Title
Pityriasis Lichenoides Following SARS-CoV-2 Infection/Vaccination

Journal
Current Dermatology Reports, 12(1)

ISSN
2162-4933

Authors
Feschuk, Aileen M
Green, Maxwell
Kashetsky, Nadia
et al.

Publication Date
2023

DOI
10.1007/s13671-023-00380-1

Peer reviewed

Current Dermatology Reports (2023) 12:27–32
https://doi.org/10.1007/s13671-023-00380-1

REVIEW

Pityriasis Lichenoides Following SARS-CoV-2 Infection/Vaccination

Aileen M. Feschuk[1] · Maxwell Green[2] · Nadia Kashetsky[1] · Howard I. Maibach[3]

Accepted: 4 December 2022 / Published online: 17 January 2023

Abstract

Purpose of Review Pityriasis lichenoides (PL) is a spectrum of dermatological conditions involving polymorphous lesions. Natural history of the condition ranges from acute to chronic. Cases of PL following SARS-CoV-2 infection/vaccination have been reported, but not yet comprehensively reviewed. Hence, the objective of this article is to review and summarize cases of PL following SARS-CoV-2 infection/vaccination in order to guide clinicians in its diagnosis and management.

Recent Findings PubMed, Embase, and Web of Science were searched for relevant articles. Thirteen articles, consisting of 14 cases of PL following SARS-CoV-2 infection/vaccination, were identified. Males represented 64.3% of cases, and the average age of those affected was 41.4 years. The majority of cases ($N=9$, 64.3%) were following SARS-CoV-2 vaccination, the most commonly implicated being Pfizer-BioNTech ($n=8/10$, 80%), while four (28.6) followed infection. The overall latency period ranged from 5 days to 1 month. Treatments varied greatly. However, at the time of follow-up, 12/14 patients (85.7%) had either marked improvement or complete resolution of lesions.

Summary This review cannot determine causality. However, a temporal association was observed with the case reports, and one case of PL followed SARS-CoV-2 infection and recurred with subsequent vaccination, suggesting an association. Nevertheless, risk of developing PL following SARS-CoV-2 infection/vaccination is likely extremely low. There is also the possibility these cases are purely coincidental. Still, clinicians should be aware of this possible etiology when diagnosing a new or exacerbated case of PL. Finally, given that the majority of patients had marked improvement or complete resolution of lesions at the time of follow-up, clinicians should provide reassurance to their affected patients.

Keywords COVID-19 · Immunization · Pityriasis lichenoides · PLEVA · PLC · SARS-CoV-2 · Vaccination

Introduction

Pityriasis lichenoides (PL) is a spectrum of histopathologically and clinically overlapping dermatological conditions, the two main types being pityriasis lichenoides et varioliformis acuta (PLEVA) and pityriasis lichenoides chronica (PLC) [1, 2]. PLEVA onsets acutely/subacutely with the eruption of polymorphous lesions ranging from macules, to hemorrhagic papules, to ulcers [1, 2]. PLEVA may involve burning, pruritus, and occasionally constitutional symptoms, and typically resolves within weeks to months [1, 2]. PLC onsets insidiously, is typically asymptomatic, and may relapse and remit for years [1, 2]. PLC is characterized by reddish-brown maculopapules containing centrally located micaceous scales [1, 2]. Both PLEVA and PLC lesions can leave hyper or hypopigmented pox-like scars [1, 2].

PL is diagnosed clinically, supported by skin biopsy demonstrating interface dermatitis and dense and diffuse lymphocytic infiltrate [1, 2]. Gradual acute and chronic type histopathological differences exist between PLEVA and PLC [1, 2]. Evidence on the treatment of PL is limited; however, a systematic review by Bellinato et al. (2019) recommended narrow-band ultraviolet B phototherapy (nb-UVB-PT) as first-line therapy and oral erythromycin or methotrexate with or without topical corticosteroids (TCS) as second-line therapies [3].

Recently, cases of PL following SARS-CoV-2 infection/vaccination have been reported, but not yet comprehensively reviewed. Cases of other dermatoses following SARS-CoV-2 infection/

✉ Aileen M. Feschuk
amfeschuk@mun.ca

[1] Faculty of Medicine, Memorial University of Newfoundland, 300 Prince Philip Dr.Newfoundland & Labrador, St. John's A1B 3V6, Canada

[2] Tulane University School of Medicine, New Orleans, LA, USA

[3] Department of Dermatology, University of California San Francisco, San Francisco, CA, USA

vaccination have been reviewed [4•]. Therefore, this review comprehensively summarizes PL cases following SARS-CoV-2 infection/vaccination to guide its diagnosis and management.

Methods

PubMed, Embase, and Web of Science were comprehensively searched in October of 2022 using the following: ("pityriasis lichenoides" OR "pityriasis lichenoides et varioliformis acuta" OR "PLEVA" OR "pityriasis lichenoides chronica" OR "mucha habermann") AND ("covid" OR "SARS" OR "coronavirus"). Following PRISMA guidelines, title/abstract screening, full-text screening, and data extractions were completed in duplicate (Fig. 1) [5]. Articles reporting new-onset or exacerbation of PL following SARS-CoV-2 infection/vaccination were included.

Results

Thirteen articles, comprising 14 cases of PL following SARS-CoV-2 infection/vaccination, were included [6–15, 16•, 17, 18•]. The mean age of those affected was 41.4 years (median

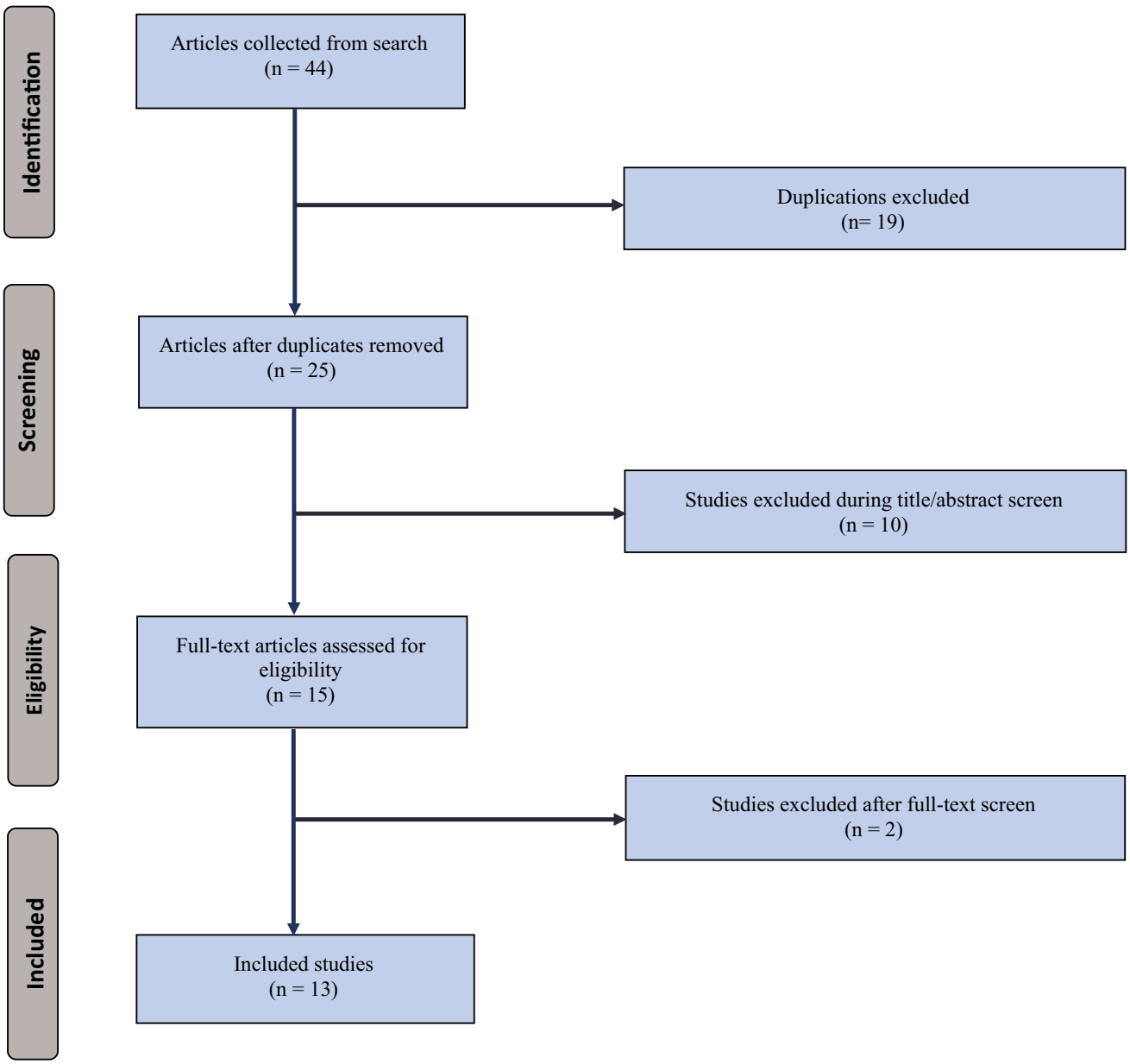

Fig. 1 Search strategy employed to identify cases of pityriasis lichenoides following SARS-CoV-2 infection and/or vaccination

41.0 years, range 6.0–81.0 years) and 64.3% of those affected were male. Of these cases, ten (71.4%) were PLEVA/ "PLEVA-like" and four (28.6%) were PLC. Thirteen cases (92.9%) were new-onset, while one (7.1%) was an exacerbation of previous PL disease. The majority of cases ($N=9$, 64.3%) were associated with SARS-CoV-2 vaccination, while four (28.6%) were associated with SARS-CoV-2 infection. One case (7.1%) followed infection, and recurred following subsequent vaccination. The majority of vaccine-associated cases ($n=8/10$, 80%) followed the Pfizer-BioNTech vaccine, while one (10.0%) followed the Oxford-AstraZeneca vaccine and one (10.0%) followed the Sinopharm vaccine. Additionally, 40.0% ($n=4/10$) following vaccination followed the first dose, while 40% ($n=4/10$) followed the first dose, with worsening after the second, and 20% ($n=2/10$) followed the second dose. Latency period ranged from 5 days to 1 month overall and for cases following vaccination, and 10 to 17.5 days for cases following infection. The mean latency period was 13.8 days overall and for cases following infection, and 13.7 days for cases following vaccination. The most common lesion location was the limbs, affected in 11 cases (78.6%), followed by the torso affected in ten (71.4%), the face/scalp affected in three (21.4%), and finally the neck affected in one (7.1%). Cases' scores on Naranjo's Adverse Drug Reaction Probability Scale (ADRPS) averaged 6.3 and ranged from 5.0 to 8.0 [19].

Two patients (14.3%) received no treatment, and treatment use was not reported in two cases (14.3%). However, all four of these cases (100.0%) reported complete resolution at unspecified time points.

One patient (7.1%) received oral corticosteroids with complete resolution at 1 month. Oral corticosteroids with TCS were used in two cases (14.3%) with complete resolution at 1 and 5 months. Oral azithromycin with TCS was used in one case (7.1%) with marked improvement at 5 months. Oral doxycycline with TCS was used in one case (7.1%) with no improvement at 1 month. Oral doxycycline was used alone in two cases (14.3%), with one reporting complete resolution at 3 months, while the other did not report follow-up. Topical fusidic acid with TSC and nb-UVB-PT was used in one case (7.1%) with complete resolution at 10 weeks, while oral azithromycin with TCS and topical immunosuppressant was used in one case (7.1%) with marked improvement at 2 months. Finally, nb-UVB-PT was used alone in one case (7.1%) with complete resolution at 2 months. Results are summarized in Table 1.

Discussion

While the etiology of PL remains unknown, proposed mechanisms of disease include immune-mediated hypersensitivity vasculitis, inflammatory response to T-cell dyscrasia, or infectious or drug-related hypersensitivity reaction [2]. The latter is supported by the fact that many viruses (e.g., human immunodeficiency virus, Epstein-Barr, varicella-zoster, parvovirus B19, cytomegalovirus, and adenovirus) and vaccinations (measles, mumps, and rubella (MMR); tetanus; diphtheria; influenza; and human papilloma virus) have been linked to PL [1, 2, 20–23]. While the link between vaccinations/infections and PL is not fully understood, it is thought that viral antigens serve as an epidermal target, and PL is the cutaneous manifestation of this cytotoxic hypersensitivity [5].

While this review cannot determine causality, Naranjo's ADRPS suggests SARS-CoV-2 may be a "probable" cause of PL [19]. However, this scale is not well validated [24, 25]. These cases could also be due to chance coincidence, as many people have been infected with, or vaccinated for, SARS-CoV-2, and not been affected by PL. If this association is in fact not due to chance, causality still cannot be established, and the risk of PL with SARS-CoV-2 is likely extremely small and at this time should not deter individuals from receiving vaccination. More infection/vaccination challenge may lead to more evidence into the relationship between SARS-CoV-2 and PL, and the etiology of PL in general.

It is of the utmost importance that possible side effects of vaccines are reported. These can be reported via platforms such as the Vaccine Adverse Event Reporting System (VAERS) (co-sponsored by the Food and Drug Administration (FDA) and the CDC), and the Canadian Adverse Events Following Immunization Surveillance System [26, 27]. Additionally, these platforms perform active surveillance of case reports from health professionals, health facilities, and publications in scientific journals [28]. These reports are considered a "signal," or a "preliminary indication of a product-related issue" [28]. Signals are then evaluated to determine their validity [28]. This may include conducting vaccine studies, for example, via case-crossover designs which are used to study transient effects on the risk of acute events, and involves the patient acting as his or her own control [29]. A cohort study published by Akpandak et al. (2022) assessed whether vaccination against SARS-CoV-2 was associated with an increased risk of herpes zoster infection [30]. No increased risk was found [30]. This is an example of a signal derived from case reports that was not supported by properly conducted epidemiological studies, suggesting the initial reports were coincidental. However, should vaccine studies suggest increased risk or causality, this can lead to regulatory action including but not limited to re-assessment of risk/benefit profiles of vaccines, the dissemination of risk alerts to healthcare professionals and consumers, and even market withdrawals [28].

This article highlights the importance of clinicians taking a thorough SARS-CoV-2 infection/vaccination history for new or exacerbated PL. Additionally, this article

Table 1 Summary of cases reporting pityriasis lichenoides following SARS-CoV-2 infection and/or vaccination (*TCS*, topical corticosteroid; *nb-UVB-PT*, narrow-band ultraviolet B phototherapy)

	Result	Sample size
Age (years)	Mean = 41.4; median = 41; range = 6–81	14
Sex	Male: *N* = 9, 64.3%; female: *N* = 5, 35.7%	14
Pityriasis lichenoides subtype		14
PLEVA/ "PLEVA-like"	*N* = 10, 71.4%	
PLC	*N* = 4, 28.6%	
Post vaccination or infection	*N* = 9, 64.3%: vaccination; *N* = 4, 28.6%: infection; *N* = 1, 7.1%: vaccination and infection	14
Latency period		12
Overall	Mean = 13.8 days; range = 5 days–1 month	
Post vaccination	Mean = 13.7 days; range 5 days–1 month	
Post infection	Mean = 13.8; range 10–17.5 days	
Vaccine type		10
Pfizer-BioNTech	*N* = 8, 80.0%	
Oxford-AstraZeneca	*N* = 1, 10.0%	
Sinopharm	*N* = 1, 10.0%	
Vaccine dose number		10
1st	*N* = 4, 40.0%	
1st, worsening with 2nd	*N* = 4, 40.0%	
2nd	*N* = 2, 20.0%	
Diagnosis		14
Biopsy	*N* = 13, 92.9%	
Clinical	*N* = 1, 7.1%	
Locations of lesions		14
Limbs	*N* = 11, 78.6%	
Torso	*N* = 10, 71.4%	
Face/scalp	*N* = 3, 21.4%	
Neck	*N* = 1, 7.1%	
Not reported	*N* = 2, 14.3%	
Treatment		14
Oral corticosteroid	*N* = 1, 7.1%; complete resolution at 1 month	
Oral corticosteroid + TCS	*N* = 2, 14.3%: complete resolution at 1 and 5 months	
Oral azithromycin + TCS	*N* = 1, 7.1%: marked improvement with hyper/hypopigmented scars at 5 months	
Oral doxycycline + TCS	*N* = 1, 7.1%: no improvement at 1 month	
Oral doxycycline	*N* = 1, 7.1%: complete resolution at 3 months *N* = 1, 7.1%: not reported	
Topical fusidic acid + TCS + nb-UVB-PT	*N* = 1, 7.1%: complete resolution at 10 weeks	
nb-UVB-PT	*N* = 1, 7.1%: complete resolution at 2 months (20 sessions)	
Oral azithromycin + TCS + topical immunosuppressant	*N* = 1, 7.1%: marked improvement at 2 months	
No treatment	*N* = 2, 14.3%: complete resolution (time period not reported)	
Not reported	*N* = 2, 14.3%: complete resolution (time period not reported)	
Naranjo's Adverse Drug Reaction Probability Scale scores	Mean: 6.3, median: 6.0, range: 5.0–8.0	14

provides preliminary insight into the risk window for PL in relationship to SARS-CoV-2 vaccination. The risk window is the period of time in which subjects are considered to be at an increased risk of adverse events following vaccination [31]. Based on the latency period determined in this study, which ranged from 5 days to 1 month following vaccination, with a mean of 13.7 days, the risk window is likely confined to approximately 1 month following vaccination.

The treatment of PL is not well established, and varied among these cases, as did follow-up periods making comparisons difficult. However, considering that at the time

of follow-up, 12/14 patients (85.7%) had either marked improvement or complete resolution of lesions, clinicians should provide their patients with reassurance, in addition to nb-UVB-PT or oral erythromycin or methotrexate with or without TCS, as suggested by Bellinato et al. [3].

Small sample sizes, likelihood of unreported cases, and lack of controlled studies are limitations of this review.

Conclusion

In conclusion, 14 cases of PL following SARS-CoV-2 infection/vaccination were identified. Although this review does not prove causality, the case reports observed a temporal association and in one case PL occurred after natural SARS-CoV-2 infection, and recurred with subsequent vaccination, suggesting an association. However, these cases could be due to chance coincidence, and if they are not, the risk of developing PL following SARS-CoV-2 infection/vaccination is likely still extremely minimal. This review adds to the growing body of evidence suggesting the etiology of PL to be an infectious or drug-related hypersensitivity reaction. Therefore, clinicians including dermatologists should inquire about recent SARS-CoV-2 infection/vaccination when diagnosing a new or exacerbated case of PL. Additionally, given that the majority of patients experienced marked improvement or complete resolution of lesions at the time of follow-up, clinicians should provide reassurance to those affected.

Compliance with Ethical Standards

Conflict of Interest The authors have no financial or non-financial competing interests to disclose.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance

1. Khachemoune A, Blyumin ML. Pityriasis lichenoides. Am J Clin Dermatol. 2007;8:29–36. https://doi.org/10.2165/00128071-200708010-00004.
2. Bowers S, Warshaw EM. Pityriasis lichenoides and its subtypes. J Am Acad Dermatol. 2006;55:557–72. https://doi.org/10.1016/j.jaad.2005.07.058.
3. Bellinato F, Maurelli M, Gisondi P, Girolomoni G. A systematic review of treatments for pityriasis lichenoides. J Eur Acad Dermatol Venereol. 2019;33:2039–49. https://doi.org/10.1111/jdv.15813.
4. • Zou H, Daveluy S. Pemphigus vulgaris after COVID-19 infection and Vaccination. J Am Acad Dermatol. 2022;87:709–10. https://doi.org/10.1016/j.jaad.2022.05.013. **This review highlights the association between COVID-19 infection/vaccination and an autoimmune dermatological disorder. Specifically, it summarizes four cases of pemphigus vulgaris following COVID-19 infection/vaccination**.
5. Page MJ, McKenzie JE, Bossuyt PM, et al. The Prisma 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021. https://doi.org/10.1136/bmj.n71.
6. Al Muqrin AM, Alruwaili ZM. Pityriasis lichenoides Chronica induced by COVID-19 messenger RNA vaccination. JAAD Case Rep. 2022;27:52–4. https://doi.org/10.1016/j.jdcr.2022.07.017.
7. Dawoud NM, Aslam H, Ali IM, DawoudMM. The first case report of Pityriasis lichenoides chronica following COVID-19 mRNA vaccination. Dermatol Ther. 2022;35. https://doi.org/10.1111/dth.15445.
8. De La Garza H, Saliba E, Rosales Santillan M, BremC, Vashi NA. Pityriasis lichenoides et varioliformis acuta as a complication of COVID-19 infection. Dermatopathology. 2022;9:244–50. https://doi.org/10.3390/dermatopathology9030028.
9. Drago F, Ciccarese G, Guadagno A, Parodi A. Pityriasis lichenoides Chronica after BNT162b2 pfizer-biontech vaccine: a novel cutaneous reaction after SARS-CoV-2 vaccine. J Eur Acad Dermatol Venereol. 2022. https://doi.org/10.1111/jdv.18418.
10. Durusu IN, Gurel G, Tokyol C. Un caso de pitiriasis Liquenoide Crónica en una paciente infectada por covid-19. Actas Dermosifiliogr. 2021. https://doi.org/10.1016/j.ad.2021.09.002.
11. Filippi F, Baraldi C, Zinzani PL, Casadei B, PileriA. A case of pityriasis lichenoides et varioliformis acuta developed after first dose of Oxford–AstraZeneca COVID-19 vaccine. J Eur Acad Dermatol Venereol. 2022;36. https://doi.org/10.1111/jdv.18269.
12. Gianotti R, Restano L, Cutrone M, et al. Papulo-purpuric dermatitis of childhood: a distinct PLEVA-like eruption associated to SARS-CoV-2 infection. Clinical, histopathological and immunohistochemical study of 10 cases. Pediatr Dermatol. 2021;38:1185–90. https://doi.org/10.1111/pde.14777.
13. LeWitt T, Chung C, Manton J, et al. Rare lymphomatoid reactions following SARS-CoV-2 vaccination. JAAD Case Rep. 2022;20:26–30. https://doi.org/10.1016/j.jdcr.2021.11.021.
14. Mäkilä T, Jeskanen L, Butina M, et al. Pityriasis lichenoides et varioliformis acuta after SARS-CoV-2 infection and relapse after vaccination. J Eur Acad Dermatol Venereol. 2022;36. https://doi.org/10.1111/jdv.18024.
15. Palmén J, Lepistö M, Talve L, HietaN. Pityriasis lichenoides et varioliformis acuta following COVID-19 mRNA vaccination. J Eur Acad Dermatol Venereol. 2022;36. https://doi.org/10.1111/jdv.17912.
16. • Sechi A, Pierobon E, Pezzolo E, et al. Abrupt onset of sweet syndrome, pityriasis rubra pilaris, pityriasis lichenoides et varioliformis acuta and erythema multiforme: unravelling a possible common trigger, the COVID-19 vaccine. Clin Exp Dermatol. 2021;47:437–40. https://doi.org/10.1111/ced.14970. **This review reports five cases of different rare and severe dermatoses temporally associated with COVID-19 vaccination, adding to the growing body of evidence that COVID-19 vaccinations may have the capacity to trigger immune-mediated conditions**.
17. Sernicola A, Dybala A, Gomes V, et al. Lymphomatoid drug reaction developed after BNT162b2 (Comirnaty) COVID-19 vaccine manifesting as pityriasis lichenoides et

varioliformis acuta-like eruption. J Eur Acad Dermatol Venereol. 2021;36. https://doi.org/10.1111/jdv.17807.

18.• Shakoei S, Kalantari Y, Nasimi M, et al. Cutaneous manifestations following COVID-19 vaccination: a report of 25 cases. Dermatol Ther. 2022;35. https://doi.org/10.1111/dth.15651. **A case-series reporting all patients presenting to a tertiary hospital in Iran with dermatological conditions up to 30 days after receiving a Covid-19 vaccination. Authors aimed to educate physicians so they may recognize and understand skin reactions following Covid-19 vaccination**.

19. National Institute of Diabetes and Digestive and Kidney Diseases. Adverse Drug Reaction Probability Scale (Naranjo). In: LiverTox: clinical and research information on drug-induced liver injury. 2019. https://www.ncbi.nlm.nih.gov/books/NBK548069/. Accessed 20 Oct 2022.

20. Jastrząb B, Stefaniak A, Hryncewicz-Gwóźdź A, NockowskiP, SzepietowskiJ. Pityriasis lichenoides et varioliformis acuta triggered by human papillomavirus vaccine: a case report and literature review. Acta Derm Venereol. 2021;101. https://doi.org/10.2340/00015555-3921.

21. Gunatheesan S, Ferguson J, Moosa Y. Pityriasis lichenoides et varioliformis acuta: a rare association with the measles, mumps and rubella vaccine. Australas J Dermatol. 2011;53. https://doi.org/10.1111/j.1440-0960.2011.00781.x.

22. Merlotto MR, Bicudo NP, Marques ME, Marques SA. Pityriasis lichenoides et varioliformis acuta following anti-tetanus and diphtheria adult vaccine. An Bras Dermatol. 2020;95:259–60. https://doi.org/10.1016/j.abd.2019.06.009.

23. Castro BA, Pereira JM, Meyer RL, Trindade FM, Pedrosa MS, Piancastelli AC. Pityriasis lichenoides et varioliformis acuta after influenza vaccine. An Bras Dermatol. 2015;90:181–4. https://doi.org/10.1590/abd1806-4841.20153492.

24. Liang R, Borgundvaag B, McIntyre M, Thwaites C, Ragan K, Wyllie A. Evaluation of the reproducibility of the Naranjo Adverse Drug Reaction Probability Scale score in published case reports. Pharmacotherapy. 2014;34(11):1159–66. https://doi.org/10.1002/phar.1496.

25. García-Cortés M, Lucena MI, Pachkoria K, et al. Evaluation of Naranjo Adverse Drug Reactions Probability Scale in causality assessment of drug-induced liver injury. Aliment Pharmacol Ther. 2008;27(9):780–9. https://doi.org/10.1111/j.1365-2036.2008.03655.x.

26. Vaccine Adverse Event Reporting System (VAERS). https://vaers.hhs.gov/index.html. Accessed 25 Nov 2022.

27. Government of Canada. Canadian Adverse Events Following Immunization Surveillance System (CAEFISS). https://www.canada.ca/en/public-health/services/immunization/canadian-adverse-events-following-immunization-surveillance-system-caefiss.html. Accessed 25 Nov 2022.

28. Government of Canada. Adverse reaction information. https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-information.html. Accessed 25 Nov 2022.

29. Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. Am J Epidemiol. 1991;133:144–53. https://doi.org/10.1093/oxfordjournals.aje.a115853.

30. Akpandak I, Miller DC, Sun Y, Arnold BF, Kelly JD, Acharya NR. Assessment of herpes zoster risk among recipients of COVID-19 vaccine. JAMA Netw Open. 2022;5(11):e2242240. https://doi.org/10.1001/jamanetworkopen.2022.42240.

31. Xu S, Zhang L, Nelson JC, et al. Identifying optimal risk windows for self-controlled case series studies of vaccine safety. Statist Med. 2011;30:742–52. https://doi.org/10.1002/sim.4125.