First Onset of Pityriasis Rubra Pilaris following SARS-CoV-2 Booster Vaccination: Case Report and Review of the Literature

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Abstract: There is increasing evidence of adverse events associated with the use of COVID-19 vaccines. Here, we report a case of the SARS-CoV-2-vaccination-related onset of pityriasis rubra pilaris (PRP) and provide an analysis of previously reported cases in the medical literature. A 67-year-old male presented with a 1-year history of histopathologically proven PRP that first developed 14 days after receiving a COVID-19 booster vaccination. Skin symptoms improved under ustekinumab medication after unsuccessful previous treatment approaches using systemic corticosteroids, brodalumab, and risankizumab. Among the published cases of post-COVID vaccination PRP, 12 (75%) males and 4 (25%) females were reported. The median age of the reported patients was 59 years. In 10 out of 16 patients (62.5%), PRP was diagnosed after the first vaccine dose, in 4 (25%) after the second dose, and in 2 of 15 patients (12.5%) after the third dose. The median time between COVID-19 vaccination and the onset of PRP was 9.5 days (range: 3–60 days). The majority of patients required systemic treatment, including systemic retinoids and methotrexate. PRP might be a rare adverse event after COVID-19 vaccination, particularly affecting older males. Even though most reported patients with COVID-19-vaccination-related PRP could be successfully treated with PRP standard medications, therapy refractory cases may also occur. Thus, clinicians must be aware of this rare but potentially severe complication.

Keywords: pityriasis rubra pilaris; COVID-19; SARS-CoV-2; psoriasis; autoimmune inflammatory keratinization diseases

1. Introduction

Since December 2020, expansive COVID-19 vaccination campaigns have been introduced worldwide. Currently, the vaccines in use are based on the mRNA, non-replicating virus vector, or inactivated virus material. Given the unprecedented number of worldwide vaccinations provided in such a short amount of time, there is an increasing wealth of reports on generally rare adverse events associated with the use of COVID-19 vaccines. Frequent and typically mild symptoms that have been observed include fever, headache, fatigue, chills, muscle pain, diarrhea, and local injection site reactions, as is commonly observed for most vaccines. Similar to COVID-19 infection, SARS-CoV-2 vaccination appears to have the potential to trigger a broad spectrum of similar cutaneous adverse effects, e.g., chilblain-like lesions, morbilliform, urticarial or purpuric rashes, vasculitis [1,2]. Pityriasis rubra pilaris (PRP) is a rare psoriasiform skin disease with an incidence between 1:5000 and 1:50,000 without gender predilection [3]. Including the present case, 16 patients with COVID-19-vaccination-related PRP have been published in the literature [4–13]. Here, we report a new case of SARS-CoV-2-vaccination-related PRP and provide an analysis of previously reported cases in the medical literature.
2. Case Report

A 67-year-old male presented with a 1-year history of erythematous follicular papules coalescing to sharply demarcated fine-scaly plaques on the forearms, axillae, face, upper legs and lower trunk, including numerous nappes claire. Severe palmoplantar hyperkeratosis was also observed (Figure 1a–c). Psoriasis Area and Severity Index (PASI) was 24.0. Histopathology revealed hyperkeratosis alternating with parakeratosis and orthokeratosis, acanthosis with broad rete ridges, areas of hypergranulosis and mild perivascular inflammatory infiltrates in the dermis supporting a diagnosis of PRP (Figure 1d,e). These lesions initially developed 14 days after receiving an mRNA-based COVID-19 booster vaccination (Comirnaty). Two previous vector-based vaccinations (Vaxzevria) did not cause any side effects. Moreover, the patient had a history of long-standing diabetes mellitus and hyperlipidemia. He had no history of any new medication. His long-standing medication included daily metformin, omeprazole, simvastatin, pregabalin, and allopurinol.

![Figure 1](image_url)

**Figure 1.** A patient with COVID-19 vaccination-related pityriasis rubra pilaris (a) showing keratotic follicular papules (b) coalescing into scaly reddish-pinkish plaques with characteristic islands of sparing (nappes claire). Palmar keratoderma with yellowish appearance is also observed (c). Histological examination of a skin biopsy revealed hyperkeratosis alternating with parakeratosis and orthokeratosis, acanthosis with broad rete ridges, areas of hypergranulosis and mild perivascular inflammatory infiltrates in the dermis (d,e).

During the first two months after onset of PRP the patient was unsuccessfully treated with highly potent topical and tapered systemic corticosteroids stating with 150 mg prednisolone. Thereafter, brodalumab was prescribed with a 2-weekly administration. Following six months of this regimen with insufficient improvement of his skin lesions, the patient was switched to risankizumab. After two cycles of three-monthly risankizumab treatment with recalcitrant skin lesions, the patient was finally referred to our department (Figure 1a–c). Blood work revealed a slight elevation of C-reactive protein with 12 mg/L (<5). Other routine laboratory parameters, including leukocytes and neutrophils, were within normal limits. An autoantibody profile (e.g., ANA, ENA), chest X-ray, and abdominal ultrasound were unremarkable, except for fatty liver disease. Serology for HIV, hepatitis B and C was negative. Despite being on a stable dose of simvastatin, the patient displayed elevated low-density lipoprotein cholesterol and triglyceride levels. Therefore, we refrained from acitretin or isotretinoin medication and instead prescribed ustekinumab (90 mg) in the standard regimen as established for psoriasis. This intervention finally resulted in a significant reduction in erythema and scale formation after the first
application, indicated by PASI 12.6. Of note, all aforementioned biologics used were not labeled to treat PRP.

3. Discussion

Similar to generalized pustular psoriasis, PRP has recently been recognized as an autoimmune inflammatory keratinization disease [3,14,15]. Indeed, psoriasis represents an important differential diagnosis of PRP and was also considered in the present case. However, the patient’s history, normal neutrophil counts, failure to respond to usually highly effective anti-psoriatic drugs, and the overall clinical and histopathological findings strongly favored a diagnosis of PRP. Previously observed associations with PRP include, viral diseases, in particular HIV infection, and various drugs [3]. Cases of post-vaccination PRP following inoculation with attenuated virus vaccines have only rarely been reported [16,17]. The trigger mechanism of post-vaccination PRP is likely immunological and possibly based on molecular mimicry. Given the existing literature and close temporal association with COVID-19 vaccination, we suggest a causal relationship in the present case. Of note, PRP represents an exceedingly rare condition, which argues against a chance association, especially considering that since the beginning of COVID-19 vaccination campaigns, several cases of PRP have been detected worldwide. Consequently, following Lladó et al. [13], who reported post-COVID vaccination PRP for the first time, 15 further cases including the present patient have now been published [4–13] (Table 1). Regarding post-COVID-19 infection-related PRP, we identified four previously reported cases, including a case reported by us of a patient who developed PRP after SARS-CoV-2 vaccination and a concomitant breakthrough infection [5,18–20]. Moreover, Margo et al. [21] reported PRP-like cases with atypical histopathology such as an interface dermatitis.

Table 1. SARS-CoV-2 vaccination-related first onset of pityriasis rubra pilaris (PRP) reported in the medical literature.

| Patients (Present Case) | Gender | Age (Years) | SARS-CoV-2 Vaccine | PRP Onset Following (Dose) | Onset of PRP after Vaccination (Days) | Re-Exposed to SARS-CoV-2 Vaccines | Systemic Treatment |
|-------------------------|--------|-------------|-------------------|--------------------------|--------------------------------------|----------------------------------|-------------------|
| #1                     | m      | 67          | Comirnaty/Pfizer-BioNTech, 1st + 2nd Vaxzevria/AstraZeneca | 3rd | 14 | - | brodalumab, risankizumab, ustekinumab |
| #2 [4]                 | m      | 75          | Spikevax/Moderna  | 1st | 5 | yes, exacerbation | acitretin, guselkumab |
| #3 [5]                 | m      | 51          | Spikevax/Moderna, 1st Vaxzevria/AstraZeneca, 2nd Comirnaty/Pfizer-BioNTech (concomitant COVID-19 infection) | 3rd | 10 | - | guselkumab |
| #4 [6]                 | m      | 65          | Vaxzevria/AstraZeneca | 1st | 60 | - | acitretin |
| #5 [7]                 | m      | 59          | CoronaVac/Sinovac | 2nd | 4 | - | none * |
| #6 [7]                 | m      | 56          | CoronaVac/Sinovac | 2nd | 30 | - | none * |
| #7 [8]                 | m      | 50          | Vaxzevria/AstraZeneca | 1st | 9 | yes, no exacerbation | acitretin |
| #8 [8]                 | m      | 58          | Comirnaty/Pfizer-BioNTech | 2nd | 20 | - | corticosteroids, allotretinoin |
| #9 [8]                 | f      | 60          | Vaxzevria/AstraZeneca | 1st | 30 | yes, no exacerbation | acitretin, methotrexate |
| #10 [9]                | m      | 31          | Vaxzevria/AstraZeneca | 1st | 15 | - | isotretinoin |
| #11 [9]                | m      | 42          | Vaxzevria/AstraZeneca | 2nd | 8 | - | isotretinoin |
| #12 [10]               | f      | 62          | Spikevax/Moderna | 1st | 5 | - | corticosteroids |
| #13 [10]               | f      | 82          | Comirnaty/Pfizer-BioNTech | 1st | 7 | - | methotrexate |
| #14 [11]               | m      | 72          | Covishield/AstraZeneca | 1st | 21 | yes, no exacerbation | none * |
| #15 [12]               | m      | 51          | Comirnaty/Pfizer-BioNTech | 1st | 3 | yes, exacerbation | acitretin |
| #16 [13]               | f      | 63          | Vaxzevria/AstraZeneca | 1st | 9 | - | acitretin |

* topical highly potent corticosteroids.
Among the published cases of post-COVID vaccination PRP [4–13], there were 12 (75%) males and only 4 (25%) females ($p < 0.05$). This predominance in males developing post-COVID vaccination PRP appears to differ from classic adult PRP, which does not show a gender preference. The median age of the reported patients was 59 years (range: 31–82 years), matching the expected age of disease onset of patients with adult PRP. In 10 out of 16 patients (62.5%), PRP developed after the first vaccine dose, in 4 (25%) after the second dose, and in 2 out of 15 patients (12.5%) after the third dose. The median time of COVID-19-vaccination-related PRP was 9.5 days (range: 3–60 days). The majority of patients received systemic treatment, including corticosteroids, retinoids, and methotrexate [4–13]. The latter represented first-choice therapies for PRP, even though the evidence for its use in PRP patients is relatively poor.

The use of biologics for PRP treatment has increasingly been reported within the last decade. The pathophysiologic link between psoriasis and PRP suggests common pathways. Notably, flare-ups or a new onset of pustular psoriasis have been observed in the context of COVID-19 vaccination [22,23]. Interleukin 23 (IL-23)- and IL-17-directed treatment regimens, which are very successfully used for psoriasis patients, might also be beneficial for patients with PRP [24–30]. It is known that the levels of Th helper 17 and T helper 1 cytokines increase in the lesional skin of patients with PRP, including IL-17A, IL-17F, tumor necrosis factor-α, and IL-23. The IL-23/Th17 axis seems to be important in the pathogenesis of PRP due to the clinical and histopathologic improvement in the targeting IL-12/23 and IL-17A (ustekinumab, secukinumab, and ixekizumab) treatment of patients with PRP [24–29]. In a single-arm trial, analyzing changes in the PASI score showed that PASI-50, PASI-75 and PASI-90 response rates were 58%, 42%, and 17%, respectively, during ixekizumab treatment of PRP at week 24 [30]. For those five patients who failed with conventional therapies, all of them achieved clinical improvement with ustekinumab, including decreased erythema, follicular hyperkeratosis, and scaling during a 15-month follow-up period [30]. Overall, IL-17 blockers were successful in treating PRP; however, the evidence is limited. By contrast, ustekinumab is a more commonly reported biologic used in PRP, supported by case reports and case series, and small trials. We hypothesize that the inhibition of the p40 subunits of IL-12 and IL-23 reduces additional cytokine release, thus removing a crucial step for immune cell activation. Given our patient’s response to ustekinumab, our report provides further support for the effectiveness of anti-IL-12/23 agents in PRP.

4. Conclusions

Here, we present a case of difficult-to-treat COVID-19-vaccination-related PRP. Together, PRP might be a rare adverse event after COVID-19 vaccination, particularly affecting older males. Even though in most of the published cases of COVID-19 vaccination-related PRP, standard treatment regimes were successful, refractory cases may also occur. Thus, clinicians should be aware of this rare but potentially severe complication.

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References

1. Gambichler, T.; Boms, S.; Susok, L.; Dickel, H.; Finis, C.; Abu Rached, N.; Barras, M.; Stücker, M.; Kasakovski, D. Cutaneous findings following COVID-19 vaccination: Review of world literature and own experience. J. Eur. Acad. Dermatol. Venereol. 2022, 36, 172–180. [CrossRef] [PubMed]
2. Tan, S.W.; Tam, Y.C.; Oh, C.C. Skin manifestations of COVID-19: A worldwide review. JAAD Int. 2021, 2, 119–133. [CrossRef] [PubMed]
3. Wang, D.; Chong, V.C.; Chong, W.S.; Oon, H.H. A Review on Pityriasis Rubra Pilaris. Am. J. Clin. Dermatol. 2018, 19, 377–390. [CrossRef]
4. Ajebo, E.M.; Howard, J.D.; Anand, D.; Davis, L.S. Pityriasis rubra pilaris potentially triggered by messenger RNA-1273 COVID vaccine. JAAD Case Rep. 2022, 32, 261–264. [CrossRef] [PubMed]
5. Gambichler, T.; Scheel, C.H.; Arafat, Y.; Kautz, O.; Boms, S. Erythrodermic pityriasis rubra pilaris after SASRS-CoV-2 vaccination with concomitant COVID-19 infection. J. Eur. Acad. Dermatol. Venereol. 2022. [CrossRef]
6. Wada, M.; Lee, S.; Curnow, P.; Simpson, I.; Mar, A. A case of pityriasis rubra pilaris following AstraZeneca COVID-19 vaccine. JAAD Case Rep. 2022, 24, 74–77. [CrossRef] [PubMed]
7. Fernández, L.T.; Pérez-Garzar, D.M.; delaO-Escamilla, A.; Yamalled-Ortega, L.A.; Cuellar-Barboza, A.; Ocampo-Candiani, J.; Chavez-Alvarez, S. Pityriasis rubra pilaris in association with inactivated SARS-CoV-2 vaccine (CoronaVac). Dermatol. Ther. 2022, 35, e15455. [CrossRef]
8. Bramhoff, A.C.; Wesselmann, U.; Bender, S.T.; Berghoff, A.V.; Hofmann, S.C.; Balakirski, G. Pityriasis rubra pilaris nach COVID-19-Impfung: Kausaler Zusammenhang oder Koinzidenz? [Pityriasis rubra pilaris after COVID-19 vaccination: Causal relationship or coincidence?]. Der Hautarzt 2022. (In Germany) [CrossRef]
9. Criado, P.R.; Ibanez, M.; Rocha, P.S.; Miot, H.A. Pityriasis rubra pilaris (type I) following ChAdOx1 COVID-19 vaccine: A report of two cases with successful treatment with oral isotretinoin. J. Eur. Acad. Dermatol. Venereol. 2022, 36, e508–e510. [CrossRef] [PubMed]
10. Sechi, A.; Pierobon, E.; Pezzolo, E.; Gemi, L.; Trevisan, G.; Zardo, D.; Riva, G.; Mondino, S.; Naldi, L. Abrupt onset of Sweet syndrome, pityriasis rubra pilaris, pityriasis lichenoides et varioliformis acuta and erythema multiforme: Unraveling a possible common trigger, the COVID-19 vaccine. Clin. Exp. Dermatol. 2022, 47, 437–440. [CrossRef]
11. Sahni, M.K.; Roy, K.; Asati, D.P.; Khurana, U. An old entity, a new trigger: Post COVID-19 vaccine pityriasis rubra pilaris. Int. J. Risk Saf. Med. 2021, 32, 261–264. [CrossRef] [PubMed]
12. Hunjan, M.K.; Roberts, C.; Karim, S.; Hague, J. Pityriasis rubra pilaris-like eruption following administration of the BNT163b2 (Pfizer-BioNTech) mRNA COVID-19 vaccine. Clin. Exp. Dermatol. 2022, 47, 188–190. [CrossRef] [PubMed]
13. Llodó, J.; Butrón, B.; Sampredo-Ruiz, R.; Fraga, J.; de Argila, D. Pityriasis rubra pilaris after Vaxzevria® COVID-19 vaccine. J. Eur. Acad. Dermatol. Venereol. 2021, 35, e683–e685. [CrossRef] [PubMed]
14. Peña-Rosado, A.; Riera-Martí, N.; Expósito-Serrano, V.; Romani, J. Autoinflammatory keratinization diseases (AIKDs. Actas Dermosifiliogr (Engl. Ed.) 2021, 112, 891–900. [CrossRef]
15. Akiyama, M. Autoinflammatory Keratinization Diseases (AIKDs): Expansion of Disorders to Be Included. Front. Immunol. 2020, 11, 280. [CrossRef] [PubMed]
16. Mohamed, M.; Belhadjali, H.; Hammedi, F.; Ben Meriem, C.; Zili, J. Pityriasis rubra pilaris occurring after vaccination with diphtheria-pertussis-tetanus and oral poliovirus vaccines. Indian J. Dermatol. Venereol. Leprol. 2015, 81, 618–620. [CrossRef] [PubMed]
17. Naciri Bennani, B.; Cheikh Rouhou, H.; Waton, J.; Cuny, J.F.; Bassegoda, G.; Trechot, P.; Barraud, A.; Schmutz, J.L. Pityriasis rubra pilaris aprés vaccination [Pityriasis rubra pilaris after vaccination]. Ann. Dermatol. Venereol. 2011, 138, 753–756. [CrossRef]
18. Kadylyak, D.; Barańska-Rybak, W. Acute postinfectious pityriasis rubra pilaris as a cutaneous manifestation in COVID-19: A case report and its dermoscopic features. J. Eur. Acad. Dermatol. Venereol. 2021, 35, e622–e624. [CrossRef]
19. Aguilar-Gamboa, F.R.; Cubas-Alarcon, D.; Villegas-Chiroque, M.; Failoc-Rojas, V.E. Pityriasis rubra pilaris post-infection due COVID-19: Case report. Colomb. Médica (Cal.) 2021, 52, e7014577. [CrossRef]
20. Arora, A.; Mohata, A.; Ghiya, B.C.; Kumar Jangir, V. Acute postinfectious type III pityriasis rubra pilaris as a cutaneous manifestation in COVID-19: Decoding a possible trigger! J. Cosmet. Dermatol. 2022. [CrossRef]
21. Magro, C.; Crowson, A.N.; Franks, L.; Schaffer, P.R.; Whelan, P.; Nuovo, G. The histologic and molecular correlates of COVID-19 vaccine-induced changes in the skin. Clin. Dermatol. 2021, 39, 966–984. [CrossRef] [PubMed]
22. Tran, T.B.; Pham, N.T.U.; Phan, H.N.; Nguyen, H.T. Generalized erythrodemic psoriasis triggered by vaccination against severe acute respiratory syndrome Coronavirus 2. Dermatol. Ther. 2022, 35, e15464. [CrossRef] [PubMed]
23. Tachibana, K.; Kawakami, Y.; Tokuda, M.; Sato, S.; Sugihara, S.; Miyake, T.; Sugiuara, K.; Morizane, S. Flare-up of generalized pustular psoriasis following Pfizer-BioNTech BNT162b2 mRNA COVID-19 vaccine: Two cases without mutations of IL36RN and CARD14 genes. J. Dermatol. 2022. [CrossRef] [PubMed]
24. Nagai, H.; Jimbo, H.; Matsuura, S.; Tatsuoka, S.; Shiraki, E.; Nishigori, C. Successful treatment of pityriasis rubra pilaris with guselkumab: Serum CCL20 as a potential marker for the disease activity. *Dermatol. Ther.* 2020, 33, e14403. [CrossRef] [PubMed]

25. De Rosa, A.; Gambardella, A.; Licata, G.; Alfano, R.; Argenziano, G. Successful treatment of Pityriasis rubra pilaris with brodalumab. *Australas. J. Dermatol.* 2020, 61, e249–e251. [CrossRef] [PubMed]

26. Langley, R.G.; Tsai, T.F.; Flavin, S.; Song, M.; Randazzo, B.; Wasfi, Y.; Jiang, J.; Li, S.; Puig, L. Efficacy and safety of guselkumab in patients with psoriasis who have an inadequate response to ustekinumab: Results of the randomized, double-blind, phase III NAVIGATE trial. *Br. J. Dermatol.* 2018, 178, 114–123. [CrossRef]

27. Ross, N.A.; Chung, H.J.; Li, Q.; Andrews, J.F.; Keller, M.S.; Uitto, J. Epidemiologic, Clinicopathologic, Diagnostic, and Management Challenges of Pityriasis Rubra Pilaris: A Case Series of 100 Patients. *JAMA Dermatol.* 2016, 152, 670–675. [CrossRef]

28. Ricar, J.; Cetkovska, P. Successful treatment of refractory extensive pityriasis rubra pilaris with risankizumab. *Br. J. Dermatol.* 2021, 184, e148. [CrossRef]

29. Napolitano, M.; Abeni, D.; Didona, B. Biologics for pityriasis rubra pilaris treatment: A review of the literature. *J. Am. Acad. Dermatol.* 2018, 79, 353–359.e11. [CrossRef]

30. Haynes, D.; Strunck, J.L.; Topham, C.A.; Ortega-Loayza, A.G.; Kent, G.; Cassidy, P.B.; Hu, R.; Choate, K.; Wang, Z.; Liu, Y.; et al. Evaluation of Ixekizumab Treatment for Patients With Pityriasis Rubra Pilaris: A Single-Arm Trial. *JAMA Dermatol.* 2020, 156, 668–675. [CrossRef]