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LARGE DOSES OF GLUCOCORTICOID IN THE TREATMENT OF ALOPECIA AREATA

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Abstract. Severe extensive alopecia areata (totalis) was treated with prednisolone as a single 2 g dose i.v. (22 patients) or 0.5 g daily for 5 days orally (13 patients). Four of the patients responded well, 12 had a poor response and 19 had no response. There was a relapse in some at about 6 months, which could be arrested by a further single i.v. dose, but the risks of this form of therapy are unclear and it cannot be recommended for general use. The clinical response to a single dose of corticosteroid implies, however, that there may be a 'switch' mechanism in certain auto-immune diseases, with an all-or-none response.

Key words: Alopecia areata; Glucocorticoid; Prednisolone; Auto-immune disease

Alopecia areata often responds to systemic corticosteroid therapy (4, 5, 9) but the condition tends to relapse when the dose is reduced and the side-effects from prolonged steroid therapy preclude this treatment for the majority of patients. By contrast a single intradermal injection of corticosteroid into a patch of alopecia can produce prolonged regrowth (8). This suggests that a short exposure to very high doses of systemic glucocorticoids might also produce a prolonged response in the same way that the rejection of organ transplants can be inhibited for several months by a single infusion of a huge dose (1 to 2 g) of prednisolone (1, 6). Such a 'once and for all' stimulus might be superior to continuous therapy, and so we felt this treatment was worth trying in severe alopecia areata.

METHODS

We studied 35 patients with alopecia areata aged 13 to 65 years. The patients were chosen because of the severity and chronicity of their condition. 18 of them had alopecia totalis of several years' duration. The remainder had severe alopecia areata with large bald areas showing no signs of regrowth. Initially we used oral prednisone but following the reports of the use of intravenous prednisolone in the treatment of organ rejection (1, 6), we gave the drug intravenously. Patients who gave a previous history of tuberculosis, diabetes mellitus, peptic ulcer or psychosis were excluded from the trial and the patients had a chest radiograph before the prednisolone infusion.

13 patients were treated with oral prednisone 500 mg daily for 5 days. Four of these patients also applied 0.4% flucinolone acetonide in 80% dimethylsulphoxide topically to the bald areas twice daily. 22 patients were admitted to hospital for a single intravenous infusion of 2 g prednisolone in 200 ml of saline over 2 hours. Seven of these patients had measurements of skin extensibility performed before and after the infusion and the results of this test have been reported separately (2). Each patient was followed for at least 4 months after injection, and the response to treatment was graded as 'good', 'poor' or 'absent'. A good response was defined as a generalized regrowth of scalp hair sufficient to be cosmetically useful, a poor response was defined as a slight or sparse regrowth, or regrowth localized to the eyebrows and eyelashes. An absent response referred to complete lack of regrowth within 4 months of the infusion.

RESULTS

Of the 13 patients receiving oral prednisone, 5 had no response to treatment, 7 had only a poor response, and one had a good response. Topical fluocinolone made no difference to the response in this group. The patient with a good response was a 13-year-old girl who had had alopecia universalis for 10 years. Within 2 months of oral prednisone therapy her hair began to regrow and by 6 months later it had reached a length of about 5 inches. She then developed multiple new patches of alopecia which progressed rapidly. An intravenous infusion of 2 g prednisolone at this stage halted the hair loss and soon afterwards new hair again started to grow. Three months later she again started to lose hair. Because of the possible risks from repeated steroid therapy she was given only a placebo infusion this time and the hair loss continued, to complete baldness. She did retain sparse eyebrows and eyelashes, however, and this is of cosmetic benefit to her.

Of the 22 patients who had intravenous predni-

solone, 14 had no response to treatment, 5 had only a poor response and 3 had a good response, as follows. One was a woman of 44, who developed very extensive and progressive alopecia areata over a period of 6 months, with no sign of regrowth at the time of the prednisolone infusion. Within 2 months she had started to grow hair in all areas, and this has progressed to complete recovery at the present time, 2 years after the infusion. The second patient was a girl of 19 who had had alopecia areata for 5 years. The patches responded well to triamcinolone intra-lesionally, but the occurrence of a new patch every few weeks had necessitated regular out-patient treatment throughout this period. Six weeks after the i.v. prednisolone infusion there was growth of hair which progressed to complete recovery. She has had only one small patch of alopecia areata in the subsequent 18 months. The third patient to respond well was a man of 19 with chronic widespread diffuse alopecia areata which had previously responded to intra-lesional triamcinolone.

A feature of the treatment with huge doses of prednisone was the rapid and frequent regrowth of eyebrows and lashes which greatly improved the appearance even in the poor responders, in whom a wig was still necessary. This growth was more persistent than the scalp hair but not, alas, in all patients. One man with alopecia totalis grew new scalp hair sufficient to demonstrate that in the prolonged course of the disorder he had developed some male pattern baldness and this new growth, together with new eyebrows and lashes, was a great improvement. After about 6 months, however, he began to lose his scalp hair and soon after this he developed a 'cold', sneezed, and shed his lashes!

No side-effects were noted, with the exception of one patient who developed striae of the thighs within 3 days of the infusion.

DISCUSSION

We found that a very large dose of oral prednisone or intravenous prednisolone produced some regrowth of hair in 16 of 35 patients with chronic alopecia areata, and in 4 of the 16 there was a generalized growth of new hair which was prolonged. Alopecia areata often recovers spontaneously, but it is unlikely that the new growth we observed was coincidental, since the patients were chosen because of the chronicity of their alopecia. The first patient with a good response had had alopecia universalis for 10 years, and the time-course of the appearance of new hair growth in her and in the other 3 patients with a good response suggested this was directly related to the therapy. In some of the patients in whom the treatment was unsuccessful or only partially successful, subsequent intradermal injection of triamcinolone acetonide produced a tuft of hair. It is likely, therefore, that despite the huge dose of prednisolone used, an adequate tissue concentration in the scalp was not reached.

Alopecia areata may belong to the deformed family of autoimmune diseases (3, 5, 7, 10, 11). The present findings may, therefore, have important implications for the mode of action of corticosteroids in these diseases. It is generally considered that treatment of an autoimmune disease should maintain constant immunosuppression until remission occurs, and this suggests a continuing pathological process. The observation that a single high dose of corticosteroid given locally (8) or systemically can produce a prolonged remission of alopecia areata implies, to the contrary, that the pathological process has features of an 'all or none' response, with a 'switch' mechanism. Consequently it would be worth investigating whether or not other autoimmune diseases would display a similar prolonged response to single large doses of glucocorticoids.

Minor episodes of alopecia areata have a high rate of spontaneous recovery and as a rule no treatment is required. The problem is the development of extensive and progressive alopecia areata for which there is no adequate treatment. The present finding that only a small proportion of such patients had a good therapeutic response obviously precludes high dose corticosteroid therapy for routine use. It may be, however, that the success rate could be increased if the disease were treated in the early active phase, or with larger doses repeated periodically. We had proposed to do this when our observation of early formation of striae led us to measure skin extensibility. We found that the intravenous prednisolone therapy produced a surprisingly rapid increase in skin extensibility which was maximum at about 3 days (2). The mechanism of this effect is unknown and we felt that repeated therapy was not advisable in case the elasticity of connective tissue might become similarly affected throughout the body. No complications such as aortic dilatation were noted in our patients, and chest radiographs one week after treatment showed a normal aortic outline, but

it would nevertheless seem wise to keep patients at rest for about a week after such an infusion.

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