Article Type: Case Report
Volume 2, Issue 1

INTERNATIONAL JOURNAL OF CLINICAL & MEDICAL CASE STUDIES

A second case of effective eradication of alopecia areata following treatment with the dopaminergic drug dextroamphetamine

Abstract

In contrast to alopecia related to conversion of terminal hairs to vellus hairs on a genetic/hormonal basis, alopecia areata (AA), is considered to have an inflammatory basis with psychogenetic and possible genetic contribution. Thus, most treatments that have been tried for AA have been attempts to interrupt the inflammatory pathways. Many of these immune suppressant drugs have both short-term side effects and also an increased risk for serious complications e.g., osteoporosis, diabetes, infection, and even cancer. Unfortunately, these autoimmune therapies have had limited efficacy. Dopaminergic drugs have been used to successfully treat a variety of autoimmune conditions that were refractory to standard immunosuppressives. A search of the literature found only one case of AA that was treated with dextroamphetamine sulfate, which was very successful. Presented here is a recent case of AA responding very well to dextroamphetamine. The corrective mechanism has been hypothesized to be related to the increase in dopamine from sympathetic nerve fibers diminishing excessive cellular permeability at the hair shaft level thus precluding infiltration of irritants that are responsible for precipitating the initial inflammatory response.

Keywords: Alopecia areata; Dopaminergic drugs; Increased cellular permeability syndrome.

Naomi Ganpo-Nkwenkwa, BS[1]; Jerome H Check, MD, PhD[1,2]*

[1]*Cooper Medical School of Rowan University, Camden, NJ, USA.*

[2]*Cooper Institute for Reproductive Hormonal Disorders, Mt Laurel, NJ, USA.*

***Corresponding author:** **Jerome H Check**
Cooper Institute for Reproductive Hormonal Disorders, Mt Laurel, NJ, 7447 Old York Road, Melrose Park, PA 19027, USA.
Tel: 215-635-4400, Fax: 215-635-2304;
Email: megan.oneil@ccivf.com

Received: Apr 08, 2025

Accepted: Apr 25, 2025

Published Online: Apr 30, 2025

Journal: International Journal of Clinical & Medical Case Studies

Copyright: © **Check JH** (2025). *This Article is distributed under the terms of Creative Commons Attribution 4.0 International License*

Introduction

Alopecia areata (AA) is the most common immune-mediated non-scarring type of hair loss affecting approximately 0.1-0.2% of the population, with a lifetime risk of 2% in the US [1]. AA patient-population is worldwide and there are no differences among age groups, sexes, and ethnicities. Patients may experience frustration due to the unpredictable nature of their disease, for which there is no definitive treatment [2].

The hair loss is usually found to be a localized circumscribed patch or patches which can be divided into subtypes. Those include Alopecia Ophiasis (AO), an occipital band, alopecia sisaipho a crown scalp, patch of hair loss, diffuse AA, complete loss of scalp hair (alopecia totalis (AT)) and complete loss of scalp and body hair (alopecia universalis (AU)). The AA scalp hair loss can be visually categorized by the Severity of Alopecia Tool (SALT) score ranging from 0%-100% [1-3].

During examination, exclamation point hairs, dystrophic hairs and yellow dots are features of AA that can only be identified through trichoscopy; which helps to determine areas to collect for a biopsy specimen [3]. Nail changes ranging from pitting to trachyonychia are more common in children and patients with severe AA (such as AT and AU), and they have a prevalence of approximately 30% [4].

Family members of those with AA and identical twins have a higher incidence of the disease [5,6]. Mouse models suggest a polygenic nature to AA [7]. According to various studies, AA has been associated with concurrent diseases (comorbidities), including depression, anxiety, autoimmune diseases, and other conditions such as asthma, allergic rhinitis, atopic dermatitis, diabetes, hypertension vitiligo, thyroiditis and systemic lupus erythematosus [8,9]. Furthermore, psychological stressors, smoking, alcohol consumption, sleep disturbance, gut microbiota, and drugs have been postulated to play a role in the pathogenesis of AA, by exacerbating the immune response against the hair follicles [10].

The hair growth cycle follows four distinct stages including anagen (growth phase) followed by catagen (transition phase), then telogen (resting/inactive phase) and finally exogen (shedding phase). A portion of the anagen phase Hair Follicle (HF) consists of an immune privileged site similar to the anterior chamber of the eyes, pregnant uterus and the testes [10]. In HF, the immune privileged sites prevent autoimmune responses against autoantigens expressed in the bulb; this is done through three distinct theorized mechanisms. First, the HF extracellular matrix acts as a barrier to prevent immune cells from being transferred in and out the HF [11]. Second, there is downregulation of the expressions of Major Histocompatibility Complex (MHC) class I and II molecules in anagen hair bulbs, which can sequester autoantigens from being presented to CD8+ T-cells, CD4+ T-cells, and Natural Killer (NK) cells [12]. Third, the epithelium secretes local immunosuppressant molecules known as "IP guardians" which form immune inhibitory sections. They suppress interferon-gamma (IFN-γ) expression of MHC molecules to protect sequestered antigens. They include Transforming Growth Factor-β1 (TGF-β1), Interleukin-10 (IL-10), α-Melanocyte Stimulating Hormone (α-MSH), Indoleamine-2,3-Dioxygenase (IDO), somatostatin and vasoactive intestinal peptide (VIP) [13].

There have been multiple investigations to explain the autoimmune nature of AA. In AA the HF cycle becomes disrupted, leading to a dystrophic and inflammatory anagen phase, and a premature catagen phase; described as an immune privilege collapse. Environmental stress can lead to build up of reactive oxygen species in HF keratinocytes. Reported triggers including emotional stress or physical stress, vaccinations, viral infections (eg: Epstein Barr virus, severe acute respiratory syndrome coronavirus 2, Hepatitis B and C) and medications [14]. In AA initiation, there is stimulation of Cytotoxic T cells (CTLs) which activate IFN-γ, that upregulate proteins including MHC class I polypeptide-related sequence A (MICA), leading to increased expression of MHC class I [15,16]. The stressed environment could also downregulate "IP guardians". This dysregulation renders anagen HFs targets of "bee-swarm-like" lymphocytic infiltrate of NKG2D+ T-cells and natural killer (NK) cells in the growing hair bulb interacting with auto-reactive CD8+ T-cells [17]. This leads to the secretion of the key mediator of AA, IFN-γ, which binds IFN-γ receptors, leading to upregulation of IL-15 and other inflammatory chemokines (e.g., MICA and CXCL9/10/11) in the HF via the Janus Kinase- JAK-STAT pathway [13]. In CD8+ T-cells, IL-15 upregulates the production of perforin and cytotoxic granzymes, causing them to produce even more IFN-γ. It creates a positive feedback loop resulting in the destruction of HF cells and the hair growth cycle [12,18]. Furthermore, they found MHC type 2 cell involvement, for which CD4+ T-cells aggravate the process, while Tregs and iNKT cells may provide relative protection against development of AA [14].

There is little question that psychological stress plays an important role in the pathophysiology of AA; AA onset has been associated with neuropeptides which are secreted in response to psychological stress such as Substance P (SP) and Corticotropin Releasing Hormone (CRH) [19]. SP initiates the nerve response to stress by acting as a neurotransmitter and neuromodulator that delivers inflammatory and pain signals. It has been confirmed from other studies that psychological stress upregulates the expression of SP of the peripheral nervous system on the human scalp [20,21]. Recent C3H/Hej mice studies have shown that serum SP levels on immunohistochemical analysis are increased along with their receptors, Neurokinin-1-Receptors (NK1R) in the scalps of patients with AA [22]. CRH is secreted by the hypothalamus at the HPA axis, and stimulates Adrenocorticotropic Hormones (ACTH) which promotes the synthesis of glucocorticoids, such as cortisol, in response to unexpected psychological stress. According to studies, it was shown that CRH, ACTH and alpha-melanocyte-stimulating hormone (alpha-MSH) expression were significantly higher in the scalp epidermis and HFs of patients with AA [23,24]. Overall, results from studies on SP and CRH indicate a defective signaling system in the cutaneous HPA axis and/or peripheral nerves involved in the pathogenesis of AA. Furthermore, they also have both been implicated in studies demonstrating their association with induction of mast cells degranulation, which further contributes to the polarization and expansion of CD8+ T-cells in AA [25].

Due to the unpredictable nature of AA, there are a plethora of treatments available. Although AA pathogenesis is a very destructive process, the HF epithelial stem cells located in the bulge are not mainly attacked. Therefore, AA can be reversible even in the majority of severe cases. The key prerequisite to the treatment of AA is the re-establishment of HF-immune privilege for a spontaneous or long-term remission. A spontaneous recovery for hair growth is seen in 35-50% within one year after AA occurred [25]. Currently there are a wide variety of treatments available from nonmedical (e.g., microblading and hair synthetics) to medical intervention targeting the immunological pathway. There are no defined treatment guidelines available, however a useful flowchart was published by Alhanshali et al in 2023 on treatment strategy [26].

Steroids, intralesional and/or topicals are considered first-line therapy for patchy AA and more extensive AA; they contain anti-inflammatory properties that help with HF regrowth [10]. Topical immunotherapies for treatment of AA include Diphenylcyclopropenone (DPCP) or Squaric Acid Dibutylester (SADBE), altering local immune response by shifting T-cell mediated autoimmunity away from targeted HF. Minoxidil, is a form of adjunctive therapy for AA, as in either topical or oral forms. However, it is not an effective monotherapy for patients with severe AA [10]. Minoxidil has been shown to shorten hair follicle telogen phase, increase anagen phase duration, and increase hair diameter and length [28]. For treatment-resistant AA or severe forms of AA including totalis and universalis, JAK inhibitor therapy is recommended. There is now a FDA approved JAK inhibitor drug named baricitinib. However, due to its immunosuppressive potency, patients must be warned of possible side effects e.g., malignancy, major adverse cardiovascular events, leukopenia, thrombocytopenia and gastrointestinal side effects [9].

Thus, unfortunately, none of the above referenced therapies are very effective for AA and some had significant short term side effects and potential long-term risks e.g., cancer or serious infections e.g. with treatment with corticosteroids or immunosuppressives.

Case report

An 18-year-old teenage young lady was referred to a rheumatologist for joint pain. She also had a 3 cm patch of alopecia in the occipital region of her head. She had a positive serum rheumatoid factor test. The rheumatologist diagnosed her with rheumatoid arthritis and AA. She was treated with prednisone and after one year she had considerable improvement in her joint pain and the bald area started to develop terminal hairs thus after 6 months the bald occipital area was not as noticeable but slightly thinner than the rest of her head hair. It should

be noted that she was under considerable stress at age 18 because her mother was very ill.

At the age of 32 she started losing hair again in the same occipital area as at age 18 reaching a size of 6.5 cm thus leaving a larger bald spot. The AA persisted until age 35 when she sought help for infertility related to diminished oocyte reserve, severe dysmenorrhea and a past history of rheumatoid arthritis, it was considered that at least part of her infertility may be related to excessive inflammation with immune rejection of the fetus related to excessive infiltration of irritants into the pelvic tissue related to increased cellular permeability [29-33]. Drugs that release more dopamine from sympathetic nerve endings diminish cellular permeability and thus diminish the inflammation [29-33].

She was started in 15 mg amphetamine tables upon arising in the morning and at noon providing 18.8 mg dextroamphetamine sulfate per day. She noticed after 3 weeks some hairs growing in her bald spot. After 3 months the AA was totally covered by normal length hair with normal thickness.

The dosage of amphetamine salts was increased monthly until 60 mg was reached (37.6 mg dextroamphetamine). Her dysmenorrhea was also eradicated. Related to a shortage of amphetamines she did not take the dextroamphetamines for 10 days after 6 months of steady intake. There were no withdrawal symptoms, but after a week she noticed increased hair loss from the occipital spot. Upon resumption of the drug the shedding stopped.

She is now 10 months from initial treatment and for the first time since age 18 there is not even any subtle thinning in the occipital area. After failing to conceive after a few cycles of treatment with dextroamphetamine daily and progesterone vaginal suppositories in the luteal phase so she decided to have in vitro fertilization embryo transfer performed. She became pregnant with twins, and she is presently in her second trimester.

Discussion

As mentioned in the introduction, there is strong evidence that alopecia areata, alopecia totalis, and alopecia universalis has an autoimmune etiology with a strong psychogenic factor initiating autoimmune events in many cases. Because remission and exacerbation are not unusual with inflammatory alopecia, one cannot always state with certainty that the treatment rendered was responsible for the improvement.

Nevertheless, we favor that the treatment that was rendered is most likely the reason for the marked quick improvement of the AA. Dopaminergic drugs have been very successful in eradicating symptoms or signs of many chronic illnesses considered to be on an autoimmune basis despite failure with other immunosuppressive drugs in both men and women [29,31,32,34-37]. In fact, dopaminergic drugs especially dextroamphetamine treatment, have resulted in long lasting remission in certain severe treatment autoimmune conditions in which the patients were considered moribund including mesenteric sclerosis, autoimmune hepatitis, and pancreatitis [39,40,41]. Evidence that inflammation in this case was being suppressed by dextroamphetamine was demonstrated, also resulting in complete relief of dysmenorrhea. Pelvic pain and endometriosis have been associated with other pathological conditions including autoimmune conditions [33,40].

This is not the first case published suggesting that inflammatory alopecia may be improved by treatment with the dopaminergic drug cabergoline. In 2014, another convincing case report was published strongly suggesting that dextroamphetamine sulfate helped a 62-year-old woman who initially presented with alopecia areata in her head and pubic hair to full blown alopecia totalis and universalis [41]. Unfortunately, however, the most recent updates in treating AA do not mention either sympathetic amines or dopaminergic drugs to treat AA [10,13,25,26]. Dextroamphetamine has also been found to treat another autoimmune condition associated with inflammatory alopecia i.e., discoid lupus erythematosus [42].

We have seen other cases of AA respond to dopaminergic drugs but we thought that at the 10 year anniversary of our previous publication it was time to write another case report to hopefully stimulate interest in a dermatologic group who have a larger volume of patients with AA to determine if dextroamphetamine or other dopaminergic drugs are effective in only a minority of cases of AA, or whether this very safe, very well tolerated, drug can be effective for the majority of cases of AA.

There are other dopaminergic drugs e.g., cabergoline that have successfully treated chronic treatment refractory conditions related to increased cellular permeability syndrome [43-45]. Even levo dopa has been found to be very effective for vulvovaginitis [46]. In general, we have found dextroamphetamine to be more effective for treating inflammatory disorders than various immunosuppressives and much safer [29,37].

References

1. Kalil L, King B. Innovation in Alopecia Areata. Dermatol Clin. 2025; 43: 27-33.
2. Strazzulla LC, Wang EHC, Avil L, Lo Sicco K, Brinster N, Christiano AM, et al. Alopecia areata: Disease characteristics, clinical evaluation, and new perspectives on pathogenesis. J Am Acad Dermatol. 2018; 78: 1–12.
3. Tosti A, Whiting D, Iorizzo M, Pazzaglia M, Misciali C, Vincenzi C, et al. The role of scalp dermoscopy in the diagnosis of alopecia areata incognita. J Am Acad Dermatol. 2008; 59: 64-67.
4. Chelidze K, Lipner SR. Nail changes in alopecia areata: An update and review. Int J Dermatol. 2018; 57: 776-783.
5. Rodriguez TA, Fernandes KE, Dresser KL, Duvic M. Concordance rate of alopecia areata in identical twins supports both genetic and environmental factors. J Am Acad Dermatol. 2010; 62: 525–527.
6. Betz RC, Petukhova L, Ripke S, Huang H, Menelaou A, Redler S, et al. Genome-wide meta-analysis in alopecia areata resolves HLA associations and reveals two new susceptibility loci. Nat Commun. 2015; 6: 5966.
7. Sundberg JP, Silva KA, Li R, Cox GA, King LE. Adult-onset Alopecia areata is a complex polygenic trait in the C3H/HeJ mouse model. J Invest Dermatol. 2004; 123: 294–297.
8. Ahn D, Kim H, Lee B, Hahm DH. Psychological Stress-Induced Pathogenesis of Alopecia Areata: Autoimmune and Apoptotic Pathways. Int J Mol Sci. 2023; 24: 11711.
9. Chu SY, Chen JY, Tseng WC, Lin MW, Chen TJ, Hwang CY, et al. Comorbidity profiles among patients with alopecia areata: the importance of onset age, a nationwide population-based study. J Am Acad Dermatol. 2011; 65: 949–956.
10. Abarca YA, Scott-Emuakpor R, Tirth J, Moroz O, Thomas GP, Yateem D, et al. Alopecia areata: Understanding pathophysiology

and advancements in treatment modalities. Cureus. 2025; 17: e78298.

11. Żeberkiewicz M, Rudnicka L, Malejczyk J. Immunology of alopecia areata. Cent Eur J Immunol. 2020; 45: 325-333.

12. Paus R, Nickoloff BJ, Ito T. A 'hairy' privilege. Trends Immunol. 2005; 26: 32–40.

13. Zhou C, Li X, Wang C, Zhang J. Alopecia areata: An update on etiopathogenesis, diagnosis, and management. Clin Rev Allergy Immunol. 2021; 61: 403–423.

14. Bertolini M, McElwee K, Gilhar A, Bulfone-Paus S, Paus R. Hair follicle immune privilege and its collapse in alopecia areata. Exp Dermatol. 2020; 29: 703-725.

15. Ito T. Recent advances in the pathogenesis of autoimmune hair loss disease alopecia areata. Clin Dev Immunol. 2013; 2013: 348546.

16. Kang H, Wu WY, Lo BKK, Yu M, Leung G, Shapiro J, et al. Hair follicles from alopecia areata patients exhibit alterations in immune privilege-associated gene expression in advance of hair loss. J Invest Dermatol. 2010; 130: 2677–2680.

17. Lepe K, Syed HA, Zito PM. Alopecia areata. In StatPearls. StatPearls Publishing. 2024. https://www.ncbi.nlm.nih.gov/books/NBK537000/

18. Katsambas AD, Lotti TM, Dessinioti C, D'Erme AM. (Eds.). Alopecia areata. In European Handbook of Dermatological Treatments (4th ed.). Springer. 2023.

19. Rokowska-Waluch A, Pawlaczyk M, Cybulski M, Zurawski J, Kaczmarek M, Michalak M, et al. Stressful events and serum concentration of substance P in acne patients. Ann Dermatol. 2016; 28: 464–469.

20. Wang L, Guo LL, Wang LH, Zhang GX, Shang J, Murao K, et al. Oxidative stress and substance P mediate psychological stress-induced autophagy and delay of hair growth in mice. Arch Dermatol Res. 2015; 307: 171–181.

21. Kim C, Shin JM, Kim D, Park S, Hong D, Jung KE, et al. Role of substance P in regulating micro-milieu of inflammation in alopecia areata. Ann Dermatol. 2022; 34: 270–277.

22. Westphal NJ, Seasholtz AF. CRH-BP: The regulation and function of a phylogenetically conserved binding protein. Front Biosci. 2006; 11: 1878–1891.

23. Kim HS, Cho DH, Kim HJ, Lee YJ, Cho BK, Park HJ. Immunoreactivity of corticotropin-releasing hormone, adrenocorticotropic hormone and alpha-melanocyte-stimulating hormone in alopecia areata. Exp Dermatol. 2006; 15: 515–522.

24. Asadi S, Alysandratos KD, Angelidou A, Miniati A, Sismanopoulos N, Vasiadi M, et al. Substance P (SP) induces expression of functional corticotropin-releasing hormone receptor-1 (CRHR-1) in human mast cells. J Investig Dermatol. 2012; 132: 324–329.

25. Trüeb RM, Dias MF. Alopecia areata: a comprehensive review of pathogenesis and management. Clin Rev Allergy Immunol. 2018; 54: 68–87.

26. Alhanshali L, Buontempo MG, Lo Sicco KI, Shapiro J. Alopecia areata: Burden of disease, approach to treatment, and current unmet needs. Clin Cosmet Investig Dermatol. 2023; 16: 803–820.

27. Happle R. Topical immunotherapy in alopecia areata. J Invest Dermatol. 1991; 96: 71s–72s.

28. Messenger AG, Rundegren J. Minoxidil: mechanisms of action on hair growth. Br J Dermatol. 2004; 150: 186–194.

29. Check JH. Most chronic conditions in women are related to increased cellular permeability and most can be effectively treated with dopaminergic drugs. J Biomed Res Environ Sci. 2024; 5: 373-386.

30. Check JH. Treating pelvic pain and endometriosis with the goal of correcting infertility and/or preventing miscarriage. J Reprod Med Gynecol Obstet. 2024; 9: 167.

31. Check JH, Neumann B. Combined Dopaminergic Drugs with Supplemental Progesterone to Treat Recurrent Miscarriage and Ulcerative Colitis despite Diminished Egg Reserve. Gynecol Reprod Health. 2024; 8: 1-10.

32. Check JH, Check DL, Neumann B. A Novel Treatment of Crohn's Disease that is Not Only Safe in Pregnancy but Can Correct Infertility and Recurrent Miscarriages. Gynecol Reprod Health. 2024; 8: 1-9.

33. Check JH. Increased tissue permeability and sympathetic nervous system hypofunction may be the common link between dysmenorrhea, chronic pelvic pain, Mittelschmerz, and Crohn's disease. Clin Exp Obstet Gynecol. 2016; 43: 112-113.

34. Boimel P, Check JH. Marked improvement of intractable arthritic pain in a woman with rheumatoid arthritis with sympathomimetic amine treatment despite previous failure with standard therapy and possible implications for last trimester unexplained fetal demise – case report. Clin Exp Obstet Gynecol. 2007; 34: 254-256.

35. Check JH, Katsoff B, Cohen R. A case report showing that a woman with ulcerative colitis refractory to standard therapy responded well to the sympathomimetic amine dextroamphetamine sulfate. Inflam Bowel Dis. 2011; 17: 870-871.

36. Check JH, Katsoff B, Cohen R. A novel highly effective medical treatment of severe treatment refractory Crohn's disease using sympathomimetic amines – case report. Inflam Bowel Dis. 2010; 16: 1999-2000.

37. Check DL, Check JH. Various presentations of the increased cellular permeability syndrome in males responding very well to sympathomimetic amine therapy – possible treatment for end-stage Covid-19 complications. J Med Clin Res & Rev. 2020; 4: 1-7.

38. Weidner J, Check JH. Marked improvement of the autoimmune syndrome associated with autoimmune hepatitis by treatment with sympathomimetic amines. Clin Exp Obstet Gynecol. 2014; 41: 460-461.

39. Check JH, Neumann B, Check DL. Dopaminergic drugs to relieve pain from chronic pancreatitis – a novel therapy. J Med Clin Res Rev. 2024; 8: 1-4.

40. Check JH, Cohen R. The triad of luteal phase ocular migraines, interstitial cystitis, and dyspareunia as a result of sympathetic nervous system hypofunction. Clin Exp Obstet Gynecol. 2014; 41: 575-577.

41. Check JH, Cohen R. An update on the treatment of female alopecia and the introduction of a potential novel therapy. Clin Exp Obstet Gynecol. 2015; 42: 411-415.

42. Check JH, Neumann BA, Check DL. The use of dopaminergic drugs for treating cutaneous discoid lupus erythematosus: a case study. J Med Clin Res & Rev. 2024; 8: 1-3.

43. Check JH, Check D. Improvement of severe chronic pelvic pain and dysmenorrhea following treating with cabergoline. Gynecol Reprod Health. 2023; 7: 1-6.

44. Check JH, Check DL, Neumann B. Marked improvement of severe treatment resistant migraine headaches with the dopaminergic drug cabergoline. J Med-Clin Res & Rev. 2024; 8: 1-5.

45. Check JH, Lombardi G, Vaniver J. Two New Clinical Manifestations of the Increased Cellular Permeability Syndrome Responding Well to Dopaminergic Drugs: Carpel Tunnel Syndrome and Sesamoiditis. BioMed Res J. 2024; 8: 814-818.

46. Ford B, Louis ED, Greene P, Fahn S. Oral and genital pain syndromes in Parkinson's disease. Mov Disord. 1996; 11: 421-426.