Skin reaction to COVID-19 vaccine: A report of 4 cases

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Abstract

Since the beginning of the covid-vaccine campaign, a lot of local and systemic dermatologic reactions happening after the administration of Coronavirus disease 2019 (COVID-19) vaccines have been described, even if their exact biological mechanism is still debated. In this paper we report 4 cases of cutaneous manifestations arose within ten days after the first dose of messenger RNA (mRNA)-based COVID-19 vaccination: one case of giant urticaria, one case of head and neck redness and two cases of Erythema Multiforme (EM). In our experience these reactions were mild, transient and all of them resolved, not recurring after the second dose, so these manifestations shouldn't be considered as an absolute contraindication to the second dose of vaccine, that to date is fundamental.

Introduction

As of today, the Italian Drugs Agency (AIFA) has approved four different SARS-CoV-2 vaccines: Pfizer/BioNTech (mRNABNT162b2, Comirnaty) and Moderna (mRNA-1273) are messenger RNA (mRNA) vaccines, while AstraZeneca (AZD1222/ChAdOx1, Vaxzevria) and Janssen (Ad26.COV2.S) are two viral vector vaccines.[1] It's by now well-known that Coronavirus disease 2019 (COVID-19) has numerous and various cutaneous manifestations: since the beginning of the pandemic one and a half year ago a large range of skin manifestations has been associated with the infection, such as chilblain-like, urticarial, vesicular, maculopapular, livedoid and vasculitic lesions. Nevertheless, the exact pathophysiology of these manifestations is still not totally clear; various hypotheses have been proposed, including viral hypersensitivity reactions, virus induced coagulopathy, thrombotic microangiopathy, overexpression of type I interferons and direct viral damage. It stands to reason that skin reactions can occur even after vaccination especially with mRNA vaccines encoding the spike protein of SARS-CoV-2.[2]

We report 4 cases of cutaneous manifestations which appeared within ten days after the first dose of an mRNA COVID-19 vaccination (Table 1).

Case report #1

A 58-year-old man was administered the first dose of the mRNA COVID-19 vaccine Pfizer/BioNTech. In the four days following the vaccination, the patient developed severe itching with fleeting urticarial lesions lasting <24 hours and migrant in appearance with polycyclic contours associated with hand swelling. No angioedema nor respiratory symptoms were present. Laboratory investigations detected raised PCR (18.4 mg/dL) and white cell count (10.410/microL). The diagnosis was consistent with giant urticaria (Figures 1a,b). The patient was treated with 0.5 mg/kg methylprednisolone daily plus oral antihistamine which resulted in the complete resolution of skin lesions within 10 days.

Case report #2

A 59-year-old man presented to the emergency department two days after the first dose of the Moderna Covid-19 vaccine for precordial pain associated with tachycardia, paresthesia and light-headedness. In a clinical examination he presented with a persistent head and neck redness (Figures 1c,d) associated with skin-colored, well-defined macules with a peripheral keratotic ridge, which were widespread on arms and legs bilaterally. His past medical history included psoriasis, which had always been treated with a topical combination of calcipotriol/betamethasone, and anxiety for which he took Alprazolam daily. Our differential diagnoses comprised head and neck dermatitis, airborn dermatitis, photoinduced dermatitis but he had no personal nor family history of atopy nor autoimmune disorders. He was treated with oral Cetirizine 10mg/die and slowly improved.

Case reports #3 and #4

A 22-year-old girl presented with targetoid lesions symmetrically distributed on the palms and soles associated with an initial involvement of the thighs (Figure 2a,b). The patient was asymptomatic, blood test analyses were within normal values and IgM anti-HSV1, anti-HSV2, anti-Mycoplasma pneumoniae, anti-CMV, anti-EBV and anti-parvovirus B19 were all negative. Ten days previously, she had received the first dose of the Moderna Covid-19 vaccine.

Similarly, a 32-year-old man presented with pruritic concentric annular lesions bilaterally spread on the soles, palms and back of the hands, which had arisen eight days after the first dose of the Moderna Covid-19 vaccine (Figure 2c,d). Besides itching he did not complain of any systemic

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symptoms. In both patients oral and genital mucosa were spared and the clinical features suggested Erythema Multiforme (EM). The former patient was successfully treated with 0.5 mg/kg methylprednisolone daily plus oral antihistamine while the latter completely resolved within one week with oral Cetirizine 10mg/die.

All patients received the second booster of vaccine without any systemic symptoms nor skin problems.

Discussion

A large variety of both local and systemic skin reactions have recently been reported after Covid-19 vaccination, especially occurring after the mRNA types.[3]

The exact biological mechanism of these reaction is still debated, and, to date, it has not been possible to establish if the main cause is a hypersensitivity to the spike protein or to other components of the vaccine.[2,4] However, distinguishing between immediate and delayed hypersensitive reactions is essential. In particular, when manifestations such as urticaria and angioedema occur within 4 hours from the injection, a possible contraindication for the second dose can exist, especially if the skin manifestations are associated with respiratory and/or cardiovascular symptoms.[5] As in case 1, the first dose-related urticaria developed in a few days, suggesting that it may not be induced by a hypersensitivity reaction to the vaccine but rather related to the host's immune response. Indeed, the patient did not exhibit any symptoms after his second dose.

Regarding EM, it is typically associated with microbial infections, especially Herpesviridae viruses or Mycoplasma pneumonia, but in a minority of cases it can be related to drugs or vaccines, mainly in the pediatric population.[6] The two most frequently associated vaccines are the diphtheria-tetanus-pertussis and recombinant hepatitis B[7] but recently an association with Covid-19 vaccines has been recognized.[8]

Some authors hypothesize that although the vaccine does not cause de novo immune mediated adverse reactions, it may trigger a pre-existing underlying dysregulated pathway through the immunologic response, inducing immune activation of both B and T lymphocytes.[6,9,10]

Figure 1. Case reports #1 and #2.

Table 1. Summary of the 4 cases.

	Case 1	Case 2	Case 3	Case 4
Vaccine	Pfizer/BioNTech	Moderna	Moderna	Moderna
Timing of onset	4 days	2 days	10 days	8 days
Kind of reaction	Giant urticaria	Head and neck redness	EM	EM
Age	58 years old	59 years old	22 years old	32 years old
Gender	Male	Male	Female	Male
Comorbidities	None	Psoriasis, anxiety	None	None
Duration of reaction	10 days	10 days	7 days	5 days
Treatment	0.5 mg/kg methylprednisolone daily plus oral antihistamine	Oral Cetirizine 10 mg/die	0.5 mg/kg methylprednisolone daily plus oral antihistamine	Oral Cetirizine 10 mg/die

Conclusions

In conclusion, although we cannot demonstrate a true causal link, all the reported cases show a temporal relation between skin reactions and vaccine administrations. Our cases also show that the majority of skin reactions are mild, transient and resolve without recurring after the second dose, as observed by other authors.[11] Consequently these manifestations should not be considered as an absolute contraindication to a second dose of vaccine that to date is fundamental.

Meticulous reporting is necessary and further studies based on larger cohorts are needed to better understand the pathophysiology of cutaneous involvement.

Figure 2. Case reports #3 and #4.

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