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REVIEW ARTICLE

Advances in the management of alopecia areata

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ABSTRACT

Spontaneous remission occurs in up to 80% of patients with limited patchy alopecia areata (AA) within 1 year. Therefore, not all patients of AA simplex/multiplex need extensive treatments, and "wait and see" is one of the choices for some patients. However, once the hair loss show progressive course, it is really difficult to manage well and may be recalcitrant to any treatment in some cases. Hair loss symptom is not life-threatening but severely decreases quality of life. There have been two widely known guidelines for AA from the British Association of Dermatologists and the National Alopecia Areata Foundation (USA). These guidelines have been substantial and provide clues for dermatologists but needed to be updated. Recently, the Japanese Dermatological Association also published a guideline for the management of AA. This guideline suggests treatments followed by recommendations and evidence levels. Several new treatments are added such as corticosteroid pulse therapy and antihistamine drugs in addition to Japanese historical therapies. Although the highly recommended therapies are still contact immunotherapy and local injection of corticosteroid, it may result in improvement of AA by use of appropriate treatments decided by age, hair loss type, disease course and desire of the AA patient.

Key words: alopecia areata, contact immunotherapy, guideline, intralesional corticosteroid, recommendation.

INTRODUCTION

Alopecia areata (AA) is one of the most difficult skin diseases to manage well. The pathogenesis of AA is still not fully understood and clinical phenotype and disease course is variable. Recently, the pathomechanism of AA has been thought to be a tissue-specific autoimmune disease and it has been speculated that the autoantigen is a melanogenesis-related protein, such as tyrosinase.[1–3] Therefore, immunosuppressive treatments such as corticosteroid, ultraviolet (UV) irradiation and cyclosporine A have been tried on AA patients but the responses are not definite.[4] Especially, AA totalis and AA universalis often show high resistance against any treatment. Therefore, two major guidelines have been made by the British Association of Dermatologists and the National Alopecia Areata Foundation in order to lead the dermatologists who see AA patients.[5,6] The Japanese Dermatological Association (JDA) has also published an AA guideline in 2010.[7] This guideline includes several unique therapies that were historically established in Japan. In addition, this guideline clearly suggests the treatment plan by flowchart (Fig. 1). In this guideline, the principle of treatment is different between patients 16 years old and over (Fig. 1a) and 15 years old and under (Fig. 1b). Basically, the patients 15 years old and under contraindicate systemic corticosteroids and UV therapy. Next, this algorithm separates the recommended therapies into two groups by the duration of hair loss. Of course, this algorithm is not absolute but just a recommendation for non-specialists of hair loss disease.

Before starting the treatments, appropriate investigation should be demonstrated for the reliable diagnosis of AA, followed by suitable treatments by using the algorithm of the AA guideline.[7]

PHYSICAL EXAMINATION

In order to make the diagnosis of hair loss disease, the following points are important to ask the patients: duration of hair loss; location of hair loss; volume of hair loss; family history; and past history including anemia, collagen diseases, thyroid disease, sleep disorder, psychological diseases and atopic dermatitis, drugs, irritation and itching of hair loss lesions, jobs and medicine. Patients often ignore their nail changes that are actually a critical feature of AA. Nail deformity can be observed in the chronic phase of AA. Hair loss lesions are sometimes seen in a beard, an eyebrow and extremities with patchy hair loss of the scalp. Some patients also suffer from vitiligo.[8] The suspected trigger of hair loss may occur 1–3 months before the beginnings of AA (e.g. viral infection, general fatigue, lack of sleep) but the causes of many cases of hair loss are uncertain.[9]

INVESTIGATION

Although it is not necessary to investigate for the diagnosis of most cases of AA, some cases are difficult diagnose and need to be distinguished from other hair loss disease, such as alopecia induced by syphilis, thyroid disease, trichotillomania, collagen diseases,

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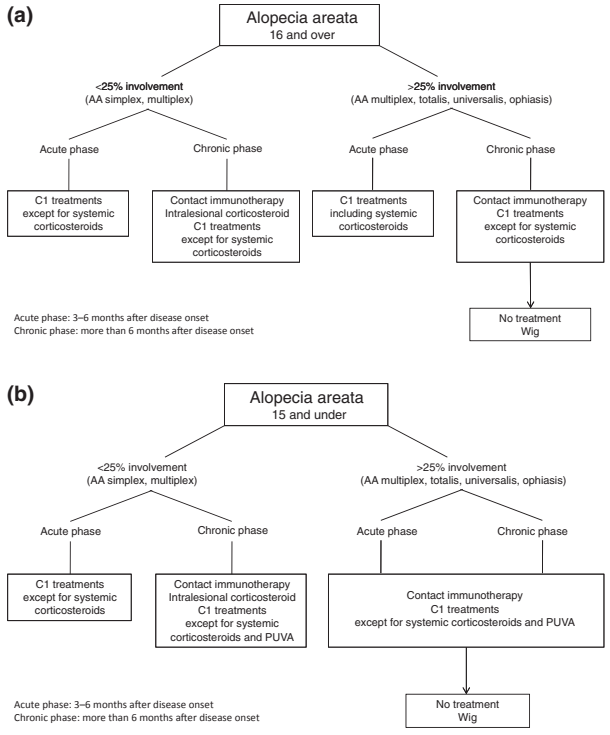

Figure 1. (a) Treatment plan for alopecia areata (AA) for patients 16 years old and over. (b) Treatment plan for alopecia areata for patients 15 years old and under. PUVA, psoralen and ultraviolet A therapy.

infection, iron deficiency and zinc deficiency. The investigation includes dermoscopy,[10] blood examination and skin biopsy.

DERMOSCOPY

Dermoscopy is easy and useful to observe hair loss disease including AA, androgenetic alopecia, cicatricial alopecia and trichotillomania.[10,11] Emersion gel is difficult to apply on the scalp lesion because of hair. Therefore, dry dermoscopy (so called trichoscopy) should be selected that has the blocking filter against light reflection from the skin surface. Characteristic trichoscopic features of AA are black dots, tapering hairs (exclamation mark hairs), broken hairs, yellow dots and short vellus hairs.[12] Black dots, yellow dots and short vellus hairs correlate with the severity of disease, and black dots, tapering hairs, broken hairs and short vellus hairs correlate with disease activity. For diagnosis, yellow dots and short vellus hairs are the most sensitive markers, and black dots, tapering hairs and broken hairs are the most specific markers.[12] Black dots and yellow dots are also seen in trichotillomania and androgenetic alopecia (AGA), respectively. However, exclamation mark hair is not observed in trichotillomania and only seen in 32% of AA cases.

BLOOD EXAMINATION

Extensive blood examination is unnecessary for most AA patients. However, the symptom of hair loss can occur possibly because of collagen disease, thyroid disease, iron deficiency anemia, zinc deficiency and syphilis.[5] Therefore, the following items can be studied: antinuclear antibody; anti-deoxyribonucleic acid antibody; free T3; free T4; thyroid stimulating hormone; antithyroid peroxidase antibody; anti-microsomal antibody; serum iron; serum zinc; and serological tests for syphilis, *Treponema pallidum*, latex agglutination, and fluorescent treponemal antibody absorption. If oral corticosteroids will be used for the treatment of AA, hepatitis B surface antigen must be examined.

SKIN BIOPSY

In many cases of AA it is unnecessary to perform skin biopsy in order to make a diagnosis. However, some cases are difficult to distinguish between acute and diffuse type alopecia of the female scalp (ADTAFS) and telogen effluvium, and skin biopsy largely helps us to decide the diagnosis.[13] In addition, skin biopsy may give us the critical information of disease activity that implies the response of treatments. In chronic lesions, lymphocytes are sparsely infiltrated in and around hair follicles, and these cases often show resistance against immunosuppressive therapies. Therefore, pathological assessments are important in deciding proper treatment. Namely, skin biopsy can be used for the diagnosis of AA and to suggest which treatment would be best.

Recently, the usefulness of a transverse section in histopathological studies of AA has become known.[14] In comparison to vertical sections, transverse sections easily show multiple hair follicles in a single section and include every part of the hair follicles, although several sections are needed to study the whole structure of hair follicles.

TREATMENT

Many cases of single, patchy type AA need no special treatments because of spontaneous resolution. However, multiple type AA, alopecia totalis (AT), alopecia universalis (AU) and alopecia ophiasis are often difficult to treat over a short duration of time and require some additional or modified therapies. Recently, the JDA published a Japanese guideline for AA management that includes treatments with strength of recommendation (A–E) and quality of evidence (I–VI) (Tables 1 and 2).[7] In addition, treatment options are offered according to a patient's age and extent of the disease (Fig. 1). For patients 15 years old and under, with less than 25% scalp involvement (S1) within 6 months of disease duration, topical and oral therapies in C1 are suggested to apply except for systemic corticosteroids, psoralen and UV-A therapy (PUVA) and minoxidil. For other patients 15 years old and under, contact immunotherapy and C1 are suggested to apply except for systemic corticosteroids, PUVA therapies and minoxidil. For patients 16 years old and over, with less than 25% scalp involvement and within 6 months of disease duration, topical and oral therapies in C1 are suggested to apply except for systemic corticosteroids and PUVA. For patients 16 years old and over, with less than 25% scalp involvement and more than 6 months of disease duration, intralesional corticosteroid, topical immunotherapy and C1 are suggested but not systemic corticosteroids and PUVA. For patients 16 years old and over, 25% scalp involvement and

Table 1. Criteria for levels of evidence and grades of recommendation

Levels of evidence	
I	Systematic review or meta-analysis
II	One or more randomized controlled trials
III	Controlled study without randomization
IV	Analytical epidemiological study (cohort study or case–control study)
V	Descriptive study (case report or case accumulation study)
VI	Expert committee reports or opinions from specialist individual
Grades of recommendation	
A	Strongly recommended to perform (there should be at least one level I or II evidence that indicates effectiveness)
B	Recommended to perform (there should be at least one level II evidence of low quality, level III of good quality or level IV of extremely good quality that indicates effectiveness)
C1	Can be considered for use, but there is insufficient evidence (level III–IV evidence of low quality, plural level V of good quality or level IV approved by the committee)
C2	Not recommended for use because there is no evidence (there is no evidence that indicates effectiveness or there is evidence that indicates no effects)
D	Recommended to avoid (there is good evidence that indicates no effect or harmful effects)

Table 2. List of alopecia areata treatments with recommendations

B	Contact immunotherapy
B	Intralesional corticosteroid
C1	Oral corticosteroid
C1	High dose pulse corticosteroid therapy
C1	Antihistamine drug
C1	Cepharanthine
C1	Mono-ammonium glycyrrhizinate
C1	Topical corticosteroid
C1	Carpronium chloride hydrate
C1	Minoxidil
C1	Cryotherapy
C1	Linear polarized infrared irradiation
C1	Psoralen and ultraviolet A therapy
C1	Wig
C2	Cyclosporin
C2	Chinese herbal drug
C2	Tranquilizer
C2	Anthralin
C2	Stellate ganglion block
C2	Hypnotherapy
D	Acupuncture and moxibustion
D	Targeted therapy

within 6 months of disease duration, pulse corticosteroid, oral corticosteroid and C1 are suggested. For patients 16 years old and over, more than 25% scalp involvement and longer than 6 months of disease duration, contact immunotherapy and C1 are recommended. Wigs can also be used.

CONTACT IMMUNOTHERAPY

Contact immunotherapy is one of the most effective treatments for AA. All three guidelines (US, British and Japanese) recommend this immunotherapy as the first-line treatment for AA.[5,6] In the therapy, three topical sensitizers have been used such as dinitrochlorobenzene (DNCB), squaric acid dibutylester (SADBE) and diphencyprone (DPCP). Topical immunotherapy has been applied on dermatoses including not only AA but also viral warts and cutaneous tumor since the 1960s. In 1974, Daman *et al.*[15] first reported the use of DNCB to induce hair growth in two patients with AA. This chemical was first found to be a potent contact allergen in 1912.[16] However, DNCB was reported to be mutagenic in the Ames assay[17] and genotoxic by sister chromatid, although there is no evidence of carcinogenicity in patients treated with DNCB. Therefore, DPCP and/or SADBE were only used in this therapy. SADBE is a strong sensitizer and is used in industry as a stabilizer and anti-fog agent in photographic emulsions. However, SADBE itself is not present in the natural environment and is not known to cross-react with other chemicals.[18] Although it is difficult to maintain its stable condition and potency in acetone dilutions because of its tendency to undergo hydrolysis, SADBE is very popular for contact immunotherapy in Japan. To prevent hydrolysis, molecular sieves are recommended in bottle of SADBE regardless of solvent.[19] DPCP is often used for contact immunotherapy in the USA and Europe compared to Japan. DPCP is made by bromination of dibenzylketone to form a precursor, a,a-dibromodibenzylketone, which is then cyclized with base to generate DPCP. a,a-Dibromodibenzylketone is a mutagenic substance and there is the possibility of it contaminating in DPCP. In addition, UV radiation and heat cause degradation to diphenylacetylene and carbon monoxide. Therefore, DPCP should be kept in brown UV-opaque bottles.

METHOD OF APPLICATION

On the initial day, sensitization may be demonstrated better on an alopecic lesion of the scalp than the upper arm in order to avoid flare-up reactions during treatment.[20] In addition, a strong sensitization reaction often induces pigmentation and induration for a long time on the arm after the sensitization. A cotton-wool swab or a paintbrush can be used as the applicator of SADBE/DPCP. A swab or a brush saturated with 1.0–2.0% SADBE/DPCP in acetone is applied to an area of at least 10 cm^2. An erythematous response may occur at around 10 days after sensitization which means successful sensitization. Only 1–2% of patients fail to sensitize by SADBE/DPCP.[21] Patients should endure the itchiness if possible but can apply corticosteroids to avoiding severe skin reactions. A second application may be performed with 1×10^{-4} SADBE/DPCP 3 weeks after the sensitization. Of course, physicians can decide the concentration of SADBE/DPCP by patch testing with several dilutions of the sensitizer on the patient's arm. However, pigmentation or induration will continue on the test area for several months. The scalp should be protected from light, with a scarf or wig, for

48 h after each application. The application is repeated once to three times per week to induce a mild contact eczema, with the concentration adjusted according to response. Once hair growth is observed on the hair loss lesion, the application should be continued even on the regrowth area. If there is no clinical improvement in the hair loss lesion, other treatments may be considered. If AA totalis or AA universalis patients are suffering from hyperpigmentation by contact eczema from the sensitizer, these patients will show poor responsiveness to contact immunotherapy. Histopathologically, the skin specimens show lichenoid or vacuolar interface dermatitis with necrotic keratinocytes and dermal melanophages, consistent with pigmented contact dermatitis (PCD). Therefore, PCD is an indicator of a poor responder for contact immunotherapy.[22] Other negative prognostic factors in the treatment with DPCP are disease severity, duration of AA before therapy and presence of nail changes.[23,24] Once complete regrowth has been observed and maintained for more than 3 months, a stepwise discontinuation in the frequency of application can be begun for more than 9 months. Eyebrows may also be treated with SADBE/DPCP although edematous and erythematous change may be seen on the face. The use of SADBE/DPCP on the eyelashes is inadvisable. Other adverse effects include severe contact eczema, exacerbation of atopic dermatitis, cervical and occipital lymphadenopathy,[25,26] headache, facial and scalp edema, contact urticaria, flu-like symptoms, erythema multiforme-like reactions,[25,27] and pigmentary disturbances (e.g. hyperpigmentation, hypopigmentation, dyschromia in confetti, and even vitiligo).

HIGH-DOSE PULSE CORTICOSTEROID THERAPY

Seiter *et al.*[28] reported the effectiveness of high-dose corticosteroid therapy for multifocal AA. They treated 30 patients with i.v. methylprednisolone on 3 consecutive days at 4-week intervals for at least three courses; 67% of their patients with AA multiplex showed more than 50% regrowth of hair, but none of the patients with AA totalis or AA universalis responded to this therapy. Tsai *et al.*[29] also reported the effectiveness of high-dose corticosteroid pulse therapy for multifocal AA lasting less than 2 years. Recently, Nakajima *et al.*[30] analyzed the outcome of high-dose corticosteroid pulse therapy on AA patients. Among the recent-onset group (duration of AA ≤6 months), 59.4% were good responders (>75% regrowth of alopecia lesions), while 15.8% with more than 6 months duration showed a good response. Recent-onset AA patients with less severe disease (≤50% hair loss) responded at a rate of 88.0%. There were no serious adverse effects in the study. In summary, high-dose corticosteroid pulse therapy is recommended in the treatment of acute phase AA lasting less than 6 months.

TOPICAL CORTICOSTEROIDS

Topical corticosteroids are widely used to treat all types of AA in office dermatology but the clinical efficacy of topical corticosteroids in AA is still controversial. A randomized controlled trial of 0.25% desoximetasone cream (commercially unavailable in Japan) in 70 patients with patchy AA (twice per day for 12 weeks) improved more than 25% of hair loss lesion but failed to show a significant effect of complete response over placebo.[31] Topical corticosteroids may have difficulty in penetration into the depth of the hair bulb. In order to increase the effect of topical corticosteroids, an occlusive dressing technique (ODT) can be applied in the treatment. Clobetasol propionate 0.05% under occlusion is effective in inducing hair regrowth in patients with AT or AT/alopecia universalis without systemic adverse effect.[32] In this study, 28 patients were enrolled and treated with a half-side test. Of the ointment, 2.5 g was applied to the right side of the scalp every night under occlusion with a plastic film. The left side of the scalp was untreated as a control. Eight patients were treated successfully with complete or almost complete (95%) hair regrowth.

Recently, a new topical formulation of clobetasol propionate 0.05% has been introduced on the market. This formulation has an enhanced delivery of the active compound through the skin.[33] In order to clarify the efficacy of the drug, 34 patients with moderate to severe AA were enrolled in a randomized, double-blind, right-to-left, placebo-controlled, 24-week trial. This study showed greater hair regrowth in 89% of the head sites treated with clobetasol versus 11% in the sites treated with placebo. This new formulation of clobetasol propionate foam is an effective, safe and well-tolerated topical treatment for AA.

INTRALESIONAL CORTICOSTEROIDS

Intralesional corticosteroids were first described in 1958 with the use of hydrocortisone.[34] Although intralesional corticosteroids are used frequently in AA, there are no randomized controlled trials on intralesional steroids. For adult AA patients with less than 50% scalp involvement, an intralesional corticosteroid with triamcinolone acetonide is considered first-line therapy. The injection is performed with triamcinolone acetonide (5–10 mg/mL) into the upper subcutis every 4 weeks. An uncontrolled study from Saudi Arabia showed complete regrowth in 63% of patients receiving monthly triamcinolone injections.[35] In addition, there are several studies that indicate the effects of corticosteroid injection for AA.[36–38] Adverse effects include transient skin atrophy and telangiectasia, which may inhibit hair regrowth. Therefore, this should be prevented by the use of smaller volumes and minimizing the number of injections per site. The eyebrow also suffers from AA and often shows resistance to treatment. Corticosteroid injection can be used with triamcinolone acetonide. Intralesional corticosteroids are useful but some AA patients are glucocorticoid resistance. This may be because of low expression of thioredoxin reductase 1 in the outer root sheath.[39]

ORAL CORTICOSTEROIDS

There are several reports that indicate the usefulness of corticosteroids in AA treatments.[40–42] Kurosawa *et al.* enrolled 51 patients with single or multiple AA and 38 patients with AT or AU who were randomly divided into three groups depending on the time of their initial visit. They were administrated: (i) oral dexamethasone 0.5 mg/day for 6 months; (ii) i.m. triamcinolone acetonide 40 mg once a month for 6 months followed by 40 mg once every 1.5 months for 1 year; and (iii) pulse therapy using oral prednisolone (PSL) 80 mg for 3

consecutive days once every 3 months. The response rate of single AA and AA multiplex was significantly better in the i.m. triamcinolone acetonide group than in the oral dexamethasone group. The overall relapse rate and that of AT/AU were significantly better in the pulse therapy group than in the oral dexamethasone group. These results indicate that i.m. triamcinolone acetonide or PSL pulse therapy is effective for AA with an acceptable level of adverse effects. Several studies have been tried on AA with oral pulse corticosteroid therapy.[40,43–45] A randomized controlled trial showed that 75% of patients receiving 200 mg PSL once weekly for 3 months were more likely to improve extensive AA than those given placebo without relapse within 3 months of discontinuation of treatment.[45] Oral steroids can be applied in recent-onset disease, but chronic phase AA such as ophiasis and universalis may show a poor response, so oral PSL is not recommended in these types of AA.[43]

ANTIHISTAMINE DRUGS

Previous clinical studies suggested the supplementary effects of antihistamine such as ebastine and fexofenadine.[46–48] Fexofenadine is a useful reagent in the treatment of extensive atopic AA with contact immunotherapy although there are no significant effects on non-atopic AA. Ebastine also showed favorable results on AA in a patient with atopic dermatitis (AD) who was refractory to contact immunotherapy and a progressive AA case with AD who did not respond to topical corticosteroids.[49] In addition, C3H/HeJ mice with AA-like lesions recovered from patchy hair loss by treatment with ebastine (1.5 mg/head per day). Histologically, CD3-positive T cells were hardly detectable around the bulbar to suprabulbar portion of anagen hair follicles in ebastine-treated AA mice. These results indicate that antihistamines can be applied for AA with AD to support other treatments.

PHOTOCHEMOTHERAPY

Photochemotherapy has been widely used in AA treatment. The response rates for oral or topical PUVA phototherapy differ widely from less than 15% to more than 70%.[50,51] There are several methods of PUVA and the response may be different between them. The PUVA turban method is unique topical PUVA to enhance the effect of photochemotherapy. After administration of psoralen lotion on the scalp lesions, a cotton towel is wrapped around the scalp as a turban. Then, UV-A is irradiated after 20 min of incubation. In one study, hair regrowth was observed in 15 patients (total regrowth in six patients and partial regrowth in nine patients) in a cohort of 20 enrolled AA patients.[52]

Mohamed *et al.*[51] reported a large retrospective study of 25 patients with AT or AU and 124 patients with AA multiplex treated with topical 8-methoxypsoralen with UV-A irradiation of the scalp. In this study, a high phototoxic dose of UV-A (erythema dose) irradiation was limited to the scalp. The UV-A dose was 6–20 J/cm^2 (average 12 J) according to the skin phototype. The treatment continued with one exposure every 3 months until hair regrowth. In AT patients, 14 (56%) had good (hair regrowth >50% of the scalp) and excellent results (hair regrowth >80% of the scalp). In multiple AA patients, 105 patients (85%) had a good or excellent result. Recurrence of hair loss was noted only in five cases after a period of 10 months to 2 years of treatment.[53] On the other hand, another study showed unfavorable results of PUVA therapy in refractory cases prior to starting PUVA. The effective success rate was at best 6.3% for AA partialis, 12.5% for AT and 13.3% for AU.[50] We demonstrated combination therapy with oral PUVA and corticosteroid for recalcitrant AA.[54] These patients were administrated 20 mg/day corticosteroid and were irradiated with UV-A on the whole body 2 h after taking methoxsalen for 1 month. The terminal hair on the whole scalp was observed after 2 months in nine enrolled patients with AA, including six patients with AT and three patients with AU. Six patients with AT and one patient with AU showed greatly increased terminal hair on the whole scalp skin after 3 months of the combination therapy. The number of regulatory T cells was increased after combination in peripheral blood nuclear cells and the lesions after the combination therapy.

MINOXIDIL

Minoxidil (2,4-diamino-6-piperidinopyrimidine-3-oxide) was originally exploited as an antihypertensive drug. However, minoxidil has been mainly used for the treatment of AGA for more than 20 years. The regrowth effect of minoxidil was found as an adverse effect of treatment for hypertension. Many mechanisms of action have been proposed, including vasodilatation,[55,56] angiogenesis,[57] enhanced cell proliferation[58,59] and potassium channel opening.[60,61] Interestingly, some studies report the immunosuppressive effects of minoxidil.[62,63] Topical minoxidil has used in the treatment of AA, and the effectiveness was evaluated in several studies. Five percent minoxidil showed an 81% response rate, defined as terminal hair regrowth, in the patients with extensive (≥75%) scalp hair loss although 1% minoxidil showed a response rate of only 38%.[63] Hair loss generally recurs after treatment is stopped because minoxidil does not change perifollicular lymphoid infiltration even in improved cases of AA.[64] In a double-blind, placebo-controlled study, Price *et al.*[65] showed hair regrowth in 63.6% and 35.7% in the 3% topical minoxidil-treated and placebo groups in extensive AA, respectively, although, cosmetically acceptable hair growth was seen only in 27.3% of the minoxidil-treated subjects.[65,66] Five percent topical minoxidil can be used as adjunctive treatment with other therapeutic options.[4]

MISCELLANEOUS

In Japan, several therapies have been historically used for decades, such as cryotherapy with liquid nitrogen, Chinese herbal medicine, carpronium chloride hydrate, cepharanthine and mono-ammonium glycyrrhizinate. These therapies have never been evaluated by double-blinded, placebo-controlled trials, except for carpronium chloride hydrate. Lei *et al.*[66] reported that cryotherapy showed hair regrowth in 60% of hair loss lesions in 97% of treated AA patients. Carpronium chloride hydrate is a parasympathetic nerve stimulant that was exploited in Japan approximately 50 years ago. In 1960, the pathogenesis of AA was thought to be an imbalance of sympathetic and parasympathetic neurons. Hyperactivity of the sympathetic nerve may contract blood vessels around hair follicles that have a possibility to induce hair loss. Therefore, stimulation of the

parasympathetic nerve may increase blood circulation around hair follicles. Only one placebo-controlled randomized trial showed the significant effect of carpronium chloride hydrate.[67] Linear polarized infrared irradiation has a similar mechanism to carpronium chloride hydrate for AA.

NO TREATMENT

Spontaneous remission occurs in up to 80% of patients with limited patchy hair loss within 1 year.[68] Therefore, not all patients of AA simplex/multiplex need extensive treatments, and ''wait and see'' is one of the choices for the patients. However, the result of no treatment is different for AT/AU patients compared to AA simplex/multiplex patients. Many patients with AT/AU may have been treated with several therapies for a long time that resulted in no improvement. These patients finally may understand the fact that there is no hope of recovery. All treatments have a high failure rate in AT/AU patients, and some patients avoid medical treatments, especially with corticosteroids. In the Japanese guideline, a wig is the final option of the algorithm until restarting treatments for AA.

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