

COVID-19 vaccination related exacerbations of hair loss in patients with moderate-to-severe alopecia areata on systemic therapy



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Key words: alopecia areata; COVID-19; hair loss; hair shedding; infection; vaccine.

INTRODUCTION

Vaccine-induced adverse events are a concern among both healthy individuals and those with preexisting conditions. The concern is that the safety of any vaccine cannot be easily generalizable to populations who are not routinely included in clinical trials, such as patients with chronic autoimmune and inflammatory disorders.¹ The paucity of data and concerns related to disease exacerbations of these preexisting inflammatory conditions can serve as a source of vaccine hesitancy among patients. Several studies have observed exacerbations of preexisting autoimmune or autoinflammatory disorders in at-risk populations postvaccination.² The current literature describes exacerbations of preexisting rheumatoid arthritis, subcutaneous lupus erythematosus, pemphigus vulgaris, and bullous pemphigoid following COVID-19 vaccinations.³⁻⁵ Although alopecia exacerbation following COVID-19 vaccinations is rarely reported, it is a frequent concern among patients. Alopecia areata (AA) has been observed following routine vaccinations, such as influenza, zoster, and human papilloma virus vaccines, thus an association cannot be ignored.^{6,7} In our clinic, we have a well-established population of patients with AA using systemic therapies who are closely followed with clinical photographs, creating a small, yet ideal, study group to evaluate the validity of these concerns. Here, we evaluate our patients with stable AA for new-onset hair loss episodes, potentially associated with a recent COVID-19 vaccination.

Abbreviations used:

AA:	alopecia areata
JAKi:	janus kinase inhibitor
mRNA:	messenger RNA
SALT:	Severity of Alopecia Tool
TLR:	toll-like receptors

METHODS

The study design is based on data analysis of medical records of patients with moderate-to-severe AA. All patients were from our alopecia registry, on systemic therapy (janus kinase inhibitors [JAKis]), and had had stable disease for at least 3 months (January–November 2021; n = 69; average therapy duration, 16 months). As a control, patients with moderate-to-severe AA who did not receive any COVID-19 vaccinations were used as a comparative group.

As a standard of care, all patients with AA in our clinic are followed closely (on average, every 1–2 months) with assessments of hair loss (Severity of Alopecia Tool [SALT] score), a review of systems, medical history, photographs, and a clinical examination at every visit. All patients were confirmed to have had stable hair loss or regrowth in the 3 months preceding their vaccination event. As part of their history, patients were asked to report any hair loss on the scalp, eyebrow/eyelash, or body between visits. Any reports of purported changes after receiving a COVID-19 vaccination were temporally confirmed, as well as the onset and duration of these exacerbations.

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Funding sources: None.

IRB approval status: Approved.

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JAAD Case Reports 2022;29:181-5.
2352-5126

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<https://doi.org/10.1016/j.jidcr.2022.08.016>

Table I. Demographic information of vaccinated patients with alopecia areata (n = 49). B, COVID-19 vaccination history and observed change in SALT score of patients with hair loss after COVID-19 vaccination

Demographics	Hair loss after vaccination	
	Yes, n = 3	No, n = 45
Age (mean)	30.6	37.2
Sex, n (%)		
Male	2 (66.6)	23 (50.0)
Female	1 (33.3)	23 (50.0)
Race, n (%)		
White	3 (100)	20 (44.4)
Asian or Pacific Islander	0 (0)	15 (33.3)
American Indian or Alaska Native	0 (0)	0 (0)
Black or African American	0 (0)	2 (4.4)
Other	0 (0)	8 (17.8)
Hispanic, Latino, or Spanish origin, n (%)		
Yes	1 (33.3)	5 (11.1)
No	2 (66.6)	40 (89.9)

F, Female; M, male; Mo, Moderna mRNA vaccine; P, BioNTech-Pfizer vaccine; SALT, Severity of Alopecia Tool.

RESULTS

We identified a total of 69 patients with stable moderate-to-severe AA on systemic JAKi therapy, 49 of whom received COVID-19 vaccinations (25 men, 24 women; average age, 36.9 years; range, 14-72 years) and 20 unvaccinated patients (12 men, 8 women; average age, 36.1 years; range, 27-62 years). All patients had a documented clinical course with stable hair loss/regrowth for at least 3 months (previous hair loss episodes duration, 1-9 years) (Tables I and II). The majority of patients received the BioNTech/Pfizer BNT162b2 vaccine (n = 29; 59.2%), followed by the Moderna messenger RNA (mRNA)-1273 vaccine (n = 14, 28.6%), and the Ad26.COVS vaccine from Johnson & Johnson (n = 6, 12.2%) (Table III).

In this case series, only 3 patients reported hair loss (n = 2 BioNTech/Pfizer, n = 1 Moderna mRNA) (2 men, 1 woman; average age, 30.6 years). These patients denied any other associated vaccination symptoms, changes in health, medications, or stress/lifestyle. None had a prior history of COVID-19 infection. Two of the affected patients identified as White, and 1 as Hispanic/Latino. Hair loss in these patients occurred an average of 2 weeks after receiving the vaccine and lasted up to 20 weeks. Observed hair loss was measured by an increase in patient SALT scores as follows: (1) patient 1, SALT 66 to SALT 99 at 2 weeks after the first dose of the

BioNTech/Pfizer vaccine (Fig 1); (2) patient 2, SALT 34 to SALT 59 at 2 weeks after the second dose of the BioNTech/Pfizer vaccine (Fig 2); and (3) patient 3, SALT 62 to SALT 70 at 2 weeks after the first dose of the Moderna mRNA vaccine (Fig 3).

Patient 1 was seen in clinic 3 weeks before receiving the first dose of the BioNTech/Pfizer vaccine (December 21, 2020, SALT 66). She reported a rapid onset of hair shedding within 2 weeks after the vaccine, which continued and intensified after receiving the second dose a month later, resulting in near complete loss of scalp hair on follow-up (March 01, 2021, SALT 99). The hair loss persisted with minimal changes at 3 and 6 months (June 29, 2021, SALT 99 and September 20, 2021, SALT 95). Patient 2 did not experience any hair loss for 4 months after his initial vaccination (BioNTech/Pfizer) (May 13, 2021, SALT 33). However, he reported hair loss 2 weeks after receiving the second vaccine dose (September 1, 2021, SALT 59). He opted not to receive a booster vaccine within the study period. Patient 3 was seen in clinic 1 week before receiving the first dose of the Moderna mRNA vaccine (June 23, 2021, SALT 62). Similar to the others, he reported hair shedding that occurred 2 weeks after receiving the first dose, which continued after receiving the second vaccine dose. He was evaluated 1 month after his second dose with an increase in the SALT score (September 8, 2021, SALT 70). He has not received the booster vaccine. Eyebrow/eyelash hair loss was only reported in 1 patient.

In these patients, all laboratory data, including complete blood cell count, comprehensive metabolic panel, and lipid panel showed no significant changes or abnormalities after COVID-19 vaccination (range; 1-2 months before and after event). Additionally, none of the 3 affected patients exhibited clinical signs of a more robust immunologic response, such as severe fever, fatigue, myalgias, or arthralgias, after the COVID-19 vaccination as compared with the other vaccinated patients. Potential additional telogen effluvium triggers, such as significant weight loss, change in diet or nutritional deficiency, severe acute or chronic illness, infection, emotional stress or trauma, medication changes, or changes in overall health were not observed in the vaccinated patients during our 6-month review period. No dose changes or treatment interruptions in JAKi systemic therapy were reported in our vaccinated cohort at any time. All vaccinated patients, irrespective of hair loss, reported that they would still recommend the COVID-19 vaccine to other patients with AA.

Table II. COVID-19 vaccination history and observed change in SALT score of patients with hair loss after receiving COVID-19 vaccine

Patient	Age (y)	Gender	COVID-19 vaccination 1st	COVID-19 vaccination 2nd	COVID-19 vaccination 3rd	SALT before vaccination	SALT after vaccinations	Total SALT Δ increase
1	33	F	P* Hair loss [‡]	P* Hair loss [‡]	P* Hair loss [‡]	66	99	33
2	27	M	P*	P* Hair loss [‡]	†	34	59	25
3	32	M	Mo* Hair loss [‡]	Mo* Hair loss [‡]	†	62	70	8

F, Female; M, male; Mo, Moderna mRNA vaccine; P, BioNTech-Pfizer vaccine; SALT, Severity of Alopecia Tool.

*Received COVID-19 vaccination.

†Did not receive COVID-19 vaccination.

‡Flares following vaccination.

Table III. COVID-19 vaccination history and hair loss after COVID-19 vaccination

Vaccination history	Vaccinated subjects n = 49 (%)
1. Patients who received the COVID-19 vaccine:	
Yes	49 (100)
No	0 (0.0)
2. Patients who received the second injection of the COVID-19 vaccine if required:	
Yes	48 (97.9)
No	1 (2.1)
3. Type of COVID-19 vaccine:	
Moderna	14 (28.6)
Pfizer	29 (59.2)
Johnson & Johnson	6 (12.2)
AstraZeneca	0 (0.0)
BioNTech	0 (0.0)
Inovio	0 (0.0)
4. COVID-19 vaccine exacerbated patient hair loss:	
Yes	3 (6.1)
No	46 (93.9)
5. Areas with increased hair loss after receiving the COVID-19 vaccine(s):	
Scalp hair loss	3 (100)
Eyebrow/eyelash hair loss	1 (2.0)
Body hair loss	0 (0.0)
6. Patients who made changes to any medications owing to the COVID-19 vaccine:	
Yes	0 (0.0)
No	49 (100)

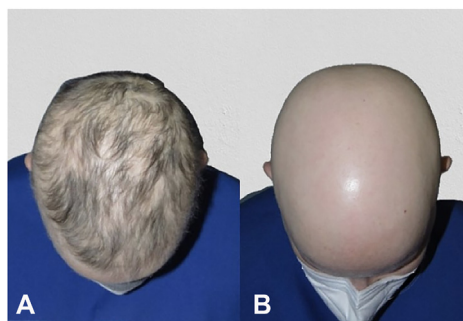


Fig 1. A 33-year-old women with moderate-to-severe alopecia areata (A) before (SALT 66%) and (B) 2 weeks after (SALT 99%) receiving the BioNTech/Pfizer BNT162b2 COVID-19 vaccine (first dose). SALT, Severity of Alopecia Tool.



Fig 2. A 27-year-old man with moderate-to-severe alopecia areata (A) before (SALT 34%) and (B) 2 weeks after (SALT 59%) receiving the BioNTech/Pfizer BNT162b2 COVID-19 vaccine (second dose). SALT, Severity of Alopecia Tool.

In contrast, in our unvaccinated cohort, there was only 1 documented case of hair loss that interestingly following a SARS-CoV-2 infection, defined as mild (not resulting in hospitalization). A 50-year-old-woman reported hair loss 3 weeks after initially testing positive for SARS-CoV-2. The increase observed in her SALT scores were: SALT 8 to SALT

50 at 3 weeks after testing positive, with subsequent shedding that lasted up to 16 weeks. This patient did not report significant weight loss, change in diet or nutritional deficiency, severe acute or chronic illness, infection, emotional stress, or trauma. Additionally,



Fig 3. A 32-year-old man with moderate-to-severe alopecia areata (**A**) before (SALT 62%) and (**B**) 2 weeks after (SALT 70%) receiving the Moderna mRNA-1273 COVID-19 vaccine (first dose). *SALT*, Severity of Alopecia Tool.

no dose changes or treatment interruptions in JAKi systemic therapy or other medications were reported.

DISCUSSION

Hair loss following COVID-19 vaccination has been poorly defined and reported cases remain few, yet patients' forums and social media propagate them swiftly. Based on our observations, a rare, yet undeniable association, may exist based on our population of closely followed patients with moderate-to-severe AA. We could not identify any rare attributes of the 3 patients who appeared to be adversely impacted by the COVID-19 vaccine, except that they were relatively younger (average age, 30.6 years) than those not affected (average age, 37.2 years). The hair loss exacerbation onset occurred relatively early (within 2 weeks after vaccination) and was seen in patients who received both types of mRNA vaccines (BioNTech/Pfizer and Moderna mRNA). Two patients experienced worsening hair loss following the first dose and 1 after the second. Notably, on extended follow-up, the 2 vaccinated patients who had hair loss following their first vaccine (BioNTech/Pfizer and Moderna mRNA) have since received their second dose and, again, experienced hair shedding. All affected patients reported a reluctance to receive the third dose of mRNA vaccines. In the literature, a single case of hair loss has been described in a patient with AA who received the AstraZeneca—Oxford University COVID-19 (AZD1222/ChAdOx1) vaccination, and we have also encountered a patient with symptom of new-onset patchy AA after receiving the Johnson & Johnson COVID-19 vaccination (senior author clinic patient, not published, but reported to the company).^{8,9}

In contrast, AA flares are now well associated with SARS-CoV-2 infection, both as exacerbations of the preexisting disease or as novel diagnoses.^{9,10} Among

our nonvaccinated AA cohort, the only case of hair loss exacerbation was observed following a SARS-CoV-2 infection. A large report assessing new-onset AA following COVID-19 infection from South Korea ($n = 226,737$; COVID-19 cases = 7,958) failed to observe a significant association of new-onset AA after contracting the SARS-CoV-2 infection (incidence rate ratio [95% CI]: 0.78 [0.48-1.27]).¹¹

To date, 3 reports have described a recurrence of AA flares (both patchy and widespread patterns) in patients with disease stability after COVID-19 vaccinations.^{8,9,12} Implicated vaccines include the BioNTech/Pfizer ($n = 7$), Moderna mRNA ($n = 3$) and AstraZeneca AZD1222/ChAdOx1 ($n = 2$) vaccines.^{8,9,12} Recent studies suggest inflammatory storms following COVID-19 vaccinations may contribute to the increased incidence and relapses in autoimmune diseases observed during the pandemic. Both mRNA and adenoviral vector vaccines display systemic immune activation following exposure. mRNA-based vaccines are known to stimulate innate immune reactions through the activation of toll-like receptors (*TLR7* and *TLR8* genes), which lead to the release of inflammatory cytokines and type I interferons implicated in AA pathology.¹³ In theory, such aforementioned cytokine and chemokine responses to RNA-based COVID-19 vaccinations may contribute to disease flares in predisposed patients. An alternate theory suggests that molecular mimicry with respect to viral and self-peptides may induce disease flares caused by autoreactive T and B cells.² These foregoing, proposed mechanisms have further encouraged the discussion of the theoretical risk of autoimmune disease relapse triggered by COVID-19 vaccines.

In this population, all of the patients were on a systemic therapeutic immunomodulator, however, the preventative or associated role of this systemic intervention cannot be determined. It is important to note that these patients experienced hair loss despite being on systemic JAKi therapy. In addition, there may be the unexplained possibility that interaction between systemic JAKi therapy and COVID-19 vaccination contributes to observed hair loss. This study is limited by the small sample size but reflects our intent to obtain the best-controlled study population. This limitation makes it challenging to assess a definitive link between COVID-19 vaccines and worsening hair loss. Therefore, we cannot extrapolate the data from this study to the general population or make assumptions about the prevalence or incidence of the observed events. Despite our best efforts, we cannot definitively dismiss the possibility that these events were coincidental because of the unpredictable nature of the disease.

CONCLUSION

Although an association between hair loss and COVID-19 vaccinations may be present, these exacerbation events are infrequent. The benefits from COVID-19 vaccinations considerably outweigh the theoretical risk of autoimmune flares among susceptible individuals. Additional large-scale studies with diverse patient populations are needed to broaden our understanding of immune-mediated, postvaccination adverse effects.

Conflicts of interest

None disclosed.

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