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A literature review of COVID 19 vaccination and Lichen Planus Pigmentosus: is there a correlation?

Introduction:

The global response to the COVID-19 pandemic involved rapidly developing and distributing various vaccines to curb the spread of the SARS-CoV-2 virus. While these vaccines are effective in preventing severe illness and hospitalization due to COVID-19, they have also prompted rigorous monitoring for potential side effects and adverse events. Among the vast array of reported post-vaccination side effects, the emergence or worsening of dermatological conditions has attracted significant attention from both clinicians and researchers.

One dermatological condition linked to COVID-19 vaccinations is lichen planus pigmentosus (LPP).[1] LPP is a rare dermatosis characterized by the development of hyperpigmented macules or patches on the skin.[2] The exact etiology of LPP remains uncertain; however, one theory is that LPP is an autoimmune disease in which CD4+ and CD8+ lymphocytes are activated to attack the basal keratinocytes.[3] Many factors could trigger lymphocytes. These factors include, but are not limited to, infection and/or vaccines.[3] A potential association between COVID-19 vaccinations and LPP has recently emerged as a subject of clinical interest and scientific inquiry.

This review aims to provide an overview of current knowledge regarding the possible relationship between COVID-19 vaccinations and LPP by delving into available data from the literature, in the form of existing case reports, clinical observations, and scientific hypotheses.

Search strategy:

Keywords for literature review: The following terms were used for the search: "Covid-19," "SARS-CoV-2," "Lichen Planus Pigmentosus," "Dermatological Manifestations," "Viral Infections," "Lichen Planus Pigmentosus Etiology"

Relevant databases: Publications were searched for relevant papers employing PubMed, Google Scholar, and Web of Science databases.

Inclusion and exclusion criteria: The beginning of the time period searched was the COVID-19 outbreak date of November 17, 2019. The end point was February 2023.

Findings:

According to our search criteria, there have been 43 reports of lichen planus following various COVID-19 vaccinations; of these, only four of the reported cases were of COVID-19 vaccine-associated LPP.[1,3-5]

The first case involved a 64-year-old female with a case of LPP-inversus, who reported symptoms of LPP after receiving her first dose of the Oxford-AstraZeneca COVID-19 vaccine. She reported worsening symptoms after the second dose of the same vaccine. The patient had no prior medical history that would explain the onset of LPP. After diagnosis, the patient received treatment with topical betamethasone 0.05% ointment. After two months of treatment, a slight improvement in her symptoms was observed, which was a reduction in pigmentation.[4]

The second case of LPP involved a 43-year-old male with multiple lesions on his face. A punch biopsy of his chin lesions showed that he had developed LPP after his second dose of the Oxford-AstraZeneca COVID-19 vaccine. The patient had no prior medical history that would explain the onset of LPP. The patient was treated with topical corticosteroid mometasone cream and a slight improvement in his symptoms was observed.[5]

Medication	Description
Prednisone	An oral corticosteroid prescribed to decrease inflammation by suppressing polymorphonuclear neutrophils.[6]
Topical Betamethasone	A topical corticosteroid prescribed to decrease inflammation by suppressing polymorphonuclear leukocytes.[6]
Topical Triamcinolone	A corticosteroid taken topically, orally, or intramuscularly. Local injections at lesion sites have been effective.[6]
Topical Halobetasol	A topical corticosteroid used to decrease inflammation and improve hyperpigmentation.[6]
Topical Clobetasol Propionate	A similar topical corticosteroid used to decrease inflammation and improve hyperpigmentation.[6]
Topical Mometasone	A similar topical corticosteroid used to decrease inflammation and improve hyperpigmentation.[6]
Topical Tacrolimus	A calcineurin inhibitor that works to inhibit the calcium-dependent reactions involved in the T-cell immune response to reduce LPP symptoms.[7]
Topical Pimecrolimus	A similar calcineurin inhibitor that works to inhibit the calcium-dependent reactions involved in the T-cell immune response to reduce LPP symptoms.[7]
Topical Cyclosporine	A topical immunosuppressant that can be effective at reducing genital LPP lesions and improving hypertrophic lesions.[8]
Isotretinoin	An oral retinoid-like agent that can work to stop sebaceous gland differentiation and abnormal keratinization to help treat LPP.[9]
Oral JAK Inhibitors	Off-label indication, small molecule inhibitor that inhibits the JAK-STAT pathway.

Table 1. Medications used to treat lichen planus pigmentosus ; courtesy of Marisa Ponzo, MD
Abbreviations LPP, lichen planus pigmentosus; JAK, Janus kinase; JAK-STAT, Janus kinase-signal transducer and activator of transcription

The third case involved a 52-year-old male with LPP-inversus with nail involvement (an uncommon subtype of LPP) after receiving a third dose of the Oxford-AstraZeneca COVID-19 vaccine. The patient presented with skin lesions on the axilla, right antecubital fossa, left popliteal fossa, right inguinal region, and on various fingernails. The patient had no prior medical history that would explain the onset of LPP. The recommended treatment for this patient was topical clobetasol propionate 0.05% ointment paired with injections of triamcinolone acetonide into the matrix of the nail.[3]

The final case involved a 50-year-old male patient diagnosed with LPP after a second dose of the Oxford-AstraZeneca COVID-19 vaccine. The patient had no prior medical history that would explain the onset of LPP. The patient received treatment with topical betamethasone 0.05% ointment, which resulted in a slight improvement that was noted at a 2-month check-in appointment.[1]

Management of LPP:

Treatment for LPP is challenging and it is important to point out that no single treatment has been proven effective. However, various medications can manage the complications of LPP. For example, LPP often occurs in sun-exposed areas; thus, it is essential to use sun protection in conjunction with other treatments. Listed below in **Table 1** presents a few medications used to treat LPP. Post-inflammatory hyperpigmentation, especially in those with richly pigmented skin, can be particularly distressing to the patient as it presents its own unique treatment challenges, which are further reviewed elsewhere.

Analysis and conclusion:

The pathogenesis of lichen planus and thus LPP is thought to involve upregulation of the T helper 1 pathway. As such, cytokines including interleuken-2 (IL-2), tumour necrosis factor-α (TNF-α), and interferon-γ (IFN-γ) are involved in the development and progression of lichen planus.[3] Furthermore, reports suggest that the COVID-19 vaccine increases the levels of cytokines such as IL-2, TNF-α, and IFN-γ in humans.[3] Given the currently proposed pathogenesis including the fact that LPP is mediated by CD4+ and CD8+ lymphocytes, and their significant role in cytokine production, it is plausible to consider that LPP could result from a COVID-19 vaccination.[4] However, it is important to be mindful that these are novel studies of the development of LPP following COVID-19 vaccination. Thus, more robust research is needed to identify a correlation between LPP and COVID-19 vaccination. The expert opinion among dermatologists in Canada is that there is an increased prevalence of LPP following the pandemic. However, concrete data to support this expert opinion are lacking. Moreover, while LPP is a rare condition, it has been reported to occur more commonly in individuals with richly pigmented skin, particularly those of Skin Type III and higher.[2] Post-inflammatory hyperpigmentation can be quite distressing to these patients; therefore, early recognition of the disease and treatment to prevent this complication is of paramount importance. In sharp contrast to its prevalence within the person of colour population, there has been a notable scarcity of research on this condition in these individuals. We must intensify our research efforts on this disease.

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