

Dramatic Response to Chloroquine and Mirtazapine for Recalcitrant Atopic Dermatitis*To the Editor:*

A 15-year-old African American male with atopic dermatitis (AD) since early childhood presented to our clinic with a severe disease flare. He reported seasonal rhinitis but no asthma. There was a strong family history of atopy. He had a known colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) and a history of multiple admissions for intravenous (IV) antibiotics for MRSA superinfections. Therapy at the time of presentation included topical tacrolimus, high-potency topical steroids, sedating antihistamines, mild soap, and heavy moisturizers. Prior therapies included topical pimecrolimus, oral steroids, and intermittent oral cyclosporine at 4 to 5 mg/kg/d for approximately 18 months. Cyclosporine had been modestly effective but had been discontinued secondary to severe hypertension.

Examination revealed an ill-appearing adolescent male in severe pain. Erythroderma with sparing of the palms and soles was present. In addition to erythema and scale, much of the body surface area was lichenified and hyperpigmented. There were multiple areas of crusting and weeping. Skin swabs were obtained for culture and antibiotic sensitivity testing, and the patient was admitted for IV antibiotics, IV steroids, and IV pain control. As with several previous hospital admissions, his condition stabilized over approximately 10 days, with a decrease in skin pain but with unchanged itch and unchanged skin lichenification. He was discharged on topical steroids, phototherapy (ultraviolet A/ultraviolet B combination therapy three times per week), and doxepin 25 mg every night at bedtime (qhs).

In addition, azathioprine at 250 mg per day was instituted at the time of discharge but was stopped after 1 week due to intolerance. Mycophenolate mofetil (MM) at a dose of 2,000 mg twice daily was started at the same time that the azathioprine was stopped. MM was continued at this dose for 3 months, without benefit. In addition, multiple brief courses (14 days) of oral steroids and oral antibiotics were necessary while the patient was on MM.

The course was complicated by two additional inpatient admissions for antibiotics, steroids, and pain control.

At the time of the last admission, MM and doxepin were discontinued. As with all prior admissions, antibiotics were administered on the basis of bacterial culture and sensitivity results, IV steroids were administered, and topical therapy with triamcinolone 0.1% ointment and tacrolimus 0.1% ointment was continued. His condition stabilized, again with decreased skin pain but with unchanged itch and unchanged eruption consisting mainly of lichenification. At discharge, his prior topical regimen was continued, chloroquine 250 mg per day was instituted (along with mirtazapine 15 mg before bed for itch control), and he was referred for allergy testing. Phototherapy was not restarted, and antibiotics were discontinued.

Within 3 weeks of the institution of chloroquine and mirtazapine, and prior to allergy testing, the patient reported a dramatic decrease in pruritus and a marked improvement in his condition. Over the ensuing several months, he has continued to do well with no need for systemic steroids, antibiotics, or inpatient admissions. There has been slow improvement in the degree of lichenification, with areas of normal skin appearing and slowly enlarging.

There are two reports in the European literature of the effectiveness of antimalarials for the treatment of AD. Chloroquine significantly benefited 54 of 62 patients with severe AD in one German report, and hydroxychloroquine was effective in a patient with recalcitrant disease in the second report.^{1,2}

Antimalarials have also shown effects (both in vivo and in vitro) in other atopic diseases, namely, asthma and allergic rhinitis. In a randomized placebo-controlled trial of 17 asthmatics, hydroxychloroquine treatment for 30 weeks led to improvement in all measured variables, including a 50% decrease in immunoglobulin E levels.³ Chloroquine caused a marked decrease in in vitro interferon- γ production following grass pollen stimulation of cultured peripheral-blood mononuclear cells isolated from patients with allergic rhinitis and grass pollen allergy.⁴

There are several reports in the literature regarding the effectiveness of mirtazapine for treating the itch associated with atopic dermatitis.^{5,6} It is impossible to know how much of this young man's improvement was due to the chloroquine and how much was due to the mirtazapine.

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These two medications have relatively benign side effect profiles. Most important, there is no consistent immunosuppression. Reports of notable side effects of chloroquine include rare reports of electrocardiogram changes and heart block, rare reports of myopathy, and a well known though often overestimated risk of retinopathy with chronic use. Consideration should be given to performing serial electrocardiography (although the optimal frequency is unknown) and to performing ophthalmologic examinations either once or twice yearly. Mirtazapine is associated with weight gain in a minority of patients, probably due to increased appetite, and with modest increases in total cholesterol and triglycerides in a minority of patients. Approximately 1 of 1,000 patients will develop reversible neutropenia while on mirtazapine. The most common side effect with mirtazapine is somnolence, which affects about 50% of patients on the medication.

This patient's dramatic response to chloroquine and mirtazapine was remarkable, especially given the severity of his disease and its resistance to multiple aggressive traditional therapies. While it is known that hospital admission can have a beneficial effect on atopic dermatitis, multiple prior admissions had resulted only in a temporary improvement in our patient, without significant alteration in disease course. However, after the institution of chloroquine and mirtazapine at the end of his last admission, his condition improved markedly. Compared with traditional

systemic medications used for severe atopy, chloroquine and mirtazapine have excellent side effect profiles. I suggest that they be considered as therapeutic options in patients with recalcitrant atopic dermatitis.

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