Case Report

A Case Study on Exploring Immune Dysregulation in Alopecia Areata – Mechanisms and Treatments Outcomes

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ABSTRACT

Alopecia areata (AA) is an autoimmune condition that causes sudden, patchy hair loss without scarring. It can have a deep emotional and psychological impact on those affected. This case report discusses a 20-year-old male who suddenly developed alopecia areata. He also had a history of vitamin B12 and vitamin D deficiencies. The report explores his symptoms, how the diagnosis was made, the treatment plan, and his outlook moving forward. The patient exhibited multiple non-scarring alopecic patches on the scalp, confirmed by a positive pull test. Treatment with systemic immunosuppressants, including cyclosporine and methylprednisolone, led to slightly hair regrowth for over the period of time. This case highlights how important it is to make an accurate diagnosis, tailor treatment to each individual, and carefully consider the potential side effects of medications when managing alopecia areata.

Keywords: Alopecia areata, immunosuppressants, cyclosporine, methylprednisolone.

INTRODUCTION

An autoimmune disorder called alopecia areata (AA) can have a major negative impact on a person's emotional and mental health and results in hair loss without scarring [1,4]. An autoimmune condition that significantly lowers a patient's quality of life, alopecia areata is still difficult to treat [3].

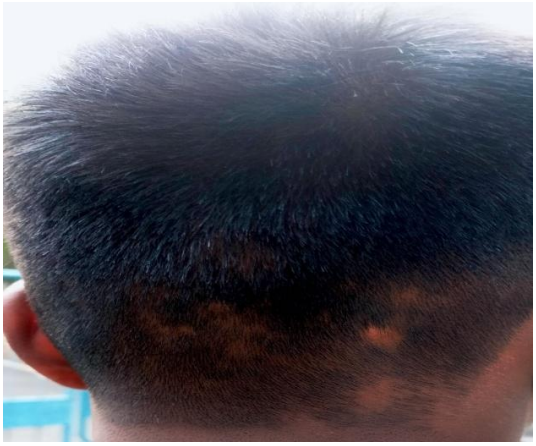

Figure 1: Onset of alopecia areata

The degree of alopecia areata (AA) varies, ranging from a little bald patch to total hair loss on the body, scalp, eyebrows, and eyelashes [5]. Many people have a transient issue; around 40% will only have one patch and, if therapy is not received, will experience full hair regrowth in six months. Even though another 27% might have further patches, they will still fully recover in a year. Nevertheless, about one-third of individuals will eventually experience a chronic or longer-lasting version of the illness. Alopecia totalis will eventually develop in 30% of those with chronic AA, 15% will have alopecia universalis, and 55% will have persistent multifocal relapsing and remitting disease if systemic treatment is not received [6].

The disorder linked to AA is exacerbated by its erratic progression and psychological suffering. Alopecia areata can be treated in a variety of ways, including as with topical creams, injections into the afflicted areas, and oral drugs [7]. Research on the efficiency of these treatments and their tolerability by patients is still scarce, nevertheless. Topical therapies such as minoxidil, topical immunotherapy, or corticosteroid creams are frequently used to promote hair regrowth in milder cases [2,8].

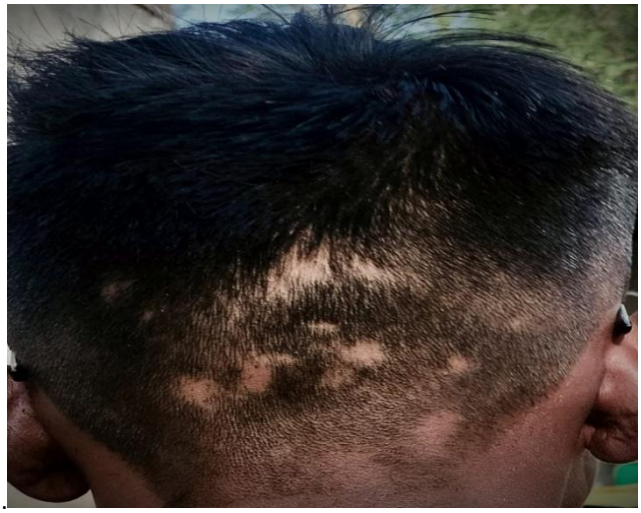

Figure 2: second stage of alopecia areata

For AA, there are no widely accepted signs that systemic treatment should be started. When hair loss occurs rapidly, when more than half of the scalp is affected, when the problem has become chronic, or when it is causing a great deal of emotional distress, systemic treatment—medication that acts throughout the body—may be appropriate. Currently available drugs for systemic treatment include tacrolimus, azathioprine, dapsone, mycophenolate mofetil, corticosteroids, ciclosporin, and

sulfasalazine. There is currently no description of the ideal therapy algorithm [6,8].

Figure 3: Alopecia areata causing severe hair fall

This consensus statement aims to provide an overview of an AA treatment algorithm which involves reasons for systemic treatment, the right systemic treatment to choose, measurements of satisfactory outcomes, and when to stop successful or unsuccessful treatment [1,5].

AVAILABLE TREATMENT PLANS-

Topical Corticosteroids-

In patients with alopecia areata, corticosteroids may promote the healing of hair follicles by lowering inflammation and calming the immune system. Approximately 25% to 57% of individuals report full hair regrowth during treatment, according to numerous studies examining the effectiveness of topical corticosteroids. Topical steroids are generally simple to apply, reasonably safe, and frequently successful. They do have certain drawbacks, though, such as the potential for skin thinning with prolonged use and the likelihood of hair loss returning once therapy is stopped (relapse rates range from 33% to 75%) [1,10].

Intra-lesional corticosteroids-

The British Association of Dermatologists national guidelines state that corticosteroid injections into the skin are the first line of treatment for tiny, patchy regions of alopecia areata. Usually administered as triamcinolone acetonide, they have been demonstrated in tests to promote hair growth in roughly 60–67% of treated areas[12,13].

Interestingly, lesser doses (2.5 mg/ml) seem to function equally as well as higher ones (10 mg/ml), without the increased risk of adverse effects such skin thinning or visible blood vessels under the skin. It is normally advised to discontinue treatment if there is no discernible improvement after six months, as these injections may still result in pain, skin whitening, or regional thinning [11,12].

Systemic corticosteroids-

For many years, systemic corticosteroids in pill form have been used to treat more common forms of alopecia areata, albeit the outcomes can differ. After using a little dose of methylprednisolone (16 mg twice a week) for six months, around 82% of patients experienced considerable hair growth, with a recurrence incidence of only 2.2% [1]. Other research, however, have shown contradictory findings. In one group of individuals, for instance, only 53 percent reacted favourably to high daily dosages of prednisolone (300–1000 mg); all of them thereafter experienced a recurrence of hair loss. Another small study found that after taking low-dose dexamethasone (5 mg twice a week), 63% of patients with diffuse alopecia areata experienced 75–95% hair regrowth, with only one recurrence [14,15].

Systemic steroids have significant drawbacks, even with these encouraging outcomes in certain situations. Relapse rates might be anything from 14% to 100% after therapy ends. Prolonged use can potentially result in serious adverse effects, including immunological suppression, mood swings, weight gain, acne, irregular periods, cataracts, excessive blood sugar, damaged bones (osteoporosis), and even Cushing's syndrome [11,16].

Minoxidil-

Minoxidil was first introduced as a powerful medication to treat excessively high blood pressure in the 1970s. It's interesting to note that excessive hair growth, one of its frequent adverse effects, prompted researchers to investigate its potential as a cure for hair loss, including alopecia areata [17,18]. A topical form of minoxidil that is safe and simple to use was subsequently developed as a result of this discovery. The precise mechanism by which minoxidil stimulates hair follicles to enter the growth phase (also referred to as the anagen phase), prolong that period, or assist hairs in transitioning from the resting phase (telogen) back into growth is not entirely understood. These days, minoxidil is frequently used as a second-line treatment or in conjunction with other treatments such as injections or creams that contain corticosteroids. Unwanted hair growth (hypertrichosis) and skin irritation (contact dermatitis) are the most frequent adverse effects. Eight Chinese patients, including those with more severe types of alopecia such as alopecia totalis and universalis, participated in a recent study that found that topical minoxidil plus non-ablative laser therapy produced encouraging outcomes with negligible adverse effects [19].

Anthralin-

A synthetic substance with a tar-like appearance, anthralin has been used to treat alopecia areata and psoriasis. Although its precise mechanism of action is unclear, some research indicates that it reduces specific immune system signals that fuel inflammation [1]. It specifically seems to reduce the release of chemicals that are involved in the body's inflammatory response, including as interleukins and tumor necrosis factor (TNF)-α. By affecting specific proteins

in the skin cells, anthralin may also have an impact on the proliferation and activity of skin cells [20,21].

Cyclosporine-

Cyclosporine is a drug that reduces inflammation in the body, namely by attacking T lymphocytes, which are immunological cells. Alopecia areata has been the subject of numerous research over the last 20 years that have examined the use of oral cyclosporine either alone or in combination with other therapies [1]. According to Gupta and colleagues' first trial, which was the first to utilize oral cyclosporine for alopecia areata, three out of six patients had discernible hair growth after 12 weeks. However, after they stopped the treatment, they all relapsed [11].

Additional research has produced conflicting findings. 32 patients participated in a carefully monitored trial, and the results showed no discernible difference between the cyclosporine-treated and placebo-treated groups, indicating that the former did not outperform the latter. The use of cyclosporine to treat alopecia areata is uncommon due to these erratic outcomes [22].

Methotrexate-

A drug called methotrexate, which inhibits folic acid, is used to treat alopecia areata, pemphigoid, psoriasis, and pemphigus infections. When used alone or in conjunction with corticosteroids, methotrexate can be a successful treatment for severe cases of alopecia areata[1,11]. Methotrexate does have some significant hazards, despite its potential benefits. Additionally, it may harm the liver, impact the respiratory and gastrointestinal systems, and raise the risk of infections like pneumonia and septic arthritis. Due of these possible adverse consequences, its use is monitored closely [23].

Photochemotherapy-

Alopecia areata has been treated using photochemotherapy, commonly referred to as PUVA (psoralen/ultraviolet A). Although the exact mechanism of action of PUVA is unknown, it is believed to be beneficial by inhibiting the immune system [1]. UVA light causes the skin to produce chemicals like prostaglandins and cytokines, which can lower the skin's concentration of immune cells like mast cells and T lymphocytes. Additionally, it aids in reducing the expression of an inflammatory protein known as ICAM-1. Furthermore, the treatment's psoralen component might aid in lowering the concentrations of specific cytokines and their receptors [26,27].

Immunotherapy-

Three distinct chemicals are used in topical immunotherapy for alopecia areata: diphenylcyclopropenone (DPCP), also known as diphencyprone; squaric acid dibutyl ester (SADBE); and 2,4-dinitrochlorobenzene (DNCB). However, due to its genotoxic and mutagenic properties, DNCB is no longer widely utilized [1].

Topical immunotherapy sensitizers' exact mode of action is still unknown; however, a number of suggestions have been put out. These include: (a) a reduction in the ratio of CD4+ to CD8+ lymphocytes from 4:1 to 1:1; (b) a decrease in intrabulbar T lymphocytes and Langerhans cells; (c) a recurrent allergic reaction in the affected area produces suppressor T cells that, through a process known as "antigenic competition," non-specifically inhibit the autoimmune reaction against the hair follicles; and (d) the expression of class I and II major histocompatibility complex molecules, which are typically present in areas affected by alopecia areata, vanishes following repeated immunotherapy [11,24].

Janus kinase inhibitors-

The molecules Janus kinase (JAK) and signal transducers and activators of transcription (STATs) are part of a crucial pathway that facilitates the function of numerous immune system signals, often known as cytokines. This has led to a growing understanding of the role that JAK/STATs play in the emergence of immune-related disorders such as alopecia areata, psoriasis, and rheumatoid arthritis [1]. The JAK-STAT signalling system is disrupted by JAK-based therapies, which function by inhibiting the activity of one or more JAK enzymes (JAK1, JAK2, JAK3, and TYK2). You can apply these inhibitors straight to your skin or take them orally. In dermatology, first-generation JAK inhibitors such as tofacitinib and ruxolitinib are frequently utilized [9].

A summary of research on JAK inhibitor therapy and alopecia areata may be found in Significant success was shown in certain investigations. For instance, following six months of tofacitinib treatment, 9 out of 13 (70%) teenage patients with alopecia areata, ages 12 to 17, showed clinically significant hair regrowth, despite modest side effects. According to retrospective research by Lui and associates, 77% of 90 patients receiving tofacitinib experienced a clinical response. greater recently, two groups of patients with severe (greater than 30% scalp involvement) alopecia areata were treated with oral tofacitinib and ruxolitinib. The effectiveness, adverse effects, and durability of these treatments were examined[24].

Platelet-rich plasma-

A portion of your blood that contains more platelets than normal is called platelet-rich plasma (PRP). Platelet-derived growth factor, insulin-like growth factors, fibroblast growth factor, and more than 20 additional growth factors are all present in abundance. By concentrating on the bulge region of the hair follicle, these growth factors aid in the promotion of hair growth. By promoting hair growth and halting hair loss, they contribute to the development of a more robust, healthy follicle for further hair growth [1,25].

CASE PRESENTATION

Patient Profile-

Patient Name- known patient (name of patient is confidential to prohibit unethical practices.)

Patient ID- 122936

AGE And Gender-20Y/Male

Relevant Medical History- Patient with a history of a body ache and easily fatigue with vitB12 and vit D deficiency from 2019.

Onset And Progression of Alopecia Areata- The sudden onset of AA was found in patient in Dec 2021. The patient observes the significant hair fall and small patches on his scalp at starting period of AA. The condition was worse with days and the patient suffering from multiple patches on scalp, eyebrows, eyelids and also with facial hair loss. The pull test was positive at the margins of the lesions, indicating active disease.

Symptoms-

- Gradual thinning on top of head.
- Circular/patchy bald spots.
- Scaling patches that appear all over the scalp.
- Full body hair loss.
- Anxiety.
- Itching.
- Small dents on nails.

Diagnosis-

- Clinical Examination-
  - Visual inspection- The dermatologist examines the scalp and other areas of hair loss for characteristic patchy pattern.
  - Nail changing- AA can also affect nails, leading to pitting and ridging.
- Medical History-
  - Timeline of hair loss- Dermatologist understanding when the hair loss began, how quickly it progressed, and whether there's family history of AA.
  - Associated Symptoms- Some individuals may report tingling, burning or itching on skin before hair loss.
- Diagnostic Tests-
  - Pull test- This involves gently pulling on a few strands of hair to see if they come out easily.
  - Trichoscopy (Dermoscopy)- A handheld magnifier is used to examine the scalp and hair. It allowing the closer look at the hair follicles.

Treatment protocol and follow-up-

The current treatments for AA focus on immunosuppression or immunomodulation of the disease's activity, although they typically produce unsatisfactory results and have a high relapse rate, particularly in more severe cases. Estimating the effectiveness of therapy is challenging because of the disease's unpredictable course and the frequent spontaneous remissions that occur within the first year. Novel, more effective medicines are still desperately needed because the current therapeutic alternatives do not appear to affect the disease's long-term trajectory.

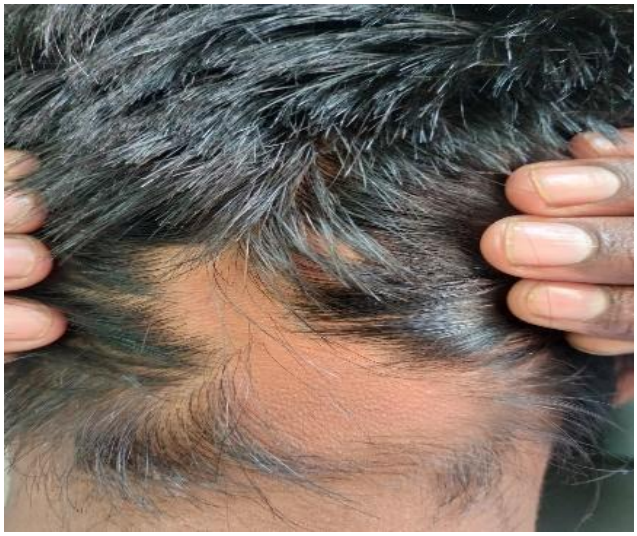

Figure 4: recalcitrant alopecia areata

Table 1: Oral Medications

Date	Drug	Dose	Duration	Progress	Side effect
9/3/2022	Prednisolone 10mg	2tabs after breakfast.	0-3 weeks	No hair regrowth form.	No side effect shown at starting of treatment.
	Rebeprazole 20mg and domperidone 30mg	Once a day before meal.	0-3 weeks	Reduces acid reflux in stomach.	
26/3/2022	Prednisolone 10mg	2tabs after breakfast.	3-13 weeks	Mild patchy regrowth obtained.	Mood changes and indigestion.
	Rebeprazole 20mg and domperidone 30mg	Once a day before meal.	3-13 weeks	Reduces acid reflux in stomach.	
	Azathioprine 50mg	Once a day (night).	3-13 weeks	Mild patchy regrowth obtained.	Mood changes and indigestion.
7/6/2022	Cyclosporine 100mg	Once a day (night).	13-17 weeks	Progressive hair regrowth obtained with new lesions on face (eyebrow) and scalp.	Stomach upset and restlessness

20/7/2022	Prednisolone 10mg	2tabs after breakfast	17-25 weeks	Progressive hair regrowth obtained with new lesions on face (eyebrow) and scalp.	Mood changes and indigestion.
	Rebeprazole 20mg and domperidone 30mg	Once a day before meal.	17-25 weeks		
	Azathioprine 50mg	Once a day (night).	17-25 weeks	Progressive hair regrowth obtained with new lesions on face (eyebrow) and scalp.	Mood changes and indigestion.
18/10/2022	Methyl prednisolone 16mg	Saturday and Sunday one tablet.	25-29 weeks	Satisfactory hair regrowth obtained on scalp.	No side effect at starting.
	Azathioprine 50mg	Once a day (night).	25-29 weeks	Satisfactory hair regrowth obtained on scalp.	Mood changes and indigestion.
24/12/2022	Prednisolone 10mg	2tabs after breakfast	29-32 weeks	Satisfactory hair regrowth obtained on scalp and in patchy regrowth in new lesions also.	vit. B12 & D Deficiency, Indigestion, stomach pain and fatigue.
	Azathioprine 50mg	Once a day (night).	29-32 weeks		
11/01/2023	Methyl prednisolone 16mg	Saturday and Sunday one tablet.	32-43 weeks	No change in previous condition; steady hair regrowth.	Nausea, restlessness and stomach pain and vit. Deficiency.
	Azathioprine 50mg	Once a day (night).			
4/4/2023	Tofacitinib 5mg	Once a day (night).	43-51 weeks	Started the satisfactory hair regrowth on scalp and eyebrow and eyelids.	Serious side effect was often on liver after 5 weeks of using tofa. (increase level of bilirubin) liver dysfuntioning. Severe nausea, vomiting, yellow skin and required intensive medical care for 1 month.
	Mineral and multi vit. Tablet.	After lunch.			

Table 2: Injectable medication

Date	Drug	Dose	Site of admin.	Progress	Side effects
10/05/2022	Triamcinolone A. 1ml	40mg/ml	Iv on scalp	Not much progress found.	Skin thinning and itching.
7/09/2022	Triamcinolone A. 1ml	10mg/ml	Iv on scalp	Hair regrowth found in patches.	Skin thinning and itching.
24/12/2022	Triamcinolone A. 1ml	40mg/ml	Iv on scalp	Progressive regrowth.	Skin thinning and itching.
11/01/2023	Triamcinolone A. 1ml	40mg/ml	Iv on scalp	Regrowth obtained but new patches not covered.	Skin thinning and itching.
4/4/2023	Triamcinolone A. 1ml	10mg/ml	Iv on scalp	Also taken in new lesions and past hair regrowth is good.	Skin thinning and itching.
24/7/2023	Triamcinolone A. 1ml	10mg/ml	Iv on scalp	Not satisfactory effect found on new patches.	Skin thinning and itching.

Table 3: Topical medications

Date	Drug	Dose	Duration	Progress	Side Effects
22/12/2021	Tacrolimus 0.03%	Apply once a day (night)	0-8 weeks	Hair loss decreased but no hair regrowth obtained.	Skin thinning, irritation
	Triamcinolone acetonide (0.1% w/w)	Apply once a day (morning)	0-8 weeks		
26/03/2022	Benzyl nicotinate, vit K & salicylic acid solution	Apply once a day (night)	8-17 weeks	Mild patchy regrowth obtained.	Burning, redness on scalp
	Clobetasol p. 0.05% w/w	Apply once a day (morning)	8-17 weeks		
07/06/2022	Benzyl nicotinate, vit K & salicylic acid solution	Apply once a day (night)	17-33 weeks	Progressive hair regrowth obtained with new lesions on face (eyebrow) and scalp.	Burning, redness on scalp
	Fluticasone 0.05% w/w	Apply once a day (morning)	17-33 weeks	Progressive hair regrowth obtained with new lesions on face (eyebrow) and scalp.	Burning, redness on scalp
18/10/2022	Minoxidile (5%), azelic acid & tretinoin solution	Twice a day	33-69 weeks	Satisfactory hair regrowth obtained on scalp.	Sometimes itching and hypersensitivity on affected/ applied areas.
	Pimecrolimus 0.1%	Once a day	33-69 weeks		
18/02/2023	Bimatoprost 0.03%	Once a day (night)	For 12 weeks	Progressive hair regrowth eyebrows& eyelashes	Irritation at applied area (eye).

Table 4: Light Therapy

Sr.No.	Date	Session no	Dose (duration in seconds)
1	15/09/2024	1	3 patches for 12 sec.
2	23/09/2024	2	3 patches for 14sec.
3	01/10/2024	3	3 patches for 16 sec.

Due to the excess use of corticosteroids the patient suffering from liver dysfunctioning and abnormal bilirubin level. The next table showing the treatment followed for liver dysfunctioning.

Table 5: Oral treatment for liver abnormal functioning

Date	Drug	Dose	Duration	Progress
30/05/2023	Ursodeoxycholic acid 300mg	Twice a day	For 1.5 month	Stable the patient and bilirubin rate
	Liver tonic	10ml daily		
	Lecithin 1gm	Once a day		
24/07/2023	Ursodeoxycholic acid 300mg	Twice a day	For 2month.	Decrease the level of bilirubin in body and reduce inflammation on liver.
	Liver tonic	10ml daily		
	Lecithin 1gm	Once a day		
26/09/2023	Ursodeoxycholic acid 300mg	Twice a day	For 2month.	Stabilizes bilirubin level and try to regulate liver function.
	Liver tonic	10ml daily		
	Lecithin 1gm	Once a day		
06/11/2023	Ursodeoxycholic acid 300mg	Twice a day	For 1 month	Small fluctuation in liver functioning and bilirubin level.

CONCLUSION

The patient was given a customized treatment plan that includes topical immunotherapy, minoxidil, and intralesional corticosteroid injections after being diagnosed with alopecia areata. With liver dysfunction as a serious side effect of oral drugs, partial hair regrowth was observed in the affected areas over time, indicating a beneficial response to treatment. Over the course of two years, the patient received monthly check-ups and thorough monitoring. Dermoscopic examinations and photographs were used to monitor progress. Periodically, new areas of hair loss emerged, and the course of treatment was modified appropriately. Psychological care was also offered in recognition of the emotional toll that hair loss takes. The patient reported feeling better about their general quality of life and attractiveness by the end of the follow-up period.

Long-term management strategies were discussed, including stress management, ongoing dermatological assessment, and the possibility of maintenance therapy to prevent relapse.

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