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Non Responder of Alopecia Totalis to Diphencyprone Responding to Addition of Betamethasone Pulse

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Abstract

Introduction: Contact sensitizers remain the mainstay of treatment of alopecia areata totalis (AT). Systemic steroids in different regimes have been tried in AT with variable success. Many authors consider that addition of systemic steroids to the contact sensitizing protocol may mitigate the effect of the latter. However, there is scarcity of studies evaluating the response to combination therapy of systemic steroids with contact sensitizers. *Case Summary*: We report the case of a 19-year-old boy with AT of 5 years duration. Diphenylcyclopropenone (DPCP) was applied to right half of the scalp as per the standard protocol. With no response even after six months of this treatment, DPCP application was stopped and oral betamethasone pulse at the dose of 0.1 mg /kg weekly was started. Within 4 weeks of Betamethasone pulse, new hair growth was visible only on the right half of the scalp. DPCP was re-instituted on the same side of the scalp along with continuation of systemic steroids. Left half of the scalp served as control. At 8 weeks, DPCP treated side showed excellent growth while the left side responded poorly. *Conclusion:* This singular split scalp treatment outcome suggests that the response of contact sensitizers like DPCP is not suppressed by systemic corticosteroids; rather seems to have a synergistic effect in the treatment of AT.

Keywords: Alopecia Totalis; Areata; Diphenylcyclopropenone; Oral Minipulse; Steroid.

Introduction

Alopecia areata (AA) is relapsing disease with a variable course. Its management is guarded with a highly variable response to DPCP.

Systemic corticosteroids have been used in severe forms of alopecia areata [1]. To minimize the side effects of daily systemic corticosteroids, oral mini-pulse (OMP) therapy with various steroids has been used with success in alopecia areata [2,3,4]. Topical immunotherapy has been variably advocated in extensive alopecia areata, efficacy of which varies from 5 to 85%. Non responders to DPCP have also been reported. The reason for non response to DPCP has not been studied extensively. There aren't any reports of combination of DPCP and systemic steroids in AA.

Hereby, we report a case of alopecia totalis (AT) a non responder to DPCP monotherapy who responded to addition of betamethasone pulse; contradicting to the assumption that steroids negate the effect of contact sensitizers.

Case Report

A nineteen year old Asian boy had total baldness on the scalp since five years. On examination, he had complete alopecia over the scalp with presence of few terminal hairs and his body hair was normal. Skin over the scalp showed no evidence of atrophy or scarring (Figure 1). The patient did not receive any treatment in the past. A clinical diagnosis of AT was made and patient was started with topical immunotherapy in the form of DPCP.

The patient was sensitized with DPCP 2% on the occipital bald area of 4cm. A mild to moderate irritant reaction as expected was noted after 48 hours. After 2 weeks of sensitization, a single coat of 0.001% DPCP was applied to the right half of the scalp using cotton tipped applicator in view of conducting a split scalp placebo control comparative study. Application was repeated weekly with gradual increase in the DPCP concentration (0.001%, 0.01%, 0.05%, 0.1%) according to the patient's response; the aim being to maintain erythema and pruritus for 48 hrs. The

patient developed mild erythema at concentration of 0.1%; therefore this concentration of DPCP was maintained for the next 6 months. However, there was no response in terms of hair growth (on the right side of the scalp) (Figure 2). Therefore, DPCP was discontinued and patient was shifted to oral minipulse (OMP) steroids in the form of oral minipulse betamethasone 0.1 mg /kg/week in two divided doses, on two consecutive days. Within four weeks of betamethasone pulse therapy, new hair growth was noted on the DPCP treated side (Figure 3). Having noticed such a dramatic response in a short period of time, DPCP was reintroduced in order to evaluate the synergistic effect of DPCP and oral steroids. In this way, the right half the scalp received DPCP while left half served as control along with continuation of oral betamethasone. Within 8 weeks of treatment, right side of the scalp (DPCP+ OMP) showed significant regrowth as compared to the left side (DPCP only) which showed poor response (Figure 4).

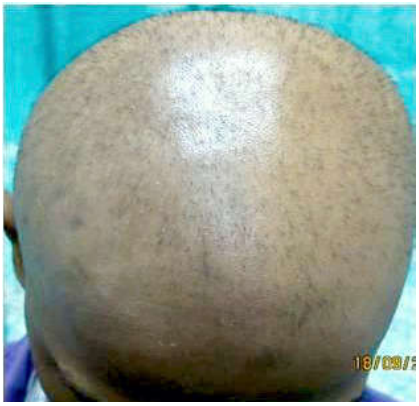

Fig. 1: Patient of alopecia totalis with presence of few terminal hairs and no evidence of atrophy or scarring

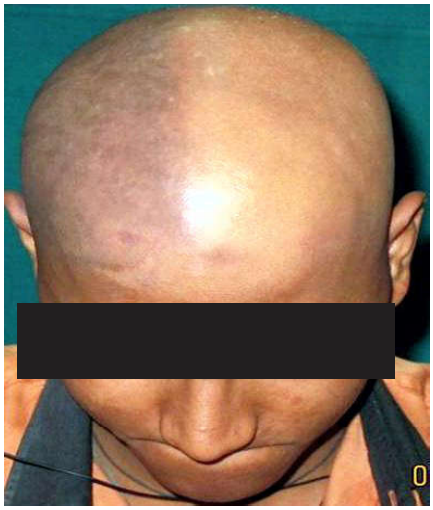

Fig. 2: No response in terms of hair growth noted on the DPCP treated right side of the scalp at the end of 6 months. Only mild erythema of DPCP seen

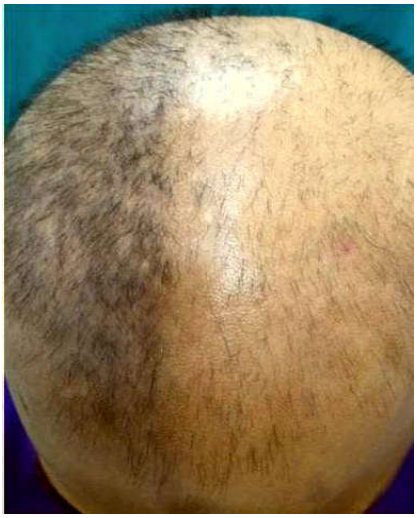

Fig. 3: New hair growth noted on the DPCP treated side within four weeks of betamethasone pulse therapy

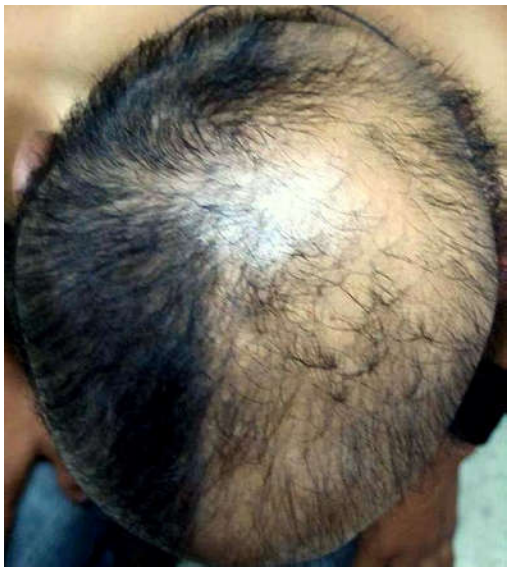

Fig. 4: Right side of the scalp (DPCP+ OMP) showing significant regrowth as compared to the left side (DPCP only) at the end of 8 weeks of treatment.

Discussion

Pathogenesis of alopecia areata is multifactorial. The recent theory on pathogenesis of alopecia areata as per Paus et al [5] focuses on a breach of immune privilege as main cause of AA, the anagen hair bulb represents an immune privileged site characterized by the absence of major histocompatibility complex (MHC) class I expression and the presence of immunosuppressive cytokines such as TGF-b (transforming growth factor b).There is induction of CD8+ and CD4+ T cells targeted to newly exposed follicular antigens, which are normally sequestered from immune recognition. This immune

dysregulation could induce hair loss in AA through multiple mechanisms including: Direct cytotoxicity by CD8+ T cells, natural killer cells (NK), or NK-T-cell activity; Antibody dependent cell-mediated cytotoxicity (ADCC) etc. Immunotherapy reverses these changes. Skin treated with topical sensitizers shows a decrease in peribulbar CD4D CD8 ratio. There is a shift in the position of T lymphocytes from the perifollicular to the interfollicular area.

Systemic steroids for AA have been used in various forms. Sharma [3] administered oral prednisolone as pulses in doses of 300 mg at 4 weeks intervals. Cosmetically acceptable hair growth was seen in 58.3% patients at 4 months of treatment and relapse was seen in 2 patients after stoppage of therapy at 3 and 9 months respectively. In another study, Sharma et al [4] have reported complete hair growth in 26.6% of patients and a good response in 36.6% of patients treated with oral mini-pulse with dexamethasone.

Topical immunotherapy has been used for the treatment of severe alopecia areata. Immune modulating effect of topical immunotherapy is unclear. Response rate with diphencyprone ranges from 5% to 85% [6-11] which has led to considerable confusion surrounding its therapeutic value and efficacy. Several prognostic criteria have been identified: presence of nail changes, personal history of atopy, duration and extent of AA, age at onset of disease. In contrast to these parameters, histopathological features that may exert an influence on the therapeutic outcome of topical immunotherapy in AA have not been much explored. Paul et al [12] have examined histopathological changes in scalp biopsy obtained from 85 patients with severe AA before initiation of Diphencyprone treatment and concluded that non responder to topical sensitizers tend to have rather pronounced inflammatory reaction with dense perifollicular lymphocytic infiltrate.

A similar study showed that the combination of corticosteroids and contact sensitizer (anthralin) showed good response in treatment resistant, extensive alopecia areata. Out of eight patients with alopecia universalis/alopecia totalis, two attained cosmetic response as early as three months, two at six months and one showing partial response; thus concluding that the combination therapy was synergistic, safe and effective [13].

This study showed synergistic response with anthralin as a contact sensitizer; whereas in our study, DPCP was used. This explains the augmented effect of corticosteroids with topical sensitizers where corticosteroids may help in reducing the pronounced inflammation around the bulb leading to a more favourable response to contact sensitizers.

This split scalp study similarly proves the synergistic effect of corticosteroids with contact sensitizers in treatment of alopecia totalis.

Conclusion

The efficacy of DPCP in the treatment of AT is poor. This split scalp study proves that the addition of systemic steroids augments the effect of DPCP.

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