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Views and Practice

Update on alopecia areata

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Alopecia areata (AA) is regarded as an organ-specific autoimmune disease affecting the hair follicles. It has a strong genetic influence.[1] Some infections e.g. Epstein-Barr virus may be a triggering factor.[2] Cell-mediated immunity seems to be the main effector with the melanogenesis-associated peptides expressed in the hair follicle of anagen hair as autoantigen.[3] It is a common cause of alopecia with a lifetime incidence of around 2%. There is no sex preference. The onset can be at any age though most of them are at the third or fourth decade of life.[4]

Patients may present with sudden onset of hair loss, usually in the form of circular patches which can be single or multiple. They are usually asymptomatic although mild itching may precede the hair loss. Pathognomonic 'exclamation mark' hairs could be found at the periphery of active lesions. When all scalp hair is lost, it is called alopecia totalis and when the eyebrows, moustache, axillary hair and pubic hair are also lost, it is termed alopecia universalis. It is also associated with other autoimmune diseases like vitiligo and lupus erythematousus.

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The course of the disease is unpredictable: some may recover spontaneously with or without relapse, while others may develop into a chronic disease. A clinical variant, the ophiasis type, is more difficult to treat. Early age of onset and extensive disease are regarded as poor prognostic factors.

The diagnosis of AA is usually clinical. However in equivocal cases, a skin biopsy may be required. Typical histology shows perifollicular lymphocytes infiltrates like a 'swarm of bees'. The hair follicles are usually preserved though injured.

Treatment of AA depends on various factors and could include topical therapies (including intralesional steroid), oral medication, phototherapy, etc. Topical immunotherapy with diphenylcyclopropenone (DPCP) and squaric acid dibutylester (SAB) has also been used in the past decades with variable success.

Recent advances on AA has thrown light on new treatment modalities: (1) Genetics: The use of genome-wide association study has identified a number of candidate genes that have important contributions to the development of autoimmunity. A more important one is the *KLRK1* gene located on chromosome 6, coding for ligands for the NKG2D receptor.[5] (2) Immunology: autoimmunity has long been known to be involved in the pathogenesis of AA and one the possible pathways has recently been discovered: the autoantigen belongs to the melanogenesis-associated peptides

which was expressed during the anagen phase of the hair cycle. The Janus Kinase (JAK) pathway is involved with a positive feedback on the maintenance of the pathogenic NK cells and hence the phenotypic manifestation.[6] (3) Mouse model: a mouse model of AA has been developed with the C3H/HeJ breed line. Of this breed, 15% will develop AA at one year of age. Affected skin grafted to the syngenetic mice results in nearly 100% transfer of the disease to recipients. Using this model and with the understanding of the immunology, scientists have used JAK blockers to treat these patients with initial promising results.[7] (4) Clinical: at the moment, AA is still incurable; conventional treatments are mostly non-specific immunosuppression with topical or systemic corticosteroids or other immunosuppressants like cyclosporine. Topical immunotherapy, like DPCP and SAB has gained some success though the long term optimal regime and the high relapse rate is a concern. Besides, it requires patients to come for treatment every week which is not very practicable. Combination treatment with Anthralin and DPCP has recently shown to be superior to DPCP alone.[8] As mentioned above, the use of JAK inhibitor could be another treatment strategy that can be further explored. (5) Psychological: hair loss can be a 'significant loss' to patients. The change of 'body image'; the fear of further hair loss; the lack of coping strategies in their daily living could make patients withdrawn, depressed with loss of self-confidence. This may pose difficulties to patients and sometimes their families especially in AA children. Worse still, patients or their family members may not even know how to get a hair-piece for camouflage or how to draw on the missing eyebrow.[9]

I have treated a cohort of 31 patients with extensive AA, who failed topical steroid therapy, with DPCP between 2009 and 2010, the results and my observations are as follows:

1. Results: Thirty-one (16 male, 15 female) Chinese patients with extensive, steroid-resistant AA and a mean age of 28.9 years (SE 10.4) were treated. The mean age of onset was 17.8 years (SE 8.8) with an average disease duration of 11.2 years (SE 7.7). Ten patients had a history of atopy and four had a history of thyroid disease. Nail changes were found in 14 patients and a family history of AA was found in two patients. Thirteen patients (41.9%) had experienced total hair loss. Two patients abandoned the treatment due to severe side effects. Of the remaining 29 patients, 4 (13.8%), 7 (24.1%), 5 (17.2%), and 13 (44.8%) achieved >90% complete response, >50-90% partial response, >10-50% minimal response, and <10% no response hair regrowth, respectively. Adverse effects included pruritus, erythema, vesiculation, scaling, cervical lymphadenopathy, dyspigmentation and urticarial reactions. Relapse occurred (>25% hair loss) in 69.23% of patients after 18 months of follow up.
2. Relatively safe: though dermatitis with tingling and burning sensation is common after treatment and especially problematic with the hot and humid weather in Hong Kong. However, simple treatment with analgesics or antihistamines is able to control the symptoms. Hyperpigmentation is again common as well as cervical lymphadenopathy. One of my patients developed vitiligo over the application site which persisted and she did not mention to us that she had a small patch of depigmentation at her right axilla. I think it is imperative to ask the patient specifically and examine thoroughly for any sign of vitiligo before embarking on treatment. Besides, patients should be forewarned.
3. Efficacy: more than 50% of patients had some improvement with hair regrowth to a certain extent. Only 10% had more than 90% hair regrowth. Yet, all relapsed several months after stopping treatment.
4. Optimal regime: so far, there is no consensus on maintenance treatment or the maximum concentration of DPCP that can be used. The choice of sensitiser, the teratogenicity of the agent used, convenience of usage as well as the efficacy have to be taken into account.

Interestingly, a recent report showed promising results when topical anthralin was added on topical DPCP.

5. Quality of life: no formal assessment of quality of life was performed in our study. One patient stated that his quality of life remained the same despite complete regrowth of his hair. Another patient who had good hair regrowth chose to shave away his regrew hair due to their patchy and non-uniform distribution. Others who had minimal hair growth decided not to pursue further with a higher dose. Some were quite satisfied with using a hair-piece as camouflage. We tried to contact unsuccessful cases for a further trial of DPCP about half a year later. However, most of them declined due to the need for frequent attendance and the side effects.
6. Extensive AA could have significant psychosocial problems. It is not uncommon to encounter patients who come into the consultation room with tears. However, the overall impact depends on a number of factors such as personality of the patients, the duration of onset, the occupation (those who work in the show business vs white collar), family support etc. It is imperative that dermatologists should be aware of this aspect of the disease. A sympathetic attitude towards the patient's feelings is essential.
7. Topical immunotherapy can be an option for treating patients with extensive AA who have failed other treatment modalities. It is superior to intralesional steroids in that the hair regrowth is more uniform compared with the patchy regrowth on isolated steroid injection sites. However, patients have to receive treatment weekly and which could be problematic. Besides the side effects may be more unpleasant than with intralesional steroids.

Despite ongoing treatment studies on this difficult problem, at the moment, there is no definite cure for the disease. For extensive and recalcitrant cases, attention can be switched to the psychosocial support of the patients, to help the patients to relieve their feeling; to correct their misconception; to suggest some practical ways to camouflage their baldness and eventually to restore their confidence to live as a 'normal' person.

In the US, patient groups have provided relief for patients with AA. Through group discussion and sharing, patients may feel less lonely and can be supported to go through 'grief reactions' and more importantly imbue a sense of confidence in their daily living. I think patient groups can be set up locally with the help of voluntary agencies like Hong Kong Rehabilitation Network and we as dermatologists, could act as medical advisors. In this way, we may inform patients of the most recent advances in treatment and help them to clarify any misconceptions or myths. Psychologists could also be incorporated into this multi-disciplinary team to teach patients relaxation techniques and coping strategies in their daily lives. Furthermore, the correct choice of hairpieces and the use of eyeliners could be taught to the patients.[10] For parents, how to deal with children with AA is also an area that can need to be explored. Further information is available in the website of National Alopecia Areata Foundation (https://www.naaf.org/).

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