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Research Article

Alopecia areata

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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 outpatient departments and clinics. The hair loss is rather rapid during the acute phase and the development into a 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, a 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 part of the body are subjected to the effect of this disease.

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 the disease. The primary medication is the use of steroids which is often supplemented by other immunomodulatory methods. Steroids can be administered in the form of a 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 an adjuvant treatment. Most of these treatments are capable of achieving some regeneration of hairs in the short term. However, the long-term effects of these treatments have yet to be confirmed, especially weighing 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 severe alopecia, it is unfortunately chronic and it usually has a great impact on the patient's psychological state. Thus, it is generally recommended to educate the 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 a dermatoscopy and a 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 single or multiple

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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 body-wide hair loss, with only 1% of the body having 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 a wave-like band around the head, especially around the temporal and occipital bone;

6. Sisaipho alopecia areata (snake-shaped) [8-10], is the opposite of opiates, which is presented as 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 option

1. When there are only a few circular bald areas and the disease is slow in progression, external application or local intradermal injection of corticosteroids is recommended, which 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 1 mg/kg/day and 0.1 mg/kg/day - 1 mg/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, pulse therapy can still have some undesirable effects, including a transient increase in blood sugar, blood pressure, palpitation, flushing, gastrointestinal discomfort, and mental symptoms. Generally, after three months of treatment, 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, 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 to the shampoo or hair tonic to treat hair loss. The recommended dosage is to apply a 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 exposure 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 alternatives only when 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 has been proven to be effective in some patients. Most patients of single-patch alopecia areata responded well to intralesional injections of corticosteroids at a 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

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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 literature 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 the oral route unless there is an 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 a 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 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 the 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 the 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 their 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 a 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 the patient's tolerance and satisfaction to determine if the medication should continue. A patient who discontinues the medication due to complete remission before the 12-month period of treatment is considered a responder. Azathioprine is usually started at a low dose (0.53mg/kg - 1 mg/kg per day) to minimize the risk of gastrointestinal distress and it is gradually titrated by 23mg/kg - 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 a 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 on the patient's response and tolerance. The dosage is gradually increased to 20 mg – 30 mg 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. There is no cure for alopecia areata, but there are treatments that help hair grow back more quickly. There are also resources to help people cope with hair loss.

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, the scalp. Several factors are thought to cause alopecia areata. Genetics appears to play a vital role since it is found that a 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 and the individual's overall health is normal, except for hair loss. A 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. Some scholars have also pointed to stress as the cause of alopecia areata. They suspect the disease is a physical manifestation of 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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