Alopecia Areata

Da-Ming Liao1，Chieh Chen 2

Dental Department, Puli Christian Hospital 1

Division of family medicine, Hualien Armed Forces General Hospital 2

Corresponding author: Chieh Chen

guppy5230@yahoo.com.tw

Address:970 No. 198, Minde 1st Street, Hualien city

Tel: 0928-698950

E-mail: guppy5230@yahoo.com.tw

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**Abstract**

Alopecia areata, which is a condition with characteristic regional hair loss on the top of the head, is quite common in the outpatient department and clinics. The hair loss is rather rapid during the acute phase and the development into severe form of alopecia may be related to the younger onset, along with nail changes, family history of atopic dermatitis, allergic rhinitis, asthmatic bronchitis, etc., or other autoimmune diseases. Physically, large area of hair loss can be observed, as well as other typical features, including broken hair roots and exclamation mark hairs. The classic histopathological sign is the infiltration of lymphocytes around the hair follicles. Moreover, alopecia is not limited to the scalp and hairs on any parts of the body are subjected to the effect of this disease.

Keywords: Alopecia Areata; canities subita; Queen Mary Syndrome.

**Introduction**

Alopecia areata is an organ-specific autoimmune disease, especially in the population inherited with specific HLA genes, even though no definite conclusion on the pathophysiological mechanism of the disease has been derived by the researchers. It is generally believed that it may be related to genetics, infections, drugs, and physical or psychological stress. Options of treatment are available depending on the severity and the duration of disease. The primary medication is the use of steroids while it is often supplemented by other immunomodulatory methods. Steroids can be administered in the form of topical agent, intralesional injection or oral medicine. Other immunomodulatory treatments include contact immunotherapy and ultraviolet light therapy [1]. Also, the rubbing of minoxidil to stimulate hair growth is considered as the adjuvant treatment. Most of these treatments are capable of achieving some regeneration of hairs in short term. However, the long-term effects of these treatments have yet to be confirmed, especially to weigh in the benefits and the side effects for the patient. In reality, alopecia areata is known to recur frequently and the more severe the condition is, the easier it is to relapse. But there were reports of stable or full recovery in one or two years if the condition were mild. As for the severe alopecia, it is unfortunately chronic that it usually has a great impact on the patient’s psychological state. Thus, it is generally recommended to educate patient with the correct understanding and expectation of the disease, to complete a more comprehensive therapeutic regime for alopecia areata [2-5].

**Classification of Alopecia Areata**

The diagnosis of alopecia areata relies on the physical examination under dermatoscope and skin biopsy may be arranged by the dermatologist when there are other conditions, such as unique hair loss pattern, pain, itching or erythematous pustules, to differentiate the disease. Alopecia areata can be classified into the following types[6,7]:

1.Patchy hair loss, typically shown as a single or multiple regions of hair loss, which may or may not connect together to form a larger patch;

2.Alopecia totalis, refers to the hair loss concentrated on the scalp, which accounts for 5% of all cases;

3.Generalized alopecia (alopecia universalis), is the body-wide hair loss, with only 1% of the body has hair intact;

4.Alopecia incognita (a.k.a. diffuse hair loss), is confirmed by a positive pull test and characterized by yellow spots or short, tiny new hair on the scalp;

5.Ophiasis (a.k.a. crawling alopecia) shows the loss of hair in the shape of wave like a band around the head, especially around the temporal and occipital bone;

6.Sisaipho alopecia areata (snake-shaped)[8-10], is the opposite of ophiasis, which is presented as the extensive hair loss in the non-scalp areas; and

7.Marie Antoinette Syndrome (a.k.a. canities subita), describes an occurrence of hair turning white overnight, which may need to differentiate from Queen Mary Syndrome, where it is an acute and diffuse hair loss and depigmentation to result in gray hair[11-15].

**The Treatments**

1.When there are only few circular bald areas and the disease is slow in progression, external application or local intradermal injection of corticosteroids is recommended, in which it may restore the hair growth within 4 to 8 weeks of administration. The injection should be repeated every 4 to 6 weeks. A major drawback of injection is the thinning of the skin at the site of topical injection. As for the topical application, the side effect is inflammation and sometimes folliculitis[14-17]. On the other hand, if large or multiple areas are affected and the disease is rapidly progressing, then systemic application of steroids is recommended. The clinical dosages for adults and children are 1mg/kg/day and 0.1-1mg/kg/day, respectively[18-20]. To avoid the side effects of long-term application of steroids, the high dosage should be given as pulse therapy, at an interval of once a month or less and for three consecutive days if intravascular injection. However, the pulse therapy can still have some undesirable effects, including transient increase of blood sugar, blood pressure, palpitation, flushing, gastrointestinal discomfort and mental symptoms. Generally, after three months of treatment, the hair loss will gradually stabilize, and hair may even start to grow after six months[17.21-24].

2.Another treatment focuses on stimulating hair growth. It involves the application of phenol (Anthralin), despite the drug’s mechanism remains unknown. The side effect includes contact dermatitis since it is believed to treat the disease by inhibiting some immunity and preventing inflammation[25,26].

3.Local immunotherapy, which is a popular choice of treatment in Canada and Europe. For example, chronic and severe alopecia areata will be treated with local application of strong allergenic substances, such as Diphenylcyclopropenone (DPCP), Dinitrochlorobenzene (DNCB) or Squaric acid dibutyl ester (SADBE), which will stimulate the production of suppressive or regulatory T-cells to control the inflammatory response at the hair follicles. Several studies have shown the treatment to be approximately 4 to 85% effective and patients may even grow hair after 6 to 12 months into the treatment. Common side effects include itching, rash, severe blisters, and cervical lymphadenopathy, contact urticaria, etc. The medication should continue once a month for another half year or a year to maintain the result, as there is evidence of recurring hair loss in one third of the patients when stopped[27-30].

4.Minoxidil hair tonic, contains the element of peripheral vasodilator. It was originally designed to treat high blood pressure. But since its effect of being a vasodilator to improve blood circulation and supply, it may directly stimulate hair growth when used on the scalp. Therefore, Minoxidil is generally added in the shampoo or hair tonic to treat hair loss. The recommended dosage is to apply 5% concentration of Minoxidil lotion every day or with Anthralin once a day for 8 to 12 weeks to start seeing hair growth. The longer the treatment continues, the more hair growth one will observe [30,31].

5.Photochemotherapy (PUVA), involves exposing the area to long-wave UVA light after a photosensitive agent, Psoralens, is applied two hours beforehand. The effectiveness of the treatment is 30% and the treatment should continue for at least half a year to achieve a desirable outcome. The primary concern of exposing to ultraviolet radiation is of course the risk of sunburn[32-35].

6.Other therapies use local immunosuppressive drugs, such as Tacrolimus or Cyclosporin. They are considered as the alternatives only when the conventional therapies fail. Other drugs include high-dose zinc, dapsone, sulfasalazine, etc [36-38].

**Conservative Treatment by Topical and Injection Steroids**

Patients sometimes may seek aggressive treatment to accelerate hair regeneration. Options include topical corticosteroids, Minoxidil, and immunotherapy (Diphenylcyclopropenone, Dinitrochlorobenzene, Dibutyl squarylate, or Dianthrene). Intradermal or subcutaneous injection of long-acting triamcinolone or betamethasone has been widely used in the treatment of alopecia areata. Both diluted and undiluted triamcinolone have been proven to be effective in some patients. Most patients of single-patch alopecia areata responded well to intralesional injection of corticosteroids at repeated interval of every 4 to 6 weeks. The result showed that 60 out of the 70 patients developed new vellus hair at the site in 4 weeks. However, the side effects of Triamcinolone may include pain, dermal atrophy or depression at the site, folliculitis, depigmentation, microvascular hyperplasia, etc. Since the tissues of alopecia areata are heavily inflamed, the external use of steroid ointment alone is not that ideal and effective[39,40].

**Systemic Steroids (via intramuscular, intravenous or oral administration)**

Long-acting corticosteroids can be given intramuscularly or intravenously as an alternative to oral intake. Although there are some suggestions in the literatures that intramuscular or intravenous administration has more side effects than oral administration, there is hardly any consensus and clinically, the drug is preferred to be given via oral route unless there is oral contraindication. Up to 80% of the patients will respond well to oral corticosteroids. 11% of the cases will be refractory to the treatment, even at high dosage. 50% of the patients will relapse shortly after reducing or stopping the treatment. The medication starts with a higher dose of oral Prednisolone (0.5-0.75 mg/kg), followed by a taper in 6 to 12 weeks, before it is maintained with Prednisolone (at a dosage of 0.25mg/kg) for 6 to 12 weeks. Or the medication may start at a lower dose of 0.1-0.2mg/kg) and increase over time based on the patient’s response and tolerance. Although most people start treatment with an initial oral dose of Prednisolone at 0.5mg/kg and tapered over 6 to 12 weeks, experts could not agree upon the optimal dosage. Furthermore, many dermatologists favor pulse dosing of oral corticosteroids, but there is little evidence of its effectiveness and safety. But it is worth mentioning that a cross-sectional study of children with severe alopecia areata under the pulse treatment of systemic corticosteroids did show some initial improvement, even though the outcome was not affected in long-term [27-29,35].

**Other Immunosuppressants and Immune-targeting Drugs (Azathioprine, Methotrexate and Cyclosporin)**

Drugs, such as Azathioprine, Methotrexate and Cyclosporin, which are the second-line systemic medication for alopecia areata, have been tested only in open-label retrospective or small prospective studies that there is no randomized trial to support the use in treatment. Nevertheless, these drugs are often used alone or in combination with Prednisolone and they appear to be more effective when used as steroid-sparing agent to prevent the recurrence of alopecia areata, than as a monotherapy. No consensus is reached on the preferred choice of steroid-sparing agent because there is no evaluation standard to assess the relative efficacy of these drugs, as this is all based on patient’s tolerance and satisfaction to determine if the medication should continue. Patient who discontinues the medication due to complete remission before 12-month period of treatment is considered responder. Azathioprine is usually started at a low dose (0.5-1 mg/kg per day) to minimize the risk of gastrointestinal distress and it is gradually titrated by 2-3mg/kg, every 4 to 6 weeks based on the patient’s response and tolerance. About one third of the patients may take Prednisolone concurrently and receive continuous injection of Triamcinolone in areas of residual hair loss. The starting dose of Methotrexate is usually 5-10mg, once every week and is also dependent of the patient’s response and tolerance. The dosage is gradually increased to 20–30mg every 4 to 6 weeks, and more than half of the patients will take Prednisolone and continuous injection of Triamcinolone at the same time [27,39].

**Results and Discussion**

It is believed that the person's genetic makeup may trigger the autoimmune reaction of alopecia areata, along with a virus or a substance the person comes into contact with. Alopecia areata is an unpredictable disease. In some people, hair grows back but falls out again later. In others, hair grows back and remains. For patients who use treatments, there are several options. However, alopecia areata cannot be "cured." As noted above, most patients experience future episodes of hair loss. Corticosteroids are anti-inflammatory medications that are used to treat alopecia areata. The most common options include: Minoxidil (Rogaine). Over-the-counter (nonprescription) minoxidil comes in liquid, foam and shampoo forms. Finasteride (Propecia): This is a prescription drug for men. Other medications: Other oral options include spironolactone (Carospir, Aldactone) and oral dutasteride (Avodart). Calcipotriol, a vitamin D analog, has been reported to be topically used in treating alopecia areata with promising results. Combination therapy of vitamin D analogs with corticosteroids might also be used in treating alopecia areata.

**Conclusion**

Most patients with alopecia areata do not need additional blood tests such as ESR, CRP, etc., for diagnosis. Only a small fraction of patients (0.4-15%) will have leukoplakia, thyroid disease, lupus erythematosus, and other autoimmune diseases, such as rheumatoid arthritis, which can be ruled out by family history or physical examination. Alopecia areata can occur anywhere on the body, such as eyebrows, armpits, and the most apparent location, scalp. Several factors are thought to cause alopecia areata. Genetics appears to play the vital role, since it is found that family history of the disease is common. Also, there is growing evidence of alopecia areata being an autoimmune disease when the temporary dysfunction of the immune system will lead the lymphocytes in the body to attack the hair follicles, cause acute inflammation and result in hair loss. The immune dysfunction is highly specific that the individual’s overall health is normal, except for the hair loss. Few patients have also shown some other autoimmune or systemic diseases at the same time, such as thyroid gland disease, leukoplakia, lupus erythematosus, diabetes, myasthenia gravis, immune anemia, etc.[40] Some scholars have also pointed to stress as the cause of alopecia areata. They suspect the disease as a physical manifestation to the pressure or the mental trauma experienced by an individual. However, there is no medical basis or evidence to support the notion, which still requires more experiments to prove the hypothesis.

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