Hydroxychloroquine is ineffective in treatment of alopecia totalis and extensive alopecia areata: A case series of 8 patients

Christoffer V. Nissen, MD, and Hans Christian Wulf, Prof, MD, DSc
Copenhagen, Denmark

Key words: alopecia; alopecia areata; alopecia totalis; hair loss; hydroxychloroquine; therapy; treatment.

INTRODUCTION
In June 2013, the Journal of the American Academy of Dermatology published a report concerning successful treatment of 2 cases of alopecia totalis with hydroxychloroquine.1 This report was encouraging, as treatment of alopecia totalis is challenging and in most cases unsuccessful. The authors explained their results with the wide range of immunomodulatory effects that are attributed to hydroxychloroquine.2 These effects include decreased secretion of proinflammatory cytokines and reduced production of lymphocytes and autoantibodies.3 As a consequence of their results, we investigated hydroxychloroquine treatment for extensive alopecia in a larger cohort.

METHODS
Eight patients (6 women, 2 men) with a mean age of 30.2 years (range, 16–53) were treated with hydroxychloroquine during 2013 and 2014. Six patients suffered from alopecia totalis, whereas 2 patients had extensive alopecia areata that involved more than 40% of the scalp. Mean duration of the disease was 3.9 years (range, 1–8), and all patients had previously tried various treatments such as topical/intralesional corticosteroids, contact immunotherapy, and ultraviolet therapy without effect. No patients were treated with oral steroids.

Before hydroxychloroquine treatment, patients were screened for retinopathy by an ophthalmologist, and a complete blood count was performed. Patients were prescribed 200 mg hydroxychloroquine perorally twice daily as monotherapy, and laboratory tests controlling blood count and liver function were done monthly. Because it takes about 2 months for hydroxychloroquine to work, patients were followed up after 3 to 4 months, and treatment was stopped if there was no sign of regrowth. In the case of regrowth, treatment was prolonged but was discontinued if the condition relapsed. Informed consent was obtained from all patients before treatment start.

RESULTS
All patients were treated with hydroxychloroquine for at least 101 days (mean, 161; range, 101–300 days). At follow-up, 5 patients discontinued treatment because of lack of regrowth; whereas 3 patients continued hydroxychloroquine. Two patients with alopecia totalis showed minimal signs of regrowth, but relapse ensued, and hydroxychloroquine was discontinued after 148 and 197 days of treatment, respectively (Fig 1). Our last patient had extensive alopecia areata and experienced widespread regrowth. However, despite continuing to take the full hydroxychloroquine dose, she suddenly suffered relapse. Thus, we concluded that her regrowth was of spontaneous origin, and hydroxychloroquine was discontinued after 300 days.

Four patients reported intermittent gastrointestinal discomfort as a side effect to hydroxychloroquine, but none discontinued treatment as a result. One patient experienced blurred vision during treatment, but ophthalmologists found no sign of retinopathy, and the patient continued hydroxychloroquine.
DISCUSSION
Extensive alopecia is a condition that often puts the physician in a dilemma. On one hand, patients are desperately seeking an effective treatment. On the other hand, the commonly used treatments rarely prove successful and cause a number of side effects.4 With a lack of randomized, placebo-controlled studies, physicians are often led to engage in treatments that are not evidence based.5 Our study illustrates this problem, as our investigation was not randomized or placebo controlled. Although our study design was not ideal, we still believe that our results are important. As researchers we are obligated to publish negative results to ensure that our colleagues and patients do not engage in time-consuming treatments that are likely to be fruitless. We based this investigation on a case report in which hydroxychloroquine had remarkable effect on treatment-resistant alopecia totalis and wished to investigate this in a similar patient population. Because none of our 8 patients experienced lasting regrowth, we cannot recommend hydroxychloroquine as treatment for extensive alopecia where other treatment modalities have failed. Taking side effects and our discouraging results further into account, it is questionable whether it is feasible to initiate a placebo-controlled trial.

REFERENCES
1. Stephan F, Habre M, Tomb R. Successful treatment of alopecia totalis with hydroxychloroquine: report of 2 cases. J Am Acad Dermatol. 2013;68(6):1048-1049.
2. Ben-Zvi I, Kivity S, Langevitz P, Shoenfeld Y. Hydroxychloroquine: from malaria to autoimmunity. Clin Rev Allergy Immunol. 2012;42(2):145-153.
3. Katz SJ, Russell AS. Re-evaluation of antimalarials in treating rheumatic diseases: re-appreciation and insights into new mechanisms of action. Curr Opin Rheumatol. 2011;23(3):278-281.
4. Delamere FM, Sladden MM, Dobbins HM, Leonardi-Bee J. Interventions for alopecia areata. Cochrane Database Syst Rev. 2008;(2):CD004413.
5. Alkhalfah A, Alsantali A, Wang E, McElwee KJ, Shapiro J. Alopecia areata update: part II. Treatment. J Am Acad Dermatol. 2010;62(2):191-202. quiz 203-194.

Fig 1. Alopecia totalis in a 22-year-old woman. A, Baseline photography before study start. B, Minimal regrowth after 4 months of hydroxychloroquine treatment. Treatment was discontinued shortly after because of relapse.