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REVIEW

Pityriasis Rosea and Pityriasis Rosea-Like Eruption Following COVID-19 Vaccination: A Narrative Review

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Abstract: COVID-19 pandemic completely changed every aspect of human life. Several measures were adopted to limit the spreading of the infection. Among these, vaccination was the main one. Globally, vaccination campaign was a success, showing to be efficient in controlling and preventing the SARS-Cov2 infection, reducing the risk of disease progression, hospitalization, and mortality. However, with the increasing number of vaccines administered, several cutaneous reactions were described, making dermatologists key players in their recognition and treatment. Among these, also viral reactivations have been described. In particular, cases of Pityriasis Rosea (PR) and PR-like reactivations have been collected. An early diagnosis is mandatory to avoid mistreatments. In this context, we conducted a review of the current literature investigating cases of PR following COVID-19 vaccination with the aim of understanding the possible pathogenetic mechanisms and causal correlation as well as to investigate the risk of this cutaneous eruption, to offer clinicians a wide perspective on the linkage between PR and COVID-19 vaccines.

Keywords: COVID-19, vaccination, pityriasis rosea, safety

Introduction

Pityriasis rosea (PR) is a dermatological condition characterized by the emergence of distinct, scaly papules and plaques that align with the Langer lines (cleavage lines) on the body's trunk and limbs.[1–3] Usually, a single herald patch on the trunk precedes this generalized rash.[1–3] This typical clinical presentation accounts for up to 90% of cases.[1–3] Prodromal symptoms such as fatigue, nausea, general malaise, enlarged lymph nodes, headaches, joint pain, fever, and sore throat are present before or during the course of PR in 69% of cases.[1–3] However, atypical cases of PR with a different rash distribution, morphology, size, and number of lesions have been described, making the diagnosis challenging.[1–4] Annually, around 170 cases of PR per 100,000 individuals are reported, usually between the ages of 10 and 35, and with a slight predominance in female subjects.[5]

As regards PR pathogenesis, a viral etiology has been proposed since intracytoplasmic and intranuclear virus-like particles have been observed.[1–3] This possible pathogenesis seems to be confirmed by the presence of an increased CD4 lymphocytes and Langerhans cells count in the dermis.[1–3] Globally, Human Herpes Virus (HHV) 6 and 7 have been linked to PV. In particular, while these viruses cause roseola infantum in children, their reactivation should be the causal agent of PR.[1–3] However, the exact pathogenetic mechanism of PR is not fully understood yet. Finally, PR-like eruptions have been described following certain medications, differing from PR for more extensive and pruritic lesions as well as histopathological differences.[5] Of interest, cases of PR reactivation have been reported following coronavirus disease 2019 (COVID-19) infection and vaccination.[6–38] As it is well-known, COVID-19 pandemic has been a global emergency, completely changing daily-routine.[39,40] These changes were reflected in clinical practice, forcing clinicians to adopt several measures (e.g hygiene measures, use of face mask, teledermatological services etc.) to reduce the risk of the spreading of the infection.[41–45] Various strategies were also adopted by local Governments such as testing and contact tracing, use of face mask, quarantine and

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isolation, lockdowns, travel restrictions, social distancing, public health messages, international cooperation, hygiene measures, and vaccination campaign.[41,42] Among these, vaccination was the main weapon to overcome the pandemic.[46] Several vaccines were studied, mainly based of two mechanisms of action: viral-vector-based vaccines and mRNA-based vaccines. Globally, 4 vaccines were licensed by the European Medicines Agency (EMA): AstraZeneca; AZD1222 and Johnson & Johnson; Ad26.COV2 (viral-vector-based), Pfizer/BioNTech; BNT162b2 and Moderna; mRNA-1273 (mRNA-based).[47,48] Other vaccines have been authorized in other countries.[47,48]

Fortunately, vaccination campaign was a success, leading to an efficient control and prevention of the COVID-19 pandemic, reducing the risk of disease progression, hospitalization, and mortality.[47,48] In this context, vaccine-related adverse events (AEs) were continuously monitored to increase public confidence.[49] The high number of administered vaccinations, led to the development of different AEs, which were often not reported in clinical trials. As regards the dermatological practice, several cutaneous reactions have been described, including cutaneous diseases (eg, psoriasis, hidradenitis suppurativa, lichen planus, etc.) and cutaneous findings (eg vesicular rashes, maculopapular, urticarial, etc.).[50–54] Of note, also cases of PR and PR-like eruptions were collected.

The aim of this systematic review is to investigate cases of PR and PR-like eruptions following COVID-19 vaccination in order to understand the possible pathogenetic mechanisms and causal correlation as well as to investigate the risk of this cutaneous eruption, to offer clinicians a wide perspective on the linkage between PR and COVID-19 vaccines.

Materials and Methods

For this review manuscript, a thorough research of the current literature was performed with the use of several databases (PubMed, Embase, Google Scholar, Cochrane Skin, EBSCO and MEDLINE) (until October 27, 2023). The following keywords were used to research data: “COVID-19”, “vaccination”, “adverse events”, “vaccine”, “skin manifestations”, “cutaneous”, “side effects”, “mRNA”, “viral-vector”, “Pfizer/BioNTech”, “BNT162b2”, “Moderna”, “mRNA-1273”, “AstraZeneca”, “AZD1222”, “Johnson & Johnson”, “Ad26.COV2.S”, “pityriasis rosea-like eruption” and “pityriasis rosea”. The investigated articles comprised meta-analyses, reviews, letter to editor, real-life studies, case reports and case series. The most relevant documents were selected. Cases of PR and PR-like eruption following vaccines which were not approved by EMA were not considered. Thus, the research was advanced by reviewing the texts and the abstracts of collected articles. The references of the selected manuscript were also evaluated to include articles that could have been missed. Only English language manuscripts were considered. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

Results

Details of the included studies are summarized in Table 1.[8–29,31,33–38] A total of 29 manuscripts reporting 113 cases of PV following COVID-19 vaccination has been collected, with the majority [35 (31.0%)] deriving from the United States,

Table 1 Pityriasis Rosea and Pityriasis Rosea-Like Eruption Following COVID-19 Vaccination

Authors	Country	Cases	Vaccines	Time	Dose
Temiz et al[8]	Turkey	31	BNT162b2: 14 AZD1222:17	Medium time: 12.7 days	First dose: 19 Second dose: 12
Freeman et al[9]	US	27	mRNA-1273: 16 BNT162b2: 8 AZD1222: 2 Ad26.COV2.S: 1	NR	First dose: 15 Second dose: 12
Català et al[20]	Spain	20	BNT162b2: 11 mRNA-1273: 5 AZD1222:4	Medium time: 6.3 days	First dose: 12 Second dose: 8
McMahon et al[31]	US	4	BNT162b2: 3 mRNA-1273: 1	Medium time: 7 days	First dose: 3 Second dose: 1

(*Continued*)

Table 1 (Continued).

Authors	Country	Cases	Vaccines	Time	Dose
Martora et al[33]	Italy	3	mRNA-1273: 3	Medium time: 8 days	First dose: 3 Second dose: 0
Busto-Leis et al[34]	Spain	2	BNT162b2: 2	Medium time: 1–7 days	First dose: 1 Second dose: 1
Cyrenne et al[35]	Canada	2	BNT162b2: 2	Medium time: 4.5 days	First dose: 1 Second dose: 1
Farinazzo et al[36]	Italy	2	BNT162b2: 2	Medium time: 2–21 days	First dose: 1 Second dose: 1
Khattab et al[37]	Greece	2	BNT162b2: 2	Medium time: 7.5 days	First dose: 1 Second dose: 1
Abdullah et al[38]	Lebanon	1	BNT162b2: 1	7 days	First dose
Adya et al[10]	India	1	AZD1222:1	4 days	First dose
Bostan et al[11]	Turkey	1	BNT162b2: 1	15 days	Second dose
Buckley et al[12]	US	1	BNT162b2: 1	7 days	First dose
Burlando et al[13]	Italy	1	BNT162b2: 1	30 days	Second dose
Carballido Vázquez et al[14]	Spain	1	BNT162b2: 1	NR	First dose
Cohen et al[15]	US	1	BNT162b2: 1	7 days	First dose
Das et al[16]	India	1	AZD1222:1	NR	NR
Dormann et al[17]	Germany	1	AZD1222:1	12 days	First dose
Larson et al[18]	US	1	mRNA-1273: 1	7 days	Second dose
Leerunyakul et al[19]	Thailand	1	AZD1222:1	14 days	First dose
Marcantonio-Santa Cruz et al[21]	Spain	1	BNT162b2: 1	7 days	Second dose
Mehta et al[22]	India	1	AZD1222:1	1 days	First dose
Niebel et al[23]	Germany	1	AZD1222:1	21 days	First dose
Pedrazini et al[24]	Brazil	1	AZD1222:1	15 days	Second dose
Shin et al[25]	Korea	1	mRNA-1273: 1	3 days	Second dose
Tihy et al[26]	Switzerland	1	BNT162b2: 1	15 days	Second dose
Valk et al[27]	US	1	BNT162b2: 1	3 days	Second dose
Wang et al[28]	Taiwan	1	mRNA-1273: 1	7 days	First dose
Yu et al[29]	Philippines	1	AZD1222:1	3 days	First dose

followed by Turkey [32 (28.3%)], and Spain [24 (21.2%)]. In particular, BNT162b2 was the most common vaccine associated with PR (53, 46.9%), followed by AZD1222 (31, 27.4%), mRNA-1273 (28, 24.8%), and Ad26.COV2.S (1, 0.9%). Medium time from vaccine to PR onset was 9 ± 6.3 days (not reported for 33 patients). Finally, the majority of PR development derived from the first dose of vaccine (67, 59.3%), instead of the second one (45, 39.8%). Of note, 1 case has not been associated with the dose of vaccination. The largest case series (31 patients) has been reported by Temiz et al.[8] Globally, no cases of severe diseases have been described. Finally, it should be reported that cases of PR have not been reported following the third dose of vaccination.

Discussion

COVID-19 pandemic was a worldwide challenge, completely revolutionizing the diagnosis and treatment scenario of cutaneous diseases, ranging from inflammatory skin conditions,[55–61] to skin cancers[62–65] PR is a common acute, self-limited cutaneous disease usually affecting children and young adults.[1–3] Despite the exact pathogenetic mechanism is not fully understood, cases of PR and PR-like eruptions were described following COVID-19 vaccination.[8–38] In this scenario, we conducted a review on the current literature to investigate the association between PR and COVID-19 vaccines. A total of 29 manuscripts reporting 113 cases were collected. Of these, BNT162b2 was the most common vaccine associated with PR (53, 46.9%), as well as the majority of PR development derived from the first dose of vaccine (67, 59.3%). Globally, medium time from vaccine to PR onset was 9 ± 6.3 days (not reported for 33 patients). Finally, no cases of severe diseases or PR following the third dose of the vaccines have been described.

As regards the possible pathogenetic mechanism, it is not clearly understood. However, cases of PR have been described following both types of vaccines (mRNA-based and viral vector-based) as well as both doses. Thus, the pathogenetic mechanism does not seem to be related with the vaccine type of dose. Probably, the exposure to the viral antigen boosts the cell-mediated immune response, increasing the production of T cells and cytokines.[66] However, this immune response can sometimes become dysregulated, leading to inflammation and reactivation of latent viral infections, including human herpesviruses HHV6 and HHV7, linked to PR.[66–68]

As far as the dermatological practice, investigating possible relationship between vaccination and cutaneous diseases is mandatory to confirm the safety of these drugs.[69–71] Vaccination was the most important strategy to overcome the pandemic.[69–71]

Globally, PR and PR-like eruptions following COVID-19 vaccines are rare, and complicated cases have not been described. Moreover, cases of PR has been also described following SARS-Cov2 infection.[72] In our opinion several cases of PR following COVID-19 vaccines have not been reported in literature due to their self-limiting and benign course, leading to an underestimation of the number of cases. Certainly, further studies are needed to understand the possible correlation in order to identify risk factors and, subsequently, "at-risk" patients.[73–76] However, it should be stated that dermatologists should keep in mind the possibility PR and PR-like eruptions following COVID-19 vaccination in order early recognize these diseases and early reassuring patients.

Strengths and Limitations

Main strengths of our work are the comprehensive literature research methods and the number of investigated articles, thanks to the rigorous quality assessment. However, the limitations of the study should be discussed. First, the number of patients is inadequate to assess the correlation between PR and COVID-19 vaccines. Moreover, clinical trials and comparative studies are absent. Similarly, the possibility of a simple causal temporal correlation between PR and COVID-19 vaccination cannot be ruled out. Finally, our assumptions must be taken simply as suggestions and not as definite proposals, as our work has not had the support of meta-analysis, which may be the generalization of our results.

Conclusions

COVID-19 vaccination campaign was the main strategy to overcome the pandemic. With the increasing number of vaccinated individuals and vaccine doses, various cutaneous reactions have been reported, often not detected in clinical trials. Among these, the possibility of viral reactivations has been described. In our review, we focused on PR and PR-like eruption following COVID-19 vaccination. Globally, the number of cases of PR and PR-like eruption is extremely low if compared with the number of vaccines administered, leading to the impossibility to demonstrate that COVID-19 vaccination may increase the risk of PR and PR-like eruption development. In our opinion, clinicians should keep in mind the possibility of the development of this cutaneous disease following vaccination. Certainly, more studies are needed to identify "at-risk" patients and adopt preventative measures. Surely, vaccination should not be discouraged.

Disclosure

The authors report no conflicts of interest in this work.

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