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An impressive case of alopecia universalis after COVID-19 vaccination: a coincidental finding or a consequence?

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Abstract. – BACKGROUND: Several cutaneous manifestations in patients undergoing COVID-19 vaccination have been described in literature.

CASE REPORT: Herein, we present a case of alopecia universalis that occurred after the first and second dose of Comirnaty vaccine. A bibliographic search was conducted and a total of 14 studies concerning the association were reviewed.

CONCLUSIONS: Given the autoimmune pathogenesis of the disease, we discussed the potential role of SARS-CoV-2 infection and vaccination as a trigger for the development of hair loss. Physicians should be aware of SARS-CoV-2 vaccine-related hair loss and properly treat this undesirable effect.

Key Words:
SARS-CoV-2 infection, COVID-19 vaccination, Hair loss, Alopecia universalis, Autoimmunity.

Introduction

Several cutaneous adverse events occurred after the anti-SARS-CoV-2 vaccination[1]. Among these, few cases of alopecia areata (AA) have been described. The autoimmune pathogenesis based on peri- and intrafollicular cluster of differentiation 4 $(CD4)^+$ and cluster of differentiation 8 $(CD8)^+$ T cells infiltrate has been extensively investigated[2].

It clinically occurs in the form of patches with complete hair loss on the scalp or other parts of the body. The major risk factors are genetic predisposition, atopy, autoimmunity, stress, hormonal changes, vaccination, and infections[3]. The most imputed are viral triggers (influenza, Cytomegalo, and the Epstein-Barr Virus)[4]. In this regard, we report a case of alopecia universalis (AU) arising after SARS-CoV-2 vaccination, suggesting a possible connection between vaccines and autoimmune diseases.

Case Report

A 48-year-old Caucasian female patient with Hashimoto's thyroiditis well-controlled, a previous episode of self-limiting AA in childhood and a familiar history of autoimmune diseases, came to our attention. She complained of a sudden hair loss starting from the parietal region of the scalp (Figure 1A). Simultaneously, she noticed a bilateral periocular edema (Figure 1B) and an impressive hair loss after routinary hair washing (Figure 1C). About 10 days before the onset of these manifestations, she received the first dose of Comirnaty [Pfizer/BioNTech (Mainz, Germany)] vaccine against SARS-CoV-2. The progressive loss of the remaining hair of the scalp, eyebrows and body's hair was reported after the second dose (Figure 1D-E). A timeline of the clinical events is reported on Figure 2. Diagnosis of AU was made. Topical clobetasol propionate solution and intralesional triamcinolone acetonide 10 mg/mL (3 sessions, 4 weeks apart) was administrated. Unfortunately, there was no response. Written consent to image recording for academic purposes was obtained.

Literature Review

A bibliographic search was conducted on PubMed database (available at: https://ncbi.nlm.nih.gov/PubMed accessed on 20 July 2022) using the key words: "alopecia" AND "COVID-19 vaccination". Basing on the abstract content, we collected pa-

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Figure 1. Clinical features 10 days after the first dose of the vaccine: **A**, Single enlarging patch of non-scarring alopecia; **B**, Periocular edema; **C**, Sudden hair loss after routinary hair washing; **D-E**, AU with total hair loss and eyebrows after the second dose of the vaccine.

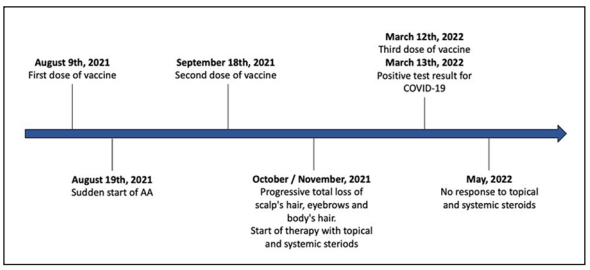

Figure 2. Timeline of ensuing clinical events after the administration of the SARS-CoV- 2 vaccine.

pers concerning this association. No restrictions for language, type or year of publication were applied. The overall search yielded 23 articles. Among these, 13 were excluded as not relevant and/or because the full text was not available, and 10 papers were selected as matching our search. The review of available medical literature is summarized in Table I.

Discussion

Since the start of the COVID-19 pandemic, multiple studies[5,6] have reported an increased incidence of several cutaneous diseases. Among them, new onset of AA might represent a cutaneous feature of SARS-CoV-2 infection[6]. Few cases showed the outbreak of AA in course of COVID-19 vaccination, thus becoming, together with telogen effluvium, the most common type of hair loss in the pandemic[6]. With regard to SARS-CoV-2 infection, two mechanisms dealing with AA occurrence have been hypothesized. The first could be the cross-reaction between the viral antigen and autoantigens, leading to a hyperimmune reaction against hair follicles or dermal papillae cells, finally resulting in hair loss. The second concerns with the cytokine storm, characterized by the increase of interleukin-6 (IL-6) levels, thus blocking the lengthening of the hair shaft and the proliferation of the matrix cells[7]. Switching to vaccination, the molecular mimicry, and the subsequent production of pathological autoantibodies, could similarly represent the pathogenic mechanism of vaccines-related alopecia. Autoimmune phenomena after vaccination could also be justified by the epitope spreading, which is a secondary autoimmune response generated after the release of neo-autoantigens caused by inflammation[8]. Finally, a further mechanism is represented by the heterologous activation of non-antigen-specific lymphocytes (bystander activation) that induce an inflammatory environment with a release of cytokines and chemokines[8]. Recent studies[7] have highlighted genetic similarities between cross-reactive human endogenous antigens and spike protein, supporting the unifying reason for common adverse events following both COVID-19 infection and vaccines. As in most of the cases of AA arising after COVID-19 vaccination described in the literature, our patient also had a personal and family history of autoimmune disease. In fact, these autoimmune reactions have been established on a typical genetic background with alopecia itself representing an additional stress factor. This can concur to a vicious circle for the patients, by activating pre-existing underlying dysregulated pathways[2,8]. With regard to the treatment of AA, several topical and systemic drugs have been widely described in literature, even if the commonest therapy is still represented by corticosteroids[9]. Additional treatments available are: minoxidil, pentoxifylline, topical calcipotriol, phototherapy with narrow band ultraviolet B radiation and Janus Kinasis inhibitors[9]. Recently, topical latanoprost, an esterified prodrug of Prostaglandin F 2α (PGF2α), has been

Table I. Patients' characteristics in studies on SARS-CoV-2 vaccines-related alopecia areata.

References	Sex/age (year)	Type of SARS-CoV-2 vaccine	Severity of hair loss	Approximate time to flare	Treatment	Outcomes
Chen et al[13]	-M/29 - F/26	- AstraZeneca - Pfizer-BioNTech	- AT of the scalp - AU	- Within 1 week after 2nd dose - Within 2 weeks after 2nd dose	Both treated with pulsed oral Methylprednisolone	No response
Gamonal et al[14]	F/27	Pfizer- BioNTech	AA of the scalp	- Within 2 weeks after 3rd dose	Not reported	Not reported
Ho et al[15]	F/51	AstraZeneca	AU	Within 1 week after 1st dose	Clobetasol propionate ointment and intralesional triamcinolone acetonide	Partial response
Lo et al[16]	F/61	Pfizer- BioNTech	AA of the scalp	Within 1 week after 2nd dose	Topical fluocinonide, tacrolimus ointment and minoxidil 5% solution, followed by intralesional triamcinolone acetonide	Complete remission
Essam et al[17]	F/32	AstraZeneca	AA of the scalp	Not reported	Not reported	Not reported
Gallo et al[18]	M/31	Pfizer- BioNTech	AA of the scalp and beard	Within 3 weeks after 2nd dose	Not reported	Not reported
Bardazzi et al[6]	- F/41 - M/24 - F/21	- Pfizer- BioNTech - Pfizer-BioNTech - Moderna	- AA of the scalp - AT of the scalp - AA of the scalp	- Within 1 week after 1st dose - Within 1 week after 1st dose - Within 2 weeks after 1st dose	- Clobetasolproprionatefoam - Intramuscolar triamcinolone and clobetasol proprionate - Intralesional triamcinolone	- Complete regrowth - Worsening to AU - Partial hair regrowth
Lee et al[19]	M/80	Pfizer-BioNTech	AT of the scalp and AA of the beard	Within 1 week after 1st dose	Topical squaric acid dibutylester and minoxidil 5% solution	No response
Scollan et al[20]	- F/33 - F/57 - F/62 - F/28 - F/29 - M/22 - M/15 - M/61 - M/16	- Moderna - Pfizer-BioNTech - Moderna - Pfizer-BioNTech - Pfizer-BioNTech - Moderna - Pfizer-BioNTech - Pfizer-BioNTech - Pfizer-BioNTech	- AA of the scalp - AA of the scalp - AU - AU - AA of the scalp - AA of the scalp and beard - AA of the scalp - AT with eyebrow, eyelash, and beard hair loss - AA of the scalp, eyebrows, and eyelashes	- Within 2 months after 2nd dose - Within 4 months after 2nd dose - Within 2 months after 2nd dose - Within 1 week after 2nd dose - Within 1 week after 2nd dose - Within 1 month after 2nd dose - Within 1 week after 2nd dose - Within 2 weeks after 1st dose - Within 1-2 weeks after 1st dose	- Tofacitinib citrate 5 mg - Tofacitinib citrate 5 mg - Tofacitinib citrate 10 mg, bimatoprost 0.03% eye drops - Tofacitinib citrate 10 mg - Intralesionaltriamcinolone - Tofacitinibcitrate 10 mg - Intralesionaltriamcinolone - Scheduled for oral tofacitinib citrate trial - Tofacitinib citrate 10 mg	Not reported
Su et al[21]	M/42	AstraZeneca	AA of the scalp	Within 3 weeks after 1st dose	- Intralesional triamcinolone	Not reported

found effective in treating AA and safer than topical betamethasone[10]. Eyelash hypertrichosis is the common complication after its chronic use similarly to other drugs[11]; however, cases of erosive pustular dermatosis have been described[12]. In conclusion, treatment of AA represents a challenge both in terms of the efficacy of the available therapies and in terms of patient compliance, since these are prolonged, related to side effects and often ineffective.

Conclusions

According with literature[13-20], several cutaneous manifestations may occur after SARS-CoV-2 vaccination. Among these, AA seems to represent a 'model' of such reactions, pathogenically linking COVID and related prophylactic measures. Although not disabling, AA may have consequences on patients' quality of life, due to its clinical presentation, and demonstrate variable response to treatments, thus requiring further clinical studies and research.

Conflict of Interest
The Authors declare that they have no conflict of interests.

Ethics Approval
Not applicable.

Informed Consent
Written consent to image recording for academic purposes was obtained.

Authors' Contribution
Conceptualization, methodology and writing, original draft preparation: Lucia Peterle, Laura Macca, Federica Li Pomi, Mario Vaccaro; data collection, methodology: Federico Vaccaro; writing, review and editing and supervision: Francesco Borgia and Mario Vaccaro. All authors have read and agreed to the published version of the manuscript.

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Study data are available at our University Hospital Archive.

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