
Pityriasis lichenoides chronica associated with rabies vaccination: a case report

Carmela Franchesca L. Miranda, MD¹; Bernadette B. Arcilla, MD, FPDS¹ ; Lian C. Jamisola, MD, FPDS, APSVI¹; Camille B. Angeles, MD, FPDS¹ and Juanita Carmela Co-Buenviaje, MD, DPDS, DPSVI¹

Abstract

Pityriasis lichenoides (PL) is an inflammatory papulosquamous condition that exists in a continuous spectrum that consists mainly of pityriasis lichenoides et varioliformis acuta and pityriasis lichenoides chronica (PLC). The condition has been reported to erupt in response to infections, radiocontrast media, medications and vaccines. Most case reports on vaccine-related eruption involve the acute PL, hence, this report aimed to present a case presenting with lesions of the chronic variant.

A 21-year-old female presented with multiple erythematous to hyperpigmented ill-defined plaques, some ulceronecrotic, topped with fine scales and excoriations on the upper and lower extremities, periumbilical area and back of 4 months duration, following rabies vaccinations.

Histopathologic findings, including interface dermatitis, parakeratosis, spongiosis, and mixed inflammatory infiltrates, confirmed the diagnosis of PLC. The patient responded well to oral corticosteroids and heliotherapy.

PL is rare and requires additional research. The potential role of vaccination as an etiologic agent represented a crucial area of this investigation. Additionally, heliotherapy should be considered as a viable therapeutic alternative when phototherapy is not feasible.. Further research is needed to elucidate the pathogenesis of PL and establish evidence-based treatment protocols.

Key words: Pityriasis lichenoides chronica, heliotherapy, vaccine, case report

Pityriasis lichenoides (PL) is an inflammatory papulosquamous condition that exists in a continuous spectrum that consists mainly of pityriasis lichenoides et varioliformis acuta (PLEVA) and pityriasis lichenoides chronica (PLC).¹⁻³ The exact prevalence, incidence, and risk factors of this condition remain unclear, yet it has been reported that the condition is more common in the pediatric age group but can affect all ages. Eruption of cutaneous

lesions may be triggered by infections, radiocontrast media, medications and vaccines.⁴⁻⁵ Although most case reports have demonstrated eruption after vaccination against viral entities, such as measles-mumps-rubella (MMR) and influenza vaccines, there is a recent report on PLEVA following vaccinations against bacterial entities, specifically anti-tetanus and diphtheria.⁵ In this case report, the authors aimed to present a case of PLC following vaccination against rabies, including their clinical experience in the diagnosis and treatment.

The Case

An otherwise healthy 21-year-old Filipino female student sought consult at the dermatology outpatient

Correspondence:

Carmela Franchesca L. Miranda, MD

Email: clmiranda.md@gmail.com

¹Section of Dermatology, University of the East Ramon Magsaysay Memorial Medical Center, Inc.

clinic (OPC) due to multiple erythematous to hyperpigmented ill-defined plaques, some ulceronecrotic, topped with fine scales and excoriations on the bilateral upper and lower extremities, periumbilical area, and back of 4-months duration (Figure 1). The patient developed the aforementioned lesions seven days after receiving the third dose of rabies vaccine (Purified vero cell rabies vaccine [Human Biologicals Institute, India]) given for a dog bite. The eruption was associated with incessant pruritus graded 10/10. There were no systemic symptoms. The patient sought consult with a dermatologist who prescribed mometasone furoate lotion to be applied once daily but it only afforded temporary improvement of the itch and a decrease in the number and size of lesions, without complete resolution. One month later, due to persistence of the lesions, unrelenting pruritus, and occasional development of new lesions prompted consultation at this institution. The patient has an unremarkable medical history, with no history of atopy and allergies to food or medication. The primary clinical impression of pityriasis lichenoides chronica was confirmed by histopathological studies which revealed microscopic

changes consistent with pityriasis lichenoides and drug reaction. The predominating pattern is subtle vacuolar interface change with parakeratosis, spongiosis, and superficial perivascular infiltrates consisting mainly of lymphocytes, with some neutrophils and eosinophils.

Oral prednisone was initiated at 0.7mg/kg/day and then slowly tapered over the course of 3 weeks. In the second week of oral prednisone, no new lesions were noted, all existing lesions were flat, hyperpigmented and there was substantial improvement in the hydration of the skin. At this point, both the pruritus and excoriations have already resolved. After 3 weeks on oral prednisone, majority of the lesions on the trunk and extremities have already resolved, with only a few erythematous to hyperpigmented thick plaques topped with scales on the patient's feet. Prednisone was discontinued, and, for the remaining lesions, betamethasone dipropionate ointment was prescribed, and tacrolimus 0.1% ointment, the latter to be applied while on steroid rest. Betamethasone dipropionate was then shifted to clobetasol propionate ointment for another 2 weeks with noted resolution. The patient was also instructed to undergo heliotherapy by exposing the affected areas to midday sun for 10-15 minutes 2-3 times per week throughout the course of treatment. Moreover, nonpharmacologic measures such as the use of emollient and mild soap were also advised and followed with good compliance.

Discussion

PL affects both children and adults, but most reports indicate that it is a predominantly pediatric condition. However, the exact worldwide prevalence in both the general and pediatric populations still remain unknown. While some studies have shown a male predominance, others have stated that there is no male or female predilection.⁶ The Philippine Dermatological Society accredited institutions reported 1,363 cases of PL from 2011 to 2021, where 563 (41.3%) are males and 800 (58.7%) are females. Out of 1,363 cases, 267 (19.6%) are pediatric cases (0-18 years old).

Three main pathogenic theories have been proposed for PL: 1) an inflammatory reaction secondary to T-cell dyscrasias, 2) an immune complex mediated hypersensitivity vasculitis, and, the most popular theory, 3) an inflammatory, immunologic response induced by infectious agents and extrinsic antigens, such as drugs and vaccines.^{5,7-9} Suggested potential mechanisms for the development of cutaneous reactions from vaccines include a) a type

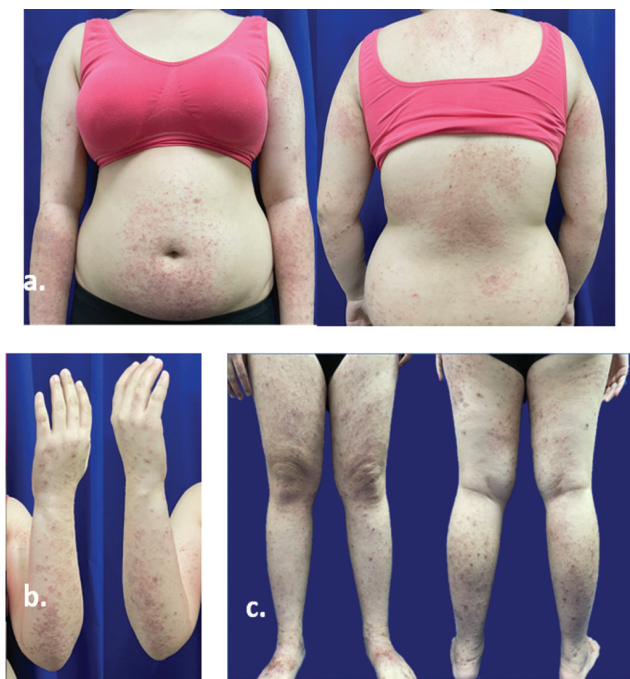


Figure 1. An adult female presented with multiple erythematous to hyperpigmented ill-defined plaques, some ulceronecrotic, topped with fine scales and excoriations on the trunk (a), and upper and lower extremities (b & c).

I or type IV hypersensitivity response oftentimes due to excipients rather than the vaccine antigen. and b) a T-cell mediated skin reaction due to molecular mimicry with a viral epitope.^{10,11} Since patient developed lesions after 24 hours post-vaccination, it is possible she developed a Type IV delayed hypersensitivity reaction to an excipient of the rabies vaccine. The administered vaccine contains the excipient thiomersol, which has been reported to cause delayed-type hypersensitivity reactions with a variety of cutaneous manifestations.¹²

A few case reports have been published on PL following vaccination, specifically on MMR, influenza, and double dose diphtheria and anti-tetanus vaccine.^{9,13} The onset of eruption ranges from 2-10 days after receiving the dose in both pediatric and adult patients. Among the case reports cited, most of the patients presented with lesions consistent with PLEVA, with only one presenting as PLC. In the aforementioned case report, lesions characteristic of PLC erupted 10 days following MMR vaccination with a clinical course lasting 10 months.¹³ The patient reported onset of eruption of her cutaneous lesions a week after receiving the 3rd dose of anti-rabies vaccine.

There have been many reports of cutaneous reactions following COVID-19 vaccination. An evaluation of clinical and histopathologic correlation of the reactions reported in an international registry on COVID-19 vaccine cutaneous reactions resulted to the identification of 13 different categories of biopsy-proven reactions, the most common being vaccine-related eruption of papules and plaques (V-REPP).^{10,11} VREPP belongs to a histopathologic spectrum of papulosquamous reactions that demonstrate some degree of spongiosis with or without both prominent interface change and eosinophils, and clinically presents as papulo-vesicular, pityriasis rosea-like and papulosquamous with subtle scales.¹⁰ Interestingly, the histological and clinical features of PLC meet the criteria of VREPP, particularly the third form.

Pityriasis lichenoides chronica is a diagnosis that warrants a high index of suspicion and confirmation by histology.¹⁴ Histopathologic examination of PLC would typically show an interface pattern. The epidermis is parakeratotic and may show acanthosis, spongiosis and focal invasion of lymphocytes and erythrocytes. Classically, a wedge-shaped moderately dense lymphohistiocytic perivascular inflammatory infiltrate that obscures the dermoepidermal junction and extends down to the reticular dermis may be appreciated. On the other hand, PLEVA would

show prominent exocytosis and dense and diffuse lymphocytic infiltration along the basal layer with features of vasculitis.^{2,4} The patient's biopsy result was consistent with PLC due to the bandlike infiltrate composed of lymphocytes and the absence of vasculitis. The presence of few neutrophils and rare eosinophils is most commonly seen in drug eruptions, which is consistent with our clinical picture being that the eruption was secondary to vaccination.¹⁵

Thus far, phototherapy is considered to be first-line therapy for PLC, together with medications which include topical corticosteroids and calcineurin-inhibitors, and oral antibiotics, particularly tetracyclines and erythromycin.^{4,5,16-17} Second line therapy includes methotrexate and cyclosporine, usually given for fulminant cases.¹⁸ The authors decided to administer oral corticosteroids to the patient because of the severity of the lesions and the significant pruritus. They aimed to commence phototherapy; however, their patient was not receptive to this option during the ongoing COVID-19 pandemic. Instead of phototherapy, their patient was advised to engage in heliotherapy by exposing the affected areas to midday sun for 10-15 minutes, 2-3 times per week during the treatment period. A systematic review on heliotherapy showed that at a frequency of only 10 days per year, 60% of patients achieved almost complete clearance of PLC for at least 2 years of treatment.¹⁸ To target the therapeutic narrowband UVB at 310 nm, heliotherapy must be conducted using midday sun, otherwise, it would be ineffective.¹⁹ The choice of potency of topical corticosteroid is upon the discretion of the physician and no recommendations have been reported. In terms of phototherapy, few uncontrolled and retrospective studies have reported improvement in majority of patients.^{16,20} Narrowband UVB treatment requires at least two to three months administered at least thrice in a week to achieve a favorable response.²¹

PLC lesions generally regress over weeks but may be followed by episodes of exacerbations and remissions that can accumulate to a clinical course that can take 1.5-31 months.^{4,22} For the patient, the clinical course lasted for more than 1 year. It is also worth noting that in a study done on cutaneous hematologic disorders in children, 4 (7%) out of 51 patients had PLC 3 to 10 years prior to being diagnosed with mycosis fungoides. Consequently, patients with PLC warrant monitoring for new lesions and follow up as needed, due to the low risk of lymphomatous

transformation and evolution to cutaneous T-cell lymphoma.²³

Conclusion

To the authors' knowledge, this is the first case report documenting PLC developing after antirabies vaccination. To date, no definite algorithm has been established in terms of its treatment. Guided by the recommended first-line and second-line therapies, treatment may vary depending on the extent of the lesions and severity of signs and symptoms, particularly pruritus. Amidst a global pandemic, heliotherapy should not be overlooked as a therapeutic option when patients are not amenable to undergo first-line conventional phototherapy.

References

1. Feola H, Mancinelli MC, Perez-Klala MV, Vereia MA. Pityriasis lichenoides chronica: Rapid response after a single cycle of azithromycin therapy. *Dermatol Ther* 2020 May;33(3):e13303. doi: 10.1111/dth.13303. Epub 2020 Apr 1.
2. Khachemoune A, Blyumin ML. Pityriasis lichenoides: pathophysiology, classification, and treatment. *Am J Clin Dermatol* 2007;8(1):29-36. doi: 10.2165/00128071-200708010-00004.
3. Zang JB, Coates SJ, Huang J, Vonderheid EC, Cohen BA. Pityriasis lichenoides: Long-term follow-up study. *Pediatr Dermatol* 2018 Mar;35(2):213-9. doi: 10.1111/pde.13396. Epub 2018 Jan 9.
4. Bowers S, Warshaw EM. Pityriasis lichenoides and its subtypes. *J Am Acad Dermatol* 2006 Oct;55(4):557-72; quiz 573-6. doi: 10.1016/j.jaad.2005.07.058.
5. Merlotto MR, Bicudo NP, Marques MEA, Marques SA. Pityriasis lichenoides et varioliformis acuta following anti-tetanus and diphtheria adult vaccine. *An Bras Dermatol* 2020 Mar-Apr;95(2):259-60. doi: 10.1016/j.abd.2019.06.009. Epub 2020 Feb 19.
6. Geller L, Antonov NK, Lauren CT, Morel KD, Garzon MC. Pityriasis Lichenoides in Childhood: Review of Clinical Presentation and Treatment Options. *Pediatr Dermatol* 2015 Sep-Oct;32(5):579-92. doi: 10.1111/pde.12581. Epub 2015 Mar 26.
7. Filippi F, Patrizi A, Sabattini E, Varotti E, Bertuzzi C, Pileri A. Pityriasis lichenoides triggered by measles-mumps-rubella vaccine injection. *J Dtsch Dermatol Ges* 2020 Jul;18(7):758-60. doi: 10.1111/ddg.14153. Epub 2020 Jul 12.
8. Gunatheesan S, Ferguson J, Moosa Y. Pityriasis lichenoides et varioliformis acuta: a rare association with the measles, mumps and rubella vaccine. *Australas J Dermatol* 2012 Nov;53(4):e76-8. doi: 10.1111/j.1440-0960.2011.00781.x. Epub 2011 Jun 13.
9. Gunatheesan S, Ferguson J, Moosa Y. Pityriasis lichenoides et varioliformis acuta: a rare association with the measles, mumps and rubella vaccine. *Australas J Dermatol* 2012 Nov;53(4):e76-8. doi: 10.1111/j.1440-0960.2011.00781.x. Epub 2011 Jun 13.
10. McMahon DE, Kovarik CL, Damsky W, Rosenbach M, Lipoff JB, Tyagi A, Chamberlin G, Fathy R, Nazarian RM, Desai SR, Lim HW, Thiers BH, Hruza GJ, French LE, Blumenthal K, Fox LP, Freeman EE. Clinical and pathologic correlation of cutaneous COVID-19 vaccine reactions including V-REPP: A registry-based study. *J Am Acad Dermatol* 2022 Jan;86(1):113-21. doi: 10.1016/j.jaad.2021.09.002. Epub 2021 Sep 10.
11. Yu JN, Angeles CB, Lim HG, Chavez C, Roxas-Rosete C. Cutaneous reactions to inactivated SARS-CoV-2 vaccine and ChAdOx1-S (recombinant) vaccine against SARS-CoV-2: a case series from the Philippines. *J Eur Acad Dermatol Venereol* 2021 Dec;35(12):e841-5. doi: 10.1111/jdv.17575. Epub 2021 Aug 17.
12. Leventhal JS, Berger EM, Brauer JA, Cohen DE. Hypersensitivity reactions to vaccine constituents: a case series and review of the literature. *Dermatitis* 2012 May-Jun;23(3):102-9. doi: 10.1097/DER.0b013e31825228cf.
13. Gil-Bistes D, Kluger N, Bessis D, Guillot B, Raison-Peyron N. Pityriasis lichenoides chronic after measles-mumps-rubella vaccination. *J Dermatol* 2012 May;39(5):492-3. doi: 10.1111/j.1346-8138.2011.01380.x. Epub 2011 Oct 4.
14. Cliff S, Cook MG, Ostlere LS, Mortimer PS. Segmental pityriasis lichenoides chronica. *Clin Exp Dermatol* 1996 Nov;21(6):464-5. doi: 10.1111/j.1365-2230.1996.tb00163.x.
15. Weyers W, Metze D. Histopathology of drug eruptions - general criteria, common patterns, and differential diagnosis. *Dermatol Pract Concept* 2011 Jan 31;1(1):33-47. doi: 10.5826/dpc.0101a09.
16. Aydogan K, Saricaoglu H, Turan H. Narrowband UVB (311 nm, TL01) phototherapy for pityriasis lichenoides. *Photodermatol Photoimmunol Photomed* 2008 Jun;24(3):128-33. doi: 10.1111/j.1600-0781.2008.00350.x.
17. Di Costanzo L, Balato N, La Bella S, Balato A. Successful association in the treatment of pityriasis lichenoides et varioliformis acuta. *J Eur Acad Dermatol Venereol* 2009 Aug;23(8):971-2. doi: 10.1111/j.1468-3083.2008.03077.x. Epub 2009 Jan 21.
18. Fernández-Guarino M, Aboin-Gonzalez S, Ciudad Blanco C, Velázquez Tarjuelo D, Lázaro Ochayta P. Treatment of adult diffuse pityriasis lichenoides chronica with narrowband ultraviolet B: experience and literature review. *Clin Exp Dermatol* 2017 Apr;42(3):303-305. doi: 10.1111/ced.13035. Epub 2017 Jan 23.
19. Koo J, Nakamura M. Heliotherapy. In: Norman R, editor. *Clinical Cases in Phototherapy*. Tampa 2017; 77-80
20. Ersoy-Evans S, Hapa AA, Boztepe G, Sahin S, Kölemen F. Narrowband ultraviolet-B phototherapy in pityriasis lichenoides chronica. *J Dermatolog Treat* 2009;20(2):109-13. doi: 10.1080/09546630802449088.

21. Takada Y, Irisawa K, Kawada A. Heliotherapy of pityriasis lichenoides chronica. *J Dermatol* 1977 Jun;4(3):91-4. doi: 10.1111/j.1346-8138.1977.tb01019.x.
22. Sibbald C, Pope E. Systematic review of cases of cutaneous T-cell lymphoma transformation in pityriasis lichenoides and small plaque parapsoriasis. *Br J Dermatol* 2016 Oct;175(4):807-9. doi: 10.1111/bjd.14605. Epub 2016 Jun 20.
23. Boccara O, Blanche S, de Prost Y, Brousse N, Bodemer C, Fraitag S. Cutaneous hematologic disorders in children. *Pediatr Blood Cancer* 2012 Feb;58(2):226-32. doi: 10.1002/pbc.23103. Epub 2011 Mar 28.