An uncontrolled, open label study of sulfasalazine in severe alopecia areata

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ABSTRACT

Background: Alopecia areata (AA) is an autoimmune disease mediated by T lymphocytes. Many treatments have been used but their results remain disappointing. There is a need to propose new therapeutic alternatives. **Methods:** During a period of 3 years, 26 patients with recalcitrant or severe AA (>40% hair loss) were enrolled in an open-label uncontrolled clinical trial. According to the response to sulfasalazine, patients were grouped into 3 categories: no hair regrowth (<10% terminal hair), partial hair regrowth (10%-90% terminal hair), and complete hair regrowth (90%-100% terminal hair). Efficacy evaluation was performed with clinical examination. **Results:** Twenty-two patients completed the treatment. Overall, 68.2% (15 of 22 patients) responded to therapy: 27.3% (6 of 22 patients) achieved complete hair regrowth, and 40.9% had partial hair regrowth. Seven (31.8%) patients had no hair regrowth. Of the 22 patients with complete and partial remission, 10 (45.5%) suffered a partial or complete relapse. Side effects following treatment were seen in 7 (31.8%) patients. **Conclusion:** Sulfasalazine could be considered as a therapeutic alternative in the treatment of AA, because of its safety profile, cosmetically acceptable efficacy, and good tolerability.

Key Words: Alopecia areata, Sulfasalazine, Treatment

INTRODUCTION

Alopecia areata (AA) is a burden for many patients; and is often resistant, even to multiple extensive therapies.[1] Topical and intra-lesional corticosteroid therapies are frequently tried, but the benefit of such treatment is often questionable or temporary. Systemic corticosteroid treatment may be effective in some cases, but the maintenance dose needed is often high. Some success has been reported with anthralin, but results seem variable. Other therapies which have been tried, with variable success, include minoxidil, cyclosporine,[2] alpha-interferon,[3] acupuncture,[4] and topical immunotherapy.[1] There are a few reports of the treatment of alopecia areata with sulfasalazine in the literature.[5,6]

Sulfasalazine is an anti-inflammatory agent composed of a sulfonamide and a salicylate. It was developed in 1938 for the treatment of rheumatoid arthritis;[7] sulfasalazine is a second-line treatment for arthritis, with efficacy similar to that of gold, d-penicillamine, and methotrexate.[8] Sulfasalazine is also used in the treatment of inflammatory bowel disease and psoriasis.

Sulfasalazine has both immunosuppressive and immunomodulatory effects, including inhibition of inflammatory cell chemotaxis, and cytokine and antibody production. Cyclosporine therapy reduces the number of T cells infiltrating the hair follicle and the perifollicular area.[2] Cyclosporine is a potent inhibitor of interleukin 2 (IL-2), a cytokine that stimulates the proliferation and activation of T lymphocytes.[2] Inhibition of the production of IL-2 may account for the efficacy of cyclosporine in patients with alopecia areata. Like cyclosporine, sulfasalazine has been shown to inhibit the release of IL-2. Another potential

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mechanism of its action includes stimulation or suppression of one or more lymphocyte subsets.[9]

Based on its use in immune-mediated diseases and its immunomodulatory properties, sulfasalazine therapy was initiated in patients with alopecia areata in the present study.

METHODS

During the period of 3 years between May 2004 and May 2007 at our Department of Dermatology, 26 patients (10 men, 16 women) with recalcitrant or severe AA were enrolled in an open-label clinical trial. Approval of the ethics committee of the university was taken. The patients were not on any other topical or systemic therapy during or immediately prior to the study period. Inclusion criteria were as follows: patients with age of 16 years or more, with recalcitrant or severe AA (>40% scalp hair loss), without any positive history of sensitivity to sulfasalazine, with no history of internal diseases (such as liver, gastrointestinal, etc.), and with no history of simultaneous treatments for AA.

Their ages ranged from 16 to 35 years (mean, 25 years). According to the response to sulfasalazine, patients were grouped into 3 categories: no hair regrowth (<10% terminal hair), partial hair regrowth (10%-90% terminal hair), and complete hair regrowth (90%-100% terminal hair). Efficacy evaluation was performed with clinical examination. In all patients, the following laboratory tests were performed at baseline, every 2 weeks for 2 months and then, every 1 month for 4 months during treatment: G6PD test (only at baseline), liver function tests, complete blood cell count, chemistry profile, urinalysis, levels of thyroid hormones, fasting blood sugar, and antinuclear antibody titers (ANA).

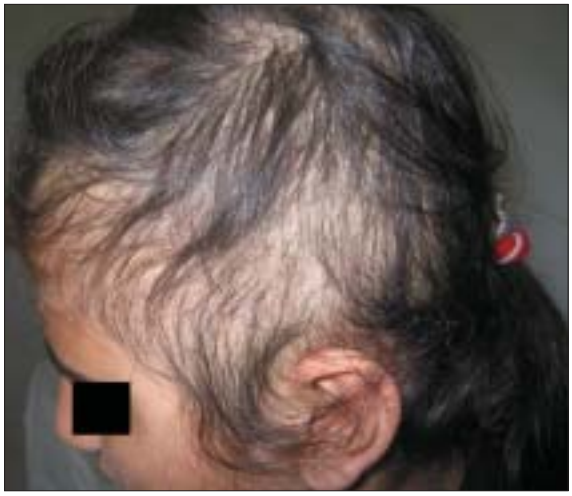

Figure 1A: A young girl with relapsing AA before treatment

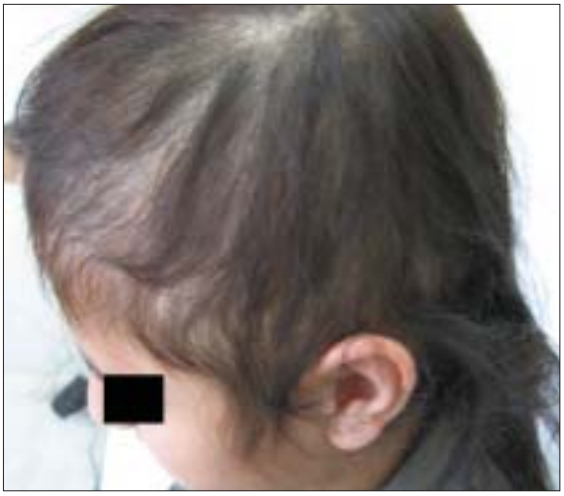

Figure 1B: The same patient (depicted in Figure 1A) after completion of treatment

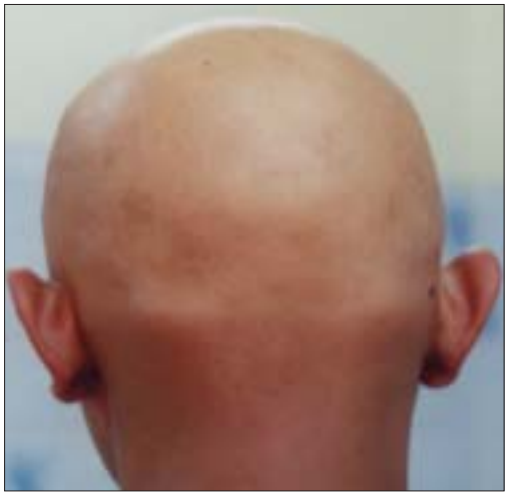

Figure 2A: A male patient with extensive AA before treatment

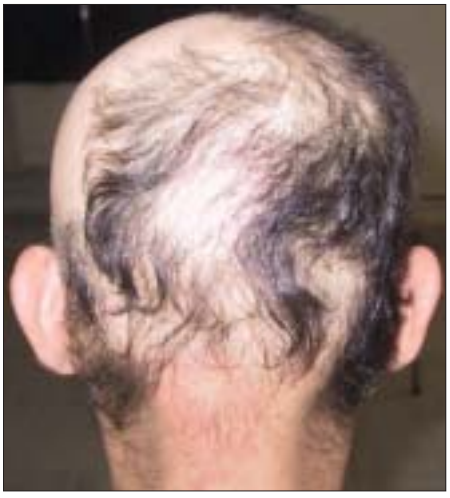

Figure 2B: The same patient (depicted in Figure 2A) after completion of treatment

Sulfasalazine was begun at 500 mg twice daily for 1 month, 1 g twice daily for 1 month, and then 1.5 g twice daily. The treatment was carried out for a further 3 months with the latter dose regimen. If no regrowth was observed even after 6 months of treatment, the patient was considered to be a non-responder and was dropped from the trial.

RESULTS

Twenty-two (8 males, 14 females) out of 26 patients completed the treatment. The disease duration before treatment ranged from 8 months to 10 years. The duration of therapy ranged from 6 to 24 months, including long-term patients with repeated sulfasalazine treatment for maintaining hair regrowth. Overall, 68.2% (15 of 22 patients) responded to therapy: 27.3% (6 of 22 patients) achieved complete hair regrowth (90%-100% terminal hair) [Figures 1A and 1B], and 40.9% (9 of 22 patients) had partial hair regrowth (10%-90% terminal hair) [Figures 2A and 2B]. Of the 9 patients with partial response, 5 patients had 10%-20% regrowth, 2 patients had 30%-40%, 1 patient had 50%, and 1 patient had 60%-70% regrowth. Seven (31.8%) patients had no hair regrowth (<10% terminal hair regrowth). Ten (45.5%) out of 22 patients suffered a complete or partial relapse either on maintenance treatment of follow-up or following termination of therapy. Side effects following treatment were seen in 7 (31.8%) of 22 patients: gastrointestinal distress, rash, laboratory abnormalities, and headache.

DISCUSSION

Treatment of AA with sulfasalazine is generally well tolerated.[11] When adverse effects occur, they usually do so in the first 3 months of treatment;[10] this is in agreement with the results of the present study. The most common reactions include nausea, vomiting, headache, fever, and rash; less common, but more serious, are hematologic abnormalities and hepatotoxicity.[11]

In a recently published study,[6] a 23-year-old had been suffering from alopecia areata for 7 years and had been successfully treated with sulfasalazine for a period of 10 months. Regrowth has been reported to be about 50% of scalp hair and lashes. Unfortunately, all hair and lashes fell out within a few months after stopping the treatment because of adverse effects such as asthenia, dizziness, and headache.

In a study by Ellis *et al.*,[5] sulfasalazine was used successfully in 7 patients with AA. Efficacy (cosmetically acceptable regrowth) and safety profiles were considered satisfactory in these patients. However, there was a relapse of hair loss when the dose of sulfasalazine was reduced. In the present study, there was 45.5% relapse rate in the patients with complete or partial remission, either simultaneously maintenance treatment of follow-up or following termination of therapy. Fortunately, this phenomenon was reversed by increasing the dose again. In the present study, about 27% of the patients achieved complete hair regrowth 6 months after treatment, which is greater than the corresponding figures previously reported in the literature.[5]

Sulfasalazine could be considered as a therapeutic alternative in the treatment of AA, because of its safety profile, cosmetically acceptable efficacy, and good tolerability. However, prospective studies that include a control group are required to confirm these findings.

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