Cryotherapy as an alternative therapy for the treatment of recalcitrant alopecia areata

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Background: The cold-induced inflammation of cryotherapy may alter the immunologic processes and structural components of the hair follicles responsible for AA. The aim of this study was to study the efficacy of cryotherapy in alopecia areata, and totalis.

Method: Forty-four patients with recalcitrant scalp alopecia areata or totalis were treated with cryotherapy. The cryo-system chosen was a closed contact CO_2 system with metallic probes. The patients were evaluated for 4-8 weeks for hair growth. Satisfactory hair growth after 8 weeks was an indication for performing cryotherapy for the remaining untreated areas.

Result: Varying degrees of hair growth were detected in 52.50% of the patients four weeks and in 65.90 % eight weeks after treatment. About 38.64% of the patients showed more than 50% hair regrowth 8 weeks after therapy.

Conclusion: Cryotherapy is effective for about two-thirds of the patients with alopecia areata, many of whom are unresponsive to conventional therapies.

Keywords: alopecia areata, alopecia totalis, cryotherapy, treatment

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INTRODUCTION

Alopecia areata is a challenging problem in dermatology. Neither the efficacy of the available therapies nor the course and the prognosis of the disease is predictable. Alopecia areata is known to be an organ-specific autoimmune disease [1]. The association of AA with other autoimmune disorders such as vitiligo, diabetes mellitus, thyroid diseases [2-7], the massive T cell infiltrations around hair follicles known as swamp of bees [8], the presence of antibodies against parts of the hair follicle and hair shaft [9], and therapeutic response to immunosuppressive agents [10] all indicate the involvement of the immune system in the pathogenesis of alopecia areata. Most available therapies are directed toward correcting or modulating the immune response. Cryotherapy is a mechanical intervention introduced for the treatment of AA.

Although cryotherapy has been reported for the treatment of alopecia areata [11,12], it is not popular in this field. In previous reports, the authors conducted a research on cases with limited involvement [11] or in combination with other modalities [12]. In this report, we attempted to study the efficacy of cryotherapy alone for the treatment of recalcitrant cases of alopecia areata including ophiasis, and alopecia totalis.

PATIENTS AND METHODS

Through a cross-sectional, non- randomized and non-blinded study, 59 recalcitrant AA patients were recruited to be treated with cryotherapy. Of these 59 patients, 15 patients did not complete the follow-up course and were excluded. In those with bilateral involvement, the right side was frozen in order to compare with the left side, which remained intact as control.

The cryo system chosen was a CO2 closed contact cryo gun with a round and flat metallic probe

which was 2 cm in diameter. After mild traction, the round probe was applied over the hairless area and the gun was triggered. Development of a 1mm frozen rim around the probe indicated the termination of freezing. The mean time for freezing was 10-15 seconds with a full CO_2 capsule. The development of a skin colored edematous wheal within 30 minutes after cryotherapy was another sign for sufficient cryotherapy. The patients could develop bulla and crust formation within the next 24 hours after cryotherapy which could be managed by repeated irrigation with normal saline and diluted povidone iodine solution. The patients were followed up 4 and 8 weeks later. Hair growth over 75% was considered as excellent, 50-75% as good, 25-50% as moderate, and less than 25% as poor. These percentages were obtained through hair counts in one square centimeter of the treated and non-affected normal hairy scalp or by counting the hair follicle orifices with or without hair.

RESULTS

Of these 59 patients, 37 patients or 62.7% were male and 22 patients were female. The mean age of the patients was 18.7 years. Fifty-one patients had alopecia areata, 12 with extensive involvement more than 50% hair loss. Six patients had alopecia totalis and the last 2 had alopecia universalis.

No Excellent response was detected 4 weeks after cryotherapy. Two patients showed excellent response 8 weeks after cryotherapy. Some of the patients with good to poor results after 4 weeks continued to improve further and upgraded to good and excellent responses after 8 weeks (Figure 1,2). The data of all responses are summarized in tables 1 and 2.

After 8 weeks, different degrees of response were observed in 29 out of 44 patients (65.90%) and 38.64 % had over 50% hair regrowth.

Eight patients developed partial leukotrichia, 14 patients had some degrees of post -inflammatory hypopigmentation, and another 2 developed post-inflammatory hyperpigmentation. All these complications resolved six months after follow-up. All the patients suffered from local pain in the beginning. Thirty-six patients had a history of bullae, erosion, and crust formation. All patients with good to excellent responses (17 cases) were among those who developed bullae and erosion. The erosion and crust resolved within a week after

Table 1. The response rate after 4 weeks.

Response	No. of the patients	Response rate
Excellent	0	0%
Good	9	20.45%
Moderate	12	27.27%
Poor	6	13.64%
No response	17	38.64%

Table 2. The response rate after 8 weeks.

Response	No. of the patients	Response rate
Excellent	2	4.55%
Good	15	34.09%
Moderate	8	18.18%
Poor	4	9.09%
No response	15	34.09%

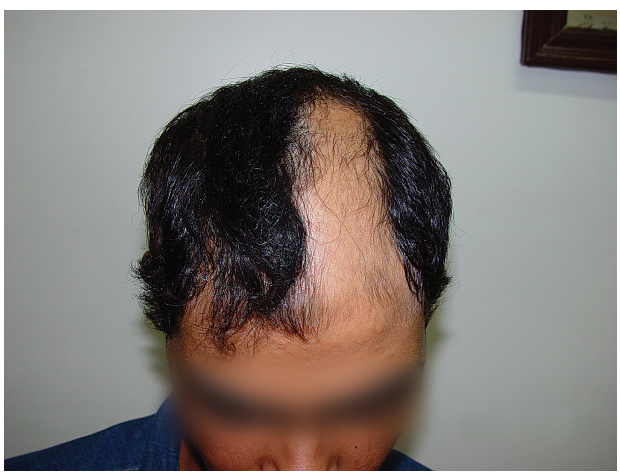

Figure 1. Ophiasis before cryotherapy.

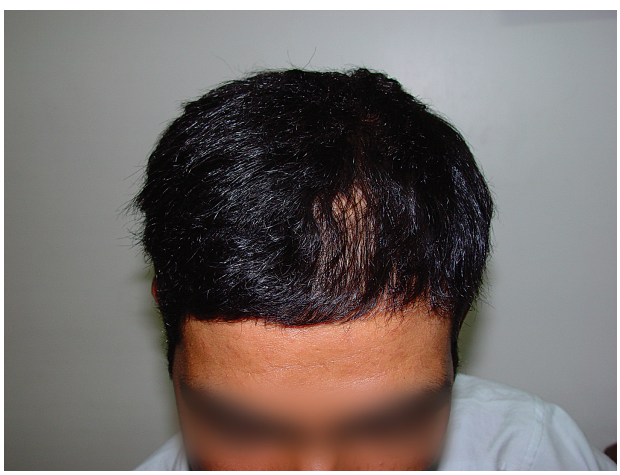

Figure 2. Ophiasis immediately after cryotherapy.

cryotherapy with no scar.

Thirteen patients had a history of repeated intralesional injections with no response. Nine among those with no response to repeated intralesional steroid responded well to cryotherapy, two with good and seven with moderate response.

DISCUSSION

Many of the available therapeutic modalities for alopecia areata are immunosuppressive agents such as corticosteroids and cyclosporine; some are contact sensitizers or irritants such as anthralene. Minoxidil is reported to have stimulatory effects on the follicular epithelium [13,14], and increase local blood flow [15]. It is also believed that minoxidil may also induce some immunologic changes by decreasing the follicular lymphocytes, perifollicular langerhans cells, activated T cells, and monocytes [14,15]. The mechanism of action for contact sensitizers and irritants are based on the production of inflammation. One common feature for all these topical modalities is to increase the local blood flow and circulation. Another possible mechanism is alteration of the immunological profile of the hair follicles.

Cryotherapy leads to local edema, inflammation, and blister formation; hence, like other sensitizers and irritants, it increases the local blood flow. The increase in local blood flow cannot be the sole mechanism, because the inflammation and edema subside within a week, while the hair starts to grow 1-2 months later. The cellular components of hair follicles are epithelial, melanocytes, T cells, and Langerhans cells [16]. All these cellular structures are altered in AA [10,16-19]. The hair follicle components involved in the pathogenesis of AA are antigenic structures, the cellular immune system including T cells and langerhans cells, and hair follicle melanocytes. Cryotherapy may damage one or all of these components as its mechanism for hair regrowth. The hair follicles in active AA are in the telogen state with little T cell infiltration. So, damage to T cells which are surrounding the hair follicles in the anagen phase is less likely to have a role. The langerhans cells are the normal component of hair follicle cells [16]. The langerhans cells are more increased in progressive AA [20]. This may indicate that intrinsic hair follicle antigens have a role in the pathogenesis of AA. The langerhans cells are also increased during sensitization with a sensitizer as diphencyprone [21]. The increase in langerhans cells is predictable in later situation, because the langerhans cells may react and proliferate during the process of antigen presentation. The damage of tissue langerhans cells may alter the process of antigen presentation, and may temporarily halt the process of antigen presentation and prevent harmful immunologic reactions and subsequent hair regrowth.

As the white hairs are not usually involved in AA, it can be suggested that the melanocytes may have an important role in AA [1]. Cryotherapy may damage or destruct the melanocytes and prevent their role in the initiation of AA. Cryotherapy can also damage keratinocytes and particularly the antigenic components, which are targeted by antibodies [8,22,23]. It can be postulated that cryotherapy may damage or denature the antigenic structures of the hair follicles and help hair regrowth as another possible mechanism. One or a combination of all these mechanisms may be the cause of hair regrowth.

Lie and co-workers reported hair growth over 90% in 97.2% of the patients. The response rate among our patients was lower. After 8 weeks, different degrees of response to cryotherapy were noted in 29 out of 44 patients (65.90%) and 38.64 % had over 50% hair regrowth.

This difference may be due to different patient selection methods. We did our study on more complicated and more extensive cases including those with ophiasis, alopecia totalis, and universalis while Lie and co-workers did their study on the cases with less than 25% scalp involvement. It is well known that patients with limited areas of involvement may respond better to therapy. Many of our patients, who responded well, were among those who did not respond to topical and intralesional steroids (9 out of 13 cases or 69.23%). Many of the patients who do not respond to steroids may respond better to cryotherapy. We also faced patients who did not respond to cryotherapy, but had satisfactory hair growth following intralesional steroid therapy. This may explain that although AA seems to be one entity clinically, it may have several subtypes with different pathogenesis. Cryotherapy can be considered as an alternative method particularly for those who do not respond to topical or intralesional steroids.

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