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Pityriasis rubra pilaris (type I) following ChAdOx1 COVID-19 vaccine: A report of two cases with successful treatment with oral isotretinoin

Dear Editor,

Pityriasis rubra pilaris (PRP) is a rare chronic papulosquamous dermatosis that can be triggered by multiple factors (e.g. drugs, infection) and influenced by a genetic background.¹ PRP was also reported following vaccination (e.g. measles-mumps-rubella, oral poliovirus, diphtheria-pertussis-tetanus and influenza).² Multiple cutaneous adverse events were associated with COVID-19 and its vaccines, to date, there are four reports of PRP related to COVID-19 vaccination.^{3–6} Here, we report two cases of

PRP after ChAdOx1 (AstraZeneca) vaccine, compare them with other similar cases and highlight a satisfactory response with oral isotretinoin.

Case 1; A 31-year-old man presented with itching salmon to erythematous scaly plaques on his upper trunk, upper and lower extremities for 60 days (Fig. 1a), sparing the periumbilical area, with palmoplantar keratoderma (Fig. 1b), without nail involvement. On 30 May 2021, he received the first dose of the immunization for SARS-CoV-2 with AstraZeneca vaccine. The patient noticed low fever and headache in the same day. After 10 days, he noticed a cutaneous rash on abdomen and face that progressed to dorsum, upper and lower limbs. There was no history of drug intake, except losartan 50 mg QD for systemic arterial hypertension during the past four years. Histopathological analysis was compatible with pityriasis rubra pilaris (Fig. 1d). The patient was treated with isotretinoin 30 mg QD and emollients for three months with total remission.

Case 2; A 42-year-old man was vaccinated with two doses of AstraZeneca vaccine, without intercurrents. After 8 days of the second dose, scaly reddish plaques were observed on his face and then progressed all over the body in one week, leaving healthy skin areas, especially on the trunk, with a citrine colour (Fig. 1c), without nail involvement or palmoplantar hyperkeratosis. There was no history of drug intake or comorbidities. The histopathological analysis was analogous to the first case (Fig. 1d) and he was treated with isotretinoin 40mg/day in two months with partial clearance and then, 20mg/day in the third month with mild erythema.

The causal relationship between COVID-19 vaccines and cutaneous immunological reactions is still not understood, but they can be due to an upregulated inflammatory immunological pathway or cross-reactivity between vital or adjuvant molecules and self-antigens.⁴

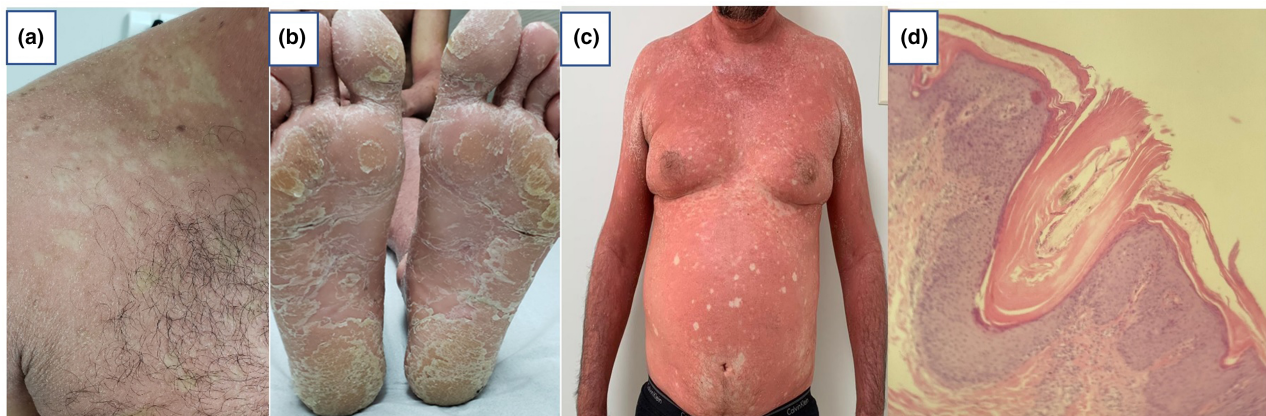


Figure 1 Clinical and histopathological features of PRP induced by COVID-19 vaccination (ChAdOx1 - AstraZeneca). (a) Case 1. Erythematous scaly plaques with areas of healthy skin; (b): Case 1. Plantar hyperkeratosis; (c): Case 2. Erythematous-citrine scaly plaques all over the body with evident areas of healthy skin in the trunk; (d): Follicular plugging, alternating orthokeratosis and parakeratosis (vertical and horizontal), epidermis with broader rete ridges than expected in a psoriasiform reaction (HE, 200X).

Table 1 Main characteristics of the reported patients with pityriasis rubra pilaris induced by COVID-19 vaccines,³⁻⁶ including our cases

Authors and country	Vaccine	Age (years)/ Sex (F, female; M, male)	Dose (1st/2nd) and time interval of first symptoms/signs	Treatment and prognosis
Criado <i>et al.</i> (Brazil)	ChAdOx1 (AstraZeneca)	31 y/M	1st, 15 days	Total clearance after 2 months of 20 mg/day oral isotretinoin and emollients
	ChAdOx1 (AstraZeneca)	42 y/M	2nd, 8 days	Total clearance after 2 months of 40 mg/day and then, 20 mg/day oral isotretinoin and emollients
Sechi, <i>et al.</i> (Italy) ³	mRNA-1273 (Moderna)	62y/F	2nd, 5 days	Progressive remission with Prednisone (1 mg/kg/day for 2 weeks), then tapered until the use of topical corticosteroids
	BNT16B2b2 (BioNTech/Pfizer)	82y/F	1st, 7 days	Clinical improvement achieved with methotrexate 15 mg/weekly with residual scaly plaques on head and neck and PP hyperkeratosis after 4 months of follow up
Sahni, <i>et al.</i> (India) ⁴	ChAdOx1 (AstraZeneca)	72y/M	1st, 3 weeks	Total clearance after emollients and topical corticosteroids without recurrence after the 2nd dose
Lladó, <i>et al.</i> (Spain) ⁵	ChAdOx1 (AstraZeneca)	63y/F	1st, 9 days	Acitretin 20 mg/day; no follow up
Hunjan, <i>et al.</i> (United Kingdom) ⁶	BNT16B2b2 (BioNTech/Pfizer)	51y/M	1st, 3 days, and 2nd, few days after.	Improvement with acitretin 20 mg/day and topical corticosteroid

Familiar cases of PRP revealed gain of function at CARD14 gene, which codifies the scaffold protein CARMA2, leading to the activation of (NF- κ B) by the complex CARMA2-BCL10-MALT1. As long as CARD14 can be induced by IL17 and PAMPS, inflammatory and infectious *stimuli* are thought to elicit PRP in genetically predisposed individuals.¹

The seven patients who developed PRP after COVID-19 vaccination are listed at the Table 1. Their age varied from 31 to 82 years, both sexes were affected and different types of PRP have been presented.³⁻⁶ Four patients presented the onset of adverse reactions in a mean time of 13 days after the first dose,³⁻⁵ one presented flare after the first and second dose⁶ and two of them after a medium of 6,5 days after the second dose.³ Four patients (57.14%) received (AstraZeneca),^{4,5} one (14.28%) mRNA-1273 (Moderna)³ and two (28,58%) BNT16B2b2 (BioNTech/Pfizer).^{3,6}

Despite the PRP might be, in most cases, persistent,⁷ in these series patients seem to improve mostly with retinoids but also with oral and topical corticosteroids.³⁻⁶ The majority of cases occurred after the first dose,³⁻⁶ but one had resolved prior to the second dose and there was no recurrence.⁴ These reactions occur in a close range of time (≤ 15 days), suggesting a pattern that could be linked to vaccination.³

PRP can be elicited by COVID-19 vaccination.²⁻⁶ Clinicians must be aware of this adverse event, probably facilitated by a genetic background, but prone to respond to treatment with a good prognosis.

Acknowledgement





The patients in this manuscript have given written informed consent to the publication of their case details.

Conflict of interests

None to declare.

Data availability statement

The data that support the findings of this study are available from the corresponding author, MI, upon reasonable request.

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Healthcare and safety of patients with melanoma during the COVID-19 Pandemic in Italy

Dear Editor,

The COVID-19 pandemic prompted drastic containment measures and a rearrangement of healthcare services. Several papers highlighted the reduction of melanoma diagnoses and related

activities^{1–5}; however, limited data are available on healthcare quality and patient safety.⁶

In Italy, the Italian Melanoma Intergroup (IMI) documented the decrease in first visits, diagnoses and surgeries related to melanoma during February–April 2020.¹ As a follow-up study, the IMI and the Italian Association of Melanoma Patients (AIMaMe) undertook a nationwide survey to evaluate the impact of the pandemic on healthcare quality and patient safety in melanoma management. AIMaMe members were invited to fill in an online questionnaire, and participants were divided into two groups based on when they received the indication for excision: pre-pandemic (Group 1, $n = 334$) and pandemic (Group 2, $n = 252$; Table 1).

Regarding patient management, we found no differences between the groups. The main reasons for the dermatology visit were a suspicious lesion (42–44%) and a routine clinical evaluation of nevi (42–45%). There were also no differences in who suggested the visit: the most frequent answers were ‘myself’ (35–36%) and ‘a dermatologist’ (36–32%). A waiting time <15 days

Table 1 Survey questionnaire

	The dermatological examination in which melanoma was diagnosed took place:				p-value†
	From January 2019 to January 2020		From February 2020 to December 2020		
Why did you undergo the dermatological examination in which melanoma was diagnosed?					
Suspicious skin lesion	141	42.2%	110	43.7%	
Regular nevus check-up	150	44.9%	105	41.7%	
Other reason	43	12.9%	37	14.7%	0.688
Who suggested to undergo a dermatological examination?					
Myself	116	34.7%	90	35.7%	
Dermatologist	119	35.6%	82	32.5%	
Family member or friend	40	12.0%	33	13.1%	
General practitioner	32	9.6%	25	9.9%	
Other medical doctor	27	8.1%	22	8.7%	0.672
How long did you have to wait for an appointment for the dermatological examination?					
<1 month	174	52.1%	151	60.0%	
1–3 months	120	35.9%	61	24.2%	
3–6 months	31	9.3%	20	7.9%	
6–12 months	9	2.7%	20	7.9%	0.001
How long did you have to wait for the surgical removal of your melanoma?					
<15 days	120	35.9%	107	42.5%	
15–60 days	175	52.4%	127	50.4%	
2–6 months	34	10.2%	15	6.0%	
6–12 months	5	1.5%	3	1.2%	0.173
How long did you have to wait to receive the histological report after surgery?					
<15 days	155	46.4%	130	51.6%	
up to 1 month	137	41.0%	99	39.3%	
>1 month	42	12.6%	23	9.1%	0.295
Did COVID-19 restrictions cause a delay of ...					
		... at least one follow-up visit?		... the first follow-up visit?	
No	259	77.5%	187	85.0%	
Yes, my decision	19	5.7%	11	5.0%	
Yes, decision by the health facility management	56	16.8%	22	10.0%	0.069