Case Report
Olgu Sunumu

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Reactivation of morphea following mRNA coronavirus disease-2019 vaccination

mRNA koronavirüs hastalığı-2019 aşısı sonrası morfea reaktivasyonu

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Abstract

Morphea is an inflammatory immune-mediated disease associated with many factors such as genetic predisposition, environmental triggers such as bacterial and viral infections, as well as intrinsic factors such as hormonal and immunological dysregulation, although its pathogenesis is largely unknown. Here, we report the first case of morphea relapse after the mRNA coronavirus disease-2019 (COVID-19) vaccine. Our case along with recent reports suggest that new associations might appear due to COVID-19 infection and vaccines.
Keywords: Morphea, COVID-19, vaccine

Öz

Morfea, patogenezi büyük ölçüde bilinmemekle birlikte, genetik yatkınlık, bakteriyel ve viral enfeksiyonlar gibi çevresel tetikleyiciler, hormonal ve immünolojik düzensizlik gibi içsel faktörler gibi birçok faktörle ilişkili olduğu düşünülen enflamatuvar immün aracılı bir hastalıktır. Burada, mRNA koronavirüs hastalığı-2019 (COVID-19) aşısından sonra morfea hastalığında nüks gelişen ilk olguyu bildiriyoruz. Mevcut güncel literatürlerle birlikte olgumuz, COVID-19 enfeksiyonu ve aşılar ile ilişkili yeni bulgularla önümüzdeki süreçte karşılaşmaya devam edeceğimizi düşündürmektedir.
Anahtar Kelimeler: Morfea, COVID-19, aşı

Introduction

The worldwide spread of severe acute respiratory syndrome-coronavirus-2, a member of the coronavirus family responsible for the coronavirus disease-2019 (COVID-19) pandemic, has put significant pressure on healthcare systems. Meanwhile, several cutaneous and extracutaneous autoimmune disorders and reactions associated with COVID-19 and its vaccines have been reported since the beginning of the pandemic[1].

Herein, we present the first case of morphea recurrence following vaccination with an mRNA vaccine for COVID-19.

Case Report

A 68-year-old woman, who was diagnosed with plaque morphea 15 years ago and remained in remission without treatment for years, presented to our outpatient clinic with the reappearance of her lesions. She had previously received clobetasol propionate ointment and methotrexate 15 mg weekly for 1 year, and her lesions were in long-term remission for the last 10 years. However, 2 weeks following the third dose of an mRNA vaccine for COVID-19, the first dose of mRNA COVID-19 vaccine, a brownish-purplish rash accompanied by pruritus and hardening of the affected

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skin suddenly reappeared on the back, abdomen, anterior and posterior thighs, including areas with previous morphea lesions. Physical examination revealed brownish-purplish plaques with mild erythematous borders and sclerosis in areas of previous morphea lesions (Figure 1). She was referred from the rheumatology to the dermatology department owing to the absence of systemic findings. Given her previous history, typical clinical findings, and refusal of a new biopsy, her morphea recurred following mRNA COVID-19 vaccination because of the absence of other possible triggers. Methotrexate 15 mg weekly with folic acid was started. Three weeks later, great improvements in the lesions were observed, which were recorded as decreased pruritus and decreased induration on palpation. The patient did not have any complaints during follow-up, and the lesions slowly improved with decreased induration and hyperpigmentation. The patient did not continue with further COVID-19 vaccination.

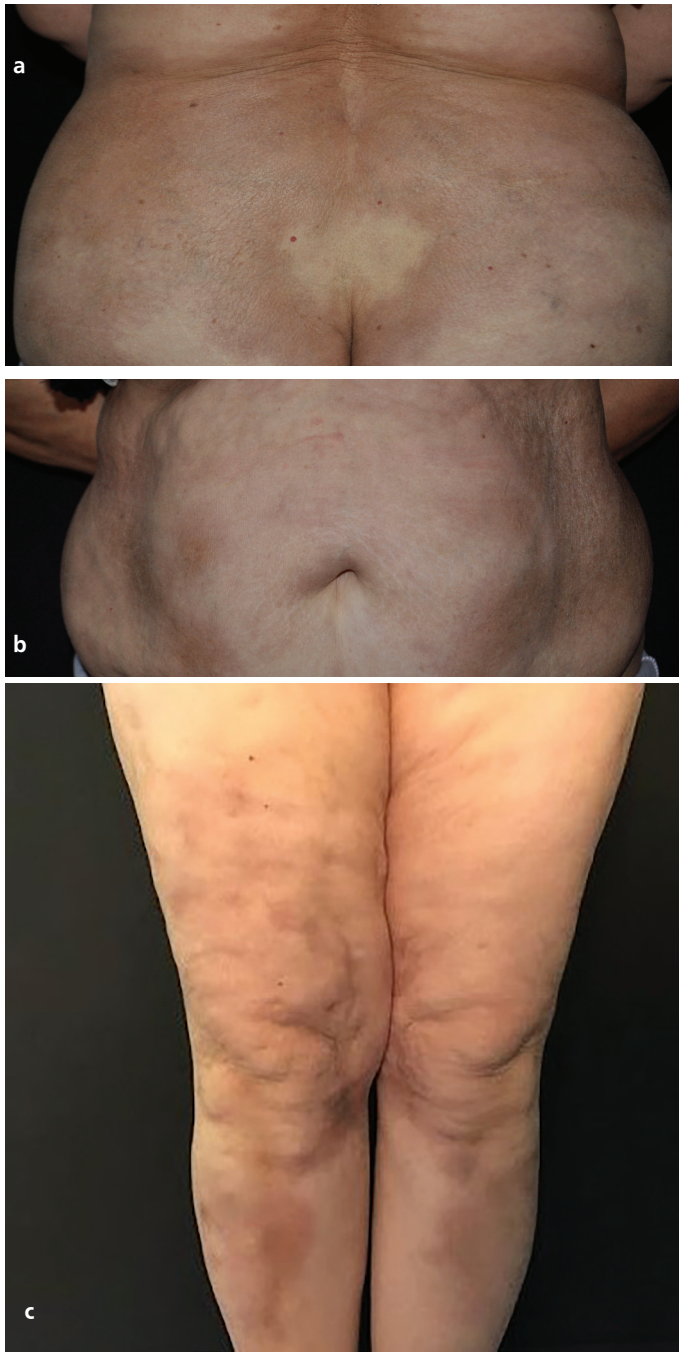

Figure 1. The presence of brownish and purplish indurated sclerotic plaques at the back (a), abdomen (b), and thighs (c)

Discussion

Exaggerated activation of the immune system following vaccination can cause autoimmune disorders such as morphea. Recently, the development of morphea following COVID-19 diagnosis has been reported in only four case reports (Table 1)[2-5].

In the literature, morphea following vaccination has been rarely reported, and the vaccines implicated include diphtheria, tetanus, pertussis, measles-mumps-rubella, hepatitis B, antitetanus, Bacillus Calmette-Guérin, Influenza, and Pneumococcal vaccines (Table 2). Considering all cases of morphea following vaccination, the majority of these cases occurred in the pediatric population. The average time between vaccination and morphea onset is approximately 10 months (2 days to 7 years). The vaccine with the shortest time to morphea occurrence (2 days) was a COVID-19 vaccine containing a viral vector[5]. Aryanian et al.[5] reported both a case of morphea following COVID-19 diagnosis and the development of morphea following COVID-19 vaccination. They reported a case of generalized morphea that started as multiple sclerotic lesions in a few days following COVID-19 diagnosis in a 29-year-old woman without any comorbid disease, and a case of generalized morphea started as diffuse maculopapular lesions on the body 2 days following COVID-19 vaccination in a 70-year-old woman. Aryanian et al.[5] attributed this to immune system activation and virus-induced inflammation leading to cross-reaction of the virus and host skin antigens.

Oh et al.[6] reported a case of morphea developing especially in the extremities 3 weeks following the second dose of mRNA COVID-19 vaccination in a 47-year-old Chinese woman. The lesions regressed after 6 months of treatment, and the patient received an inactivated COVID-19 vaccine during follow-up without any recurrence[6]. In this case, the absence of recurrence following the administration of an inactivated vaccine could be thought to be similar to the present case as the patient had not shown any recurrence following the first inactivated COVID-19 vaccination.

In their case series, Antoñanzas et al.[7] emphasized that a 45-year-old woman developed generalized morphea following the first dose of an mRNA COVID-19 vaccine, and no recurrence developed following the second dose. In another 52-year-old woman, no reaction developed following the first dose of an mRNA COVID-19 vaccine; however, complaints started following the second dose of an mRNA COVID-19 vaccine.[7]

Paolino et al.[8] further presented a case series including four patients who developed generalized morphea following vaccination. Three of these patients were female, and all cases were aged >50 years. All three women developed morphea following mRNA COVID-19 vaccination; however, the male patient developed morphea following COVID-19 vaccination with a vaccine containing a viral vector[8]. Our patient was over 50 years of age and female, similar to the cases of morphea developing following COVID-19 diagnosis and vaccination.

Table 1. Morphea cases reported following COVID-19 diagnosis and COVID-19 vaccination

Reference	Age	Sex	Type of morphea	Time of morphea onset	Treatment
Severino et al.[2]	62	Female	Plaque morphea	*	TCS
Lotfi et al.[3]	57	Female	Pansclerotic morphea	1 week	TCS
Pigliacelli et al.[4]	61	Female	Plaque morphea	1 month	TCS, vitamin E emollient
Aryanian et al.[5]	29	Female	Generalize morphea	A few days later	TCS, phototherapy
Reference	**Age**	**Sex**	**Type of vaccine**	**Time of morphea onset**	**Treatment**
Aryanian et al.[5]	70	Female	COVID-19 vaccine with viral vector	2 days	MTX and TCS
Oh et al.[6]	47	Female	mRNA COVID-19 vaccine	3 weeks	Calcipotriol and TCS
Antoñanzas et al.[7]	45	Female	mRNA COVID-19 vaccine	2 weeks	TCS and calcipotriol
	52	Female	mRNA COVID-19 vaccine	6 weeks	TCS, MTX
Paolino et al.[8]	61	Female	mRNA COVID-19 vaccine	15 days	TCS, MTX
	52	Female	mRNA COVID-19 vaccine	7 days	MTX
	64	Male	COVID-19 vaccine with viral vector	20 days	Tacrolimus 0.1% cream
	73	Female	mRNA COVID-19 vaccine	20 days	Tacrolimus 0.1% cream
Metin and Celepli[9]	55	Female	mRNA COVID-19 vaccine	7 weeks	TCS and calcipotriol
Bilgic et al.	68	Female	mRNA COVID-19 vaccine	2 weeks	MTX

COVID-19: Coronavirus disease-2019, MTX: Methotrexate, TCS: Topical corticosteroids, *Could not be reached

Table 2. Morphea cases reported caused by other vaccines

Reference†	Age (years)	Sex	Vaccination	Time of morphea onset	Treatment
Desmons et al.	7 months	Female	DTaP	Shortly after	*
Mork et al.	*	*	BCG	*	*
Bonino et al.	5	*	Antitetanus	2 years	*
	13	*	Antitetanus	*	*
Grezard et al.	*	*	Hepatitis B	*	*
Drago et al.	50	Female	Anti-tetanus	2-week	Pred
Schmutz et al.	5	Female	Hepatitis B	1 month	*
	36	Female	Hepatitis B	2-3 months	*
Dursun et al.	25	Female	Hepatitis B	A few months later	Colchicine
	23	Male	Hepatitis B	2 months	Colchicine and TCS
Torrelo et al.	8 months	Male	DTaP	2-3 weeks	*
	2	Female	MMR	Shortly after	Pred
Khelifa et al.	53	Female	Influenza	*	Doxy and TCS
Bukhari et al.	4	Female	Hepatitis B	*	*
Mlika et al.	9 months	Male	Hepatitis B	2-week	Pred
Kumar et al.	7	Female	Non-identified vaccine	*	TCA and calcipotriol
Khaled et al.	2	Female	DTaP	3 months	Pred and MTX
Viladomiu et al.	1	Male	Pneumococcal vaccine	20 days	TCS
Matsumoto et al.	8	Female	BCG	7 years	Pred and MTX
Lopez et al.	67	Female	Influenza	10 days	PUVA, Pred, and MTX

DTaP: Diphtheria, Tetanus, Pertussis, BCG: Bacillus Calmette-Guérin, PUVA: Psoralen-UV-A, Pred: Prednisone, MTX: Methotrexate, TCS: Topical corticosteroids, Doxy: Doxycycline, MMR: Measles, Mumps, and Rubella, *Full data could not be accessed. †Full list of other references are provided in Supplementary Material 1

In a recent case, Metin and Celepli[9] also described morphea development following mRNA COVID-19 vaccination[9]. They showed spike proteins in the patient tissue by immunostaining the biopsy. Thus, virus-induced inflammation leading to cross-reaction with one's tissue might be the underlying cause of these cases.

To the best of our knowledge, this is the first case report in the literature in which morphea reappeared/recurred following COVID-19 vaccination. Although the clinical findings and history of our patient point out the relationship between the reappearance of morphea and COVID-19 vaccination, a coincidental event could not be ruled out. Our

case and other new cases may indicate that new findings and newly described associations with COVID-19 and vaccines can be expected.

Ethics

Informed Consent: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.G., A.B., Concept: M.G., A.B., Design: M.G., A.B., Data Collection or Processing: M.G., A.B., Analysis or Interpretation: M.G., A.B., Literature Search: M.G., A.B., Writing: M.G., A.B.

Conflict of Interest: No conflict of interest was declared by the authors.

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