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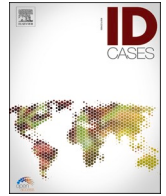
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Case report

Alopecia universalis after injection of messenger RNA COVID-19 vaccine. A case report

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ABSTRACT

Messenger RNA vaccines against SARS-CoV-2 infection, or COVID-19 dramatically changed the landscape of the fight against COVID-19 pandemic. However, they might be associated with various side effects, such as myocarditis. Herein we report a case of alopecia universalis occurring after injection of an mRNA COVID-19 vaccine in a Japanese patient. Healthcare workers should be aware of this rather rare complication after vaccinations.

Introduction

Messenger RNA vaccines against SARS-CoV-2 infection, or COVID-19 dramatically changed the landscape of the fight against COVID-19 pandemic. The vaccines are well tolerated with a fairly good safety profile [1]. However, it is not without significant adverse side effects like any other vaccines, and healthcare workers should remain to be aware of their potential risks. Here, we report a case of alopecia universalis occurring in a female who received mRNA COVID-19 vaccines.

Case report

A Japanese female patient in her 40s without significant past medical history was referred to the Kampo clinic of the hospital with hair loss in her body. She was in her usual state of health but developed acute onset hair loss 1 week after the receipt of the first dose of mRNA-1273 intramuscularly in August 2021. She lost her head hair, eyebrows, eyelashes, axillary hair, pubic hair, and hair on the arms and legs. She again received the second dose of the same vaccine a month later and there was no additional event except for a mild fever for a few days.

She denied any significant past medical and family history. She had hair dye one year prior to the vaccination without any event, and she denied any further hair dye afterward. She was not on any medication, supplements, or herbs. She also denied any change of shampoo, hair conditioner, soap, or cosmetics. She visited a dermatologist and was diagnosed with alopecia totalis. Blood tests were unremarkable with a

negative rapid plasma reagin (RPR) test, and anti-nuclear antibody (ANA) titer of 1:40. Thyroid stimulating hormone (TSH) level was also normal (0.456 μ IU/mL). She was given oral prednisone of an unknown dosage with no improvement. She also received excimer lamp treatment with few effects.

She was later prescribed oral cephalexin, and monoammonium glycyrrhizinate without success. She wished to try herbal medications and was referred to our clinic in August 2022.

On physical examination, her vital signs were normal. She had scarce gray hair on her head. Her eyebrows were also scarce, with short eyelashes. There was no axillary hair and her arms and legs also lacked hair growth (Fig. 1). Her genitalia was not examined. She has no skin lesions. The remainder of the physical examination was unremarkable. She declined a skin biopsy.

Shimotsuto, or Siwo-Tang, a Kampo herbal medicine, consisting of Rhemannia root, Peony root, Cnidium Rhizome, and Japanese Angelica root, was prescribed. She continued to receive excimer lamp treatment regularly at a dermatologist. Her alopecia improved a little but no significant change has occurred as of this writing.

Discussion

We here report a case of alopecia universalis presumably induced by mRNA-1273 injection. Alopecia areata is a common autoimmune disease that presents as nonscarring hair loss, although the exact pathogenesis of the disease remains unclear. Alopecia totalis and alopecia

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Fig. 1. The head of the patient on the initial visit.

universalis are subtypes of alopecia areata and there is a 100% loss of all scalp hair in the former, and a 100% loss of all scalp and body hair in the latter [1]. Tinea capitis and trichotillomania are two important differential diagnoses, and they are mainly seen in children. This patient did not have inflammation or scaling of the skin, which makes tinea capitis unlikely. There was no irregularity of hair loss or broken hairs, and trichotillomania is also unlikely in the patient. Systemic lupus erythematosus (SLE) and secondary syphilis are also considered in the differential diagnosis but blood tests and lack of physical findings make these also unlikely [1]. Therefore, it is reasonable to conclude that this patient suffered from alopecia universalis.

Alopecia areata could occur with multiple risk factors. Genetic factors might play a role although this patient did not have any family history of alopecia. Comorbidities such as hyperthyroidism, hypothyroidism, vitiligo, psoriasis, rheumatoid arthritis, and inflammatory bowel disease, are associated with alopecia areata, although none of these conditions existed in the patient [2]. Prevalence of atopic dermatitis, asthma, and rhinitis are common among patients with alopecia areata [2]. Herpes zoster may also be associated with alopecia areata [3]. We were not able to identify any triggering factors other than COVID-19 vaccination before the onset of alopecia universalis in the patient. Therefore, although not conclusive, it is a reasonable assumption that the vaccine had an inducing effect to develop alopecia universalis in the patient.

Alopecia areata after vaccinations such as tetanus, hepatitis B, and smallpox have been reported [4,5]. Alopecia areata also has been reported after COVID-19 vaccinations [6–8]. Gallo et al. reported a case of a male patient with alopecia areata after receiving BNT172b, another mRNA vaccine [6]. Essam et al. also reported a case of alopecia areata in a female patient after receiving ChAdOx1 nCoV-19, an adenovirus vector vaccine [7]. Rossi et al. also reported 3 cases of alopecia areata, after the receipt of either BNT172b or ChAdOx1 nCoV-19 [8].

A cross-sectional study in Italy found 24 patients who developed alopecia areata which developed within 16 weeks after COVID-19 vaccination. Fifteen patients received BNT162b2 and 5 received mRNA-1273, and 4 received ChAdOx1 nCoV-19. Four out of these 24 developed alopecia universalis. Half of these 24 patients had underlying autoimmune diseases such as Hashimoto thyroiditis, and celiac disease [9]. Another case series reported 9 cases of alopecia areata following COVID-19 vaccination [10]. Three of them received mRNA-1273 and

the rest received BNT162b2. Alopecia universalis occurred in 2 patients and one developed after the receipt of mRNA-1273. The patient was a female in her 60s and had a remote history of alopecia areata.

According to the Vaccine Adverse Event System Reporting System at Centers for Disease Control and Prevention, there were 3823 alopecia, and 44 alopecia universalis reported after COVID-19 vaccine as of the search on March 15, 2023 (12). Although the causality of these reports is not definite, it is judicious to consider that COVID-19 vaccines, either mRNA vaccines or others, could cause alopecia areata and its subtypes. As far as our literature search could find, this is the first to report the case of alopecia areata occurring in Japanese persons.

COVID-19 vaccines may play a role in the activation of immunological events leading to an aberrant autoimmune response in susceptible individuals. Both mRNA vaccine and adenovirus vector vaccine deliver the gene encoding the S protein, which induces the immune system, with antibodies production and Th1 cells activation with the release of pro-inflammatory cytokines [11]. This could explain the occurrence of autoimmune diseases including alopecia areata.

The incidence of alopecia areata and alopecia universalis after COVID-19 vaccines are unknown but are considered to be rare. Because the dosage of the vaccine is higher (59 µg) in mRNA01273 than that of BNT172b2 (30 µg), the frequency of adverse reactions such as fever, arthralgia, chill, and myalgia appear higher in the former than the latter [12]. Whether mRNA1273 causes more alopecia than other COVID-19 vaccines should be investigated in future studies. Of note, alopecia is a common phenomenon after SARS-CoV-2 infection, with a potentially similar mechanism [13]. It is still rational to prevent the infection by vaccination, and the avoidance of vaccination due to a fear of alopecia is not justifiable.

The treatment of alopecia areata or universalis remains a challenge. Oral JAK inhibitors such as baricitinib, topical or systemic corticosteroids, laser treatment, and other options exist with various efficacy. The best approach to refractory diseases remains unknown [2].

In conclusion, we report a case of alopecia universalis in a Japanese patient after receipt of the mRNA COVID-19 vaccine. Further studies will be necessary to elucidate its incidence and prevalence, and its best clinical approach.

Ethics statement

The current study is exempted from the ethics committee approval since this is a case report. A written informed consent was given by the patient to publish this work.

Ethical approval

This is the casereport and is exempted from the ethics committee approval.

Consent

A written informed consent was provided by the patient.

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CRediT authorship contribution statement

Conception of the report: KI. Drafting of the manuscript: KI. The revision and the approval of the manuscript: KI and MK.

Declaration of Competing Interest

We have no conflicts of interest.

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