HIV positive patients with extensive psoriasis-like lesions (Table 1) who were successfully treated with a once daily dose of 150mg of chloroquine phosphate at the Infectious Diseases Institute Clinic, Mulago Hospital in Kampala, Uganda.

Patient 1 (Fig. 1, Parts A and B)

A 35-year-old woman presented with a history of a recurrent itchy skin rash for 5 years with little improvement on topical steroid ointments, coal tar and antihistamines. On examination, she had severely hyperkeratotic and pitting nails (onycholysis) and silvery, scaly skin lesions discoid in shape ('leopard skin') all over her trunk, lower limbs and face. She did not have any joint swellings or dactylitis. Her skin condition led her to suspect HIV infection and she had her index HIV test at the clinic. The CD4 count at presentation was 104cells/mm³. In view of the clinical presentation of the skin lesions, a presumptive diagnosis of psoriasis was made. Topical steroids, tar and antihistamine

*Address correspondence to this author at the Institute of Tropical Medicine and University of Antwerp, Nationalestraat 155, B-2000, Antwerp, Belgium; Tel: + 3232476426; Fax: 3232476432; E-mail: bcoleb@itg.be

therapy were tried again but had no effect. Highly Active Antiretroviral Therapy (HAART) was not provided free of cost by the Hospital at the time and she was not able to afford it on her own. A decision was made to prescribe daily chloroquine in order to relieve her. A marked improvement was noted after 2 weeks of the daily chloroquine therapy alone. When HAART was available free of cost, she was started on Zidovudine, Stavudine and Nevirapine. The daily chloroquine therapy was gradually weaned off and she did not have a recurrence of the psoriatic rash. She was continued on HAART and her current CD4 count is 463cells/mm³.



Fig. (1). Part A: 35 year old female with psoriatic- like lesions before chloroquine treatment.



Fig. (1). Part B: 35 year old female after 2 weeks of chloroquine treatment.

Patient 2 (Fig. 2, Parts A and B)

A 56-year-old man presented with a 2 month history of itchy hypopigmented lesions on the trunk and upper limbs more marked on the extensor surfaces. His CD4 count at initial presentation to the clinic was 47cells/mm³. He had previously been treated with topical and oral antifungal drugs, but the rash persisted. A once daily dose of chloroquine was then introduced. Improvement was noted within 2 weeks of therapy. When HAART was offered free to the patients, he was also started on Zidovudine, Stavudine and Nevirapine. The daily chloroquine therapy was gradually weaned off. He did not have a recurrence of the psoriatic-like- rash thereafter.



Fig. (2). Part A: 56 year old male with psoriatic- like lesions before chloroquine treatment.



Fig. (2). Part B: 56 year old male after 2 weeks of chloroquine treatment.

Patient 3

A 33-year-old woman presented with a month history of a generalized pruritic and desquamating rash. She also had multiple painful joint swellings. Her CD4 count at initial presentation to the clinic was 176 cells/mm³. She was started on Non-Steroidal Anti-inflammatory Drugs and topical hydrocortisone therapy, but there was no improvement. Three months later, she developed onycholysis, the desquamating rash started weeping and became more

Table 1. Patient Characteristics

Patient	Age (Years)	Sex	CD4 Count (Cells/mm ³)#	Symptoms and Signs	Treatment Period*
Patient 1	35	Female	104	Recurrent itchy rash for 5 years. Discoid silvery scaly skin lesions. Severely hyperkeratotic and pitting nails.	2 weeks
Patient 2	56	Male	47	Itchy hypopigmented lesions for 2 months. Non scaly lesions more marked on the extensor surfaces.	2 weeks
Patient 3	33	Female	176	Generalized pruritic desquamating rash. Associated with multiple painful joint swellings.	3 weeks

#- CD4 count at first encounter with patient before treatment was started.

*-Treatment period with chloroquine before symptomatic relief was noted.

extensively distributed on her body. A presumptive diagnosis of psoriasis with psoriatic arthritis was made. She was started on daily chloroquine and marked clinical improvement was noted within 3 weeks of therapy. We were unable to follow this patient through as she stopped attending the clinic when the rash and the joint swellings subsided.

DISCUSSION

We report three HIV positive patients whose psoriasis-like lesions disappeared with chloroquine treatment. A similar effect of antimalarial treatment on psoriasis and psoriatic arthritis has been observed by others [18-22] but exacerbations of psoriasis during antimalarial treatment have also been described [23-27]. These contradictory effects of antimalarials in the treatment of psoriasis were first reported in the literature about chloroquine in 1966 [28]. Four decades later, the data about the benefit of chloroquine and other antimalarials on psoriasis are still inconclusive [17].

Chloroquine and hydroxychloroquine are both 4-aminoquinolones and have been used since the 1940s as antimalarials and since the early 1950s in the treatment of rheumatoid arthritis, systemic lupus erythematosus and other autoimmune diseases. In addition, both hydroxychloroquine and chloroquine have been shown to have anti-HIV effects *in vitro* and *in vivo*, although chloroquine has been studied more extensively. The inhibition of HIV replication by hydroxychloroquine has been observed in lymphocytes and monocytes from peripheral blood [29]. Although different mechanisms have been proposed for the anti-HIV effect of chloroquine when used alone [30-32] or in combination with protease inhibitors [33], they all suggest a direct inhibitory effect on viral replication. One preliminary study from Uganda has also shown a potential effect of chloroquine in decreasing the rate of HIV vertical transmission [34]. Chloroquine or hydroxychloroquine in combination with anti-retroviral drugs have been shown to reduce the HIV viral load in HIV-1 infected patients [35-38].

The suggestion that antimalarials may be inadvisable in the management of psoriasis [16] is supported by *in vitro* studies of hydroxychloroquine and chloroquine.

Hydroxychloroquine may induce hyperproliferation, enhancement and irregular keratinization which cause an initial break in the barrier function of the epidermis [39]. Chloroquine has also been shown to abnormally stimulate the lower lymphocyte transformation in controlled

experiments in patients with and without psoriasis [40]. The molecular mechanism that has been suggested for the role of chloroquine in the psoriasis disease process is blocking of epidermal transglutaminase, an enzyme that is pivotally involved in the terminal differentiation of keratinocytes [41]. Despite these *in vitro* experiments showing the potential deleterious effect of chloroquine in psoriasis, the patients we report all improved unequivocally. It is difficult to ascertain whether this improvement seen was caused by the anti-HIV effect of chloroquine or a direct effect of the drug on the psoriasis disease process.

Patient 1 and Patient 3 had the classical clinical features of psoriasis. Given their age and female gender, systemic lupus erythematosus would be another diagnostic consideration. A case report from Iran reported improvement of skin lesions in clinically ascertained discoid lupus erythematosus with chloroquine [42]. Anti-nuclear antibody (ANA) serological tests were not done in our patients. The lesions of Patient 2 were also suggestive of a generalized fungal skin infection but they did not respond to antifungal therapy. Chloroquine has also been shown to be effective in the treatment of fungal infections caused by *Histoplasma capsulatum* [43], *Paracoccidioides brasiliensis* [44] and *Cryptococcus neoformans* [45]. This effect is thought to be mediated by reducing the availability of iron for the intracellular pathogen [43, 46, 47]. Enhancement of the activity of mononuclear phagocytes by an iron independent pH-dependent mechanism has also been reported [45]. These actions of chloroquine are attributed to the fact that it is a weak base which raises the endocytic and lysosomal pH of eukaryotic cells [48].

A major limitation of our report is that we could not confirm that our patients had psoriasis. Skin biopsies or skin scrapings to rule out other dermatological conditions such as a fungal dermal infection were not done. The diagnosis of psoriasis has been described as one that can reasonably be made on clinical grounds, although histological examination of a skin biopsy specimen may be helpful [1]. For the diagnosis of psoriasis, no specific test, besides clinical examination has proven useful [49]. This report highlights the challenges of patient care in resource limited settings. It would have been prudent to have the diagnosis made by a dermatologist and further confirmed by histopathology. In Uganda, there is only one consultant dermatologist and the process of having histopathology before treatment is long and complicated. In a situation where the hands of the clinician were tied as to do the best to relieve symptoms of a

patient in the midst of the paucity of HAART, we had to start the patients on chloroquine. Due to the unavailability of free HAART at the time, we were unable to start our patients on definitive HIV treatment, despite all three patients having documented CD4 counts below 200cells/ml.

CONCLUSION

Our report suggests that chloroquine treatment may be beneficial in certain HIV seropositive patients with psoriasis. Although biologic-immune-response modifiers that specifically target key mechanisms of the pathogenesis of psoriasis have been shown to be effective [50-52], the costs of these drugs are prohibitively expensive for use in resource limited settings. Chloroquine on the other hand is cheap, easy to use and is a widely available drug. Based on our findings and those reported in the literature [17], a clinical trial to evaluate the effect of antimalarial therapy on psoriasis would be beneficial.

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