



Oral lichen planus following the administration of vector based COVID-19 vaccine (Ad26.COV2.S)

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3 **Oral lichen planus following the administration of vector based COVID-19**
4 **vaccine (Ad26.COV2.S)**
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3 The introduction and approval of vaccines against COVID-19 is a pivotal step in the
4 quest to break the global pandemic. Unprecedented vaccination programs have been initiated
5 worldwide with the ultimate goal to achieve herd immunity (Wouters et al., 2021). Various
6 vaccines based on different technologies are currently in use (Wouters et al., 2021, Bogdanov
7 et al., 2021): viral vector (AstraZeneca, J&J, Gameleya), mRNA (Moderna, Biontech/Pfizer)
8 and inactivated SARS-CoV-2 virus (Sinopharm). According the latest studies, the safety,
9 tolerability and efficacy profiles of all vaccines appears to be favorable (Wu et al., 2021).
10 Limited local reactions at the injection site are most commonly reported after the vaccine
11 administration followed by mild systemic discomfort like headache and flu-like symptoms
12 (Wu et al., 2021). Severe adverse events (e.g. thrombosis, thrombocytopenia, myocarditis)
13 rarely reported (0.1%) (Wu et al., 2021).
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16 While the vaccination programs are progressing, more knowledge about possible
17 vaccination side effects is surfacing. It is difficult to establish causative associations between
18 conspicuous (possibly rare) clinical findings and COVID vaccine administration and findings
19 have to be interpreted with care (Anaya-Saavedra, 2021). However, in the endeavor to
20 improve the understanding of the underlying immunologic mechanisms of action of the
21 current and future vaccines, a meticulous surveillance of possible side effects is warranted.
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24 Cutaneous and mucosal side effects (allergic and non-allergic) in the wake of
25 vaccinations (in general) are well described (Rosenblatt & Stein, 2015). A rare vaccination-
26 associated event is the onset of lichen planus (LP) or lichenoid reactions (Lai & Yew, 2017).
27 A review published in 2017 found a total of 33 cases of LP arising after various vaccinations
28 (Lai & Yew, 2017). Most cases of LP (very rarely with oral manifestations) or lichenoid
29 reactions were observed within a fortnight following a Hepatitis B, Influenza or Herpes zoster
30 vaccination (inactivated/attenuated virus vaccinations) (Lai & Yew, 2017, Tannock et al.,
31 2020).
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34 With the progress of the worldwide COVID vaccination campaign an increasing array
35 of tentative vaccine associated (muco-)cutaneous side effects are recognized (Bogdanov et al.,
36 2021). Recently published reports have associated COVID-19 vaccinations with the
37 emergence of cutaneous LP or the exacerbation of oral manifestations of LP (Hiltun et al.,
38 2021, Merhy et al., 2021, Kulkarni & Sollecito, 2021). LP and oral LP (OLP) are the clinical
39 correlate of an autoimmunologic reaction of mainly CD8+ cytotoxic T-cells against epidermal
40 basal layer keratinocytes which induces keratinocyte apoptosis via different complex humoral
41 or cytokine mediated mechanisms (Nogueira et al., 2015). This process is mainly maintained
42 and promoted by the secretion of IL-2, TNF- α and IFN- γ secreted by CD4+ (Th1)
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3 lymphocytes (Nogueira et al., 2015, Hiltun et al., 2021). The LP/OLP associated immune
4 reaction is represented histologically by the accumulation of lymphocytic infiltrates in the
5 basal epidermal layer (Müller, 2017).
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8 An important and intended effect of all COVID-19 vaccines is the broad stimulation of
9 the immune system inducing an intense T-cell driven response leading to B-cell activation
10 and antibody production (Alter et al., 2021). Long-lasting and potentially increasing
11 immunologic responses have been shown for the Ad26.COVS.2.S (Johnson&Johnson) vaccine
12 (Alter et al., 2021, Barouch et al., 2021). These responses include elevated levels of
13 proinflammatory cytokines, such as IL-2, TNF- α and IFN- γ which are implicated in the
14 development of LP and OLP.
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20 While cases of initial onset of cutaneous LP and flares of preexisting OLP have been
21 published (Hiltun et al., 2021, Merhy et al., 2021, Kulkarni & Sollecito, 2021), literature
22 searches failed to reveal descriptions of COVID-19 vaccine associated initial manifestations
23 of OLP without extraoral efflorescences. Thus, this may be the first report of OLP that
24 developed in timely association with the COVID-19 vaccination (Ad26.COVS.2.S).
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29 A 49 year old male patient presented with a 9 week history of oral mucosal
30 discomfort, burning sensations, desquamation and signs of inflammation. Further exploration
31 revealed that the symptoms had developed six days after the COVID-19 vaccination with
32 Ad26.COVS.2.S (Johnson&Johnson). The patient had suffered from flu-like symptoms for
33 three days immediately following the vaccination. The clinical examination showed the
34 classical image of OLP with Wickham striae on the buccal mucosa and extensive plaque
35 formation on the tongue (figures 1 and 2). The clinical diagnosis was confirmed by a surgical
36 biopsy. The histological image showed the defining band-like accumulation of lymphocytes
37 in the vicinity of the epidermal basal membrane with infiltration into the epidermis with signs
38 of necrotic (apoptotic) keratinocytes (figure 3). The patient was treated with a four week
39 course of topical clobetasol mouth irrigation solution (0.5mg/ml) which led to a significant
40 improvement of the symptoms.
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50 Newly arising OLP lesions have been recognized in patients suffering or convalescent
51 from COVID-19 (Burgos-Blasco et al., 2021, Fidan et al., 2021). However, the onset of OLP
52 has not been associated with COVID-19 vaccinations to date despite initial hints for the
53 emergence of cutaneous LP after COVID-19 jabs. The reported LP cases evolved in patients
54 who received mRNA based vaccines (Moderna, Biontech/Pfizer). In the present case report
55 OLP manifested after vaccination with a vector based COVID-19 vaccination
56 (Ad26.COVS.2.S, Johnson&Johnson). The induction of inflammatory cytokine release and T-
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3 cell activation is one of the main steps of the vaccines independent of the underlying
4 technology. It is plausible that this cytokine flare might be implicated in vaccination
5 associated (cutaneous) side effects such as LP and OLP the pathophysiology of which is
6 based on the infiltration of activated T-cells infiltration epidermal layers (Nogueira et al.,
7 2015). Oral mucosal disorders might have been falsely associated with COVID-19 and its
8 aftermath or COVID-19 vaccines and the limited clinical significance of single case reports
9 must be highlighted (Anaya-Saavedra, 2021). However, in an emerging knowledge base
10 concerning COVID vaccine associated side effects, even rare events should be recognized and
11 communicated in order to increase the understanding of the vaccine mechanism of action.
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22 **Figure legends**

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24 **Figure 1:** Image of the right buccal mucosa showing the typical clinical OLP image of
25 reticular white markings (Wickham striae)

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27 **Figure 2:** Image of the left lateral tongue showing plaque-like OLP manifestations

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29 **Figure 3:** Histological image of the biopsy of the buccal mucosae with the linear
30 accumulation of lymphocytes along the basal epidermal membrane with intraepidermal
31 lymphocytic infiltrates and single necrotic keratinocytes (hematoxylin-eosin stain,
32 magnification: 5x)
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Figure 1: Image of the right buccal mucosa showing the typical clinical OLP image of reticular white markings (Wickham striae)

1150x681mm (72 x 72 DPI)



Figure 2: Image of the left lateral tongue showing plaque-like OLP manifestations

851x559mm (72 x 72 DPI)

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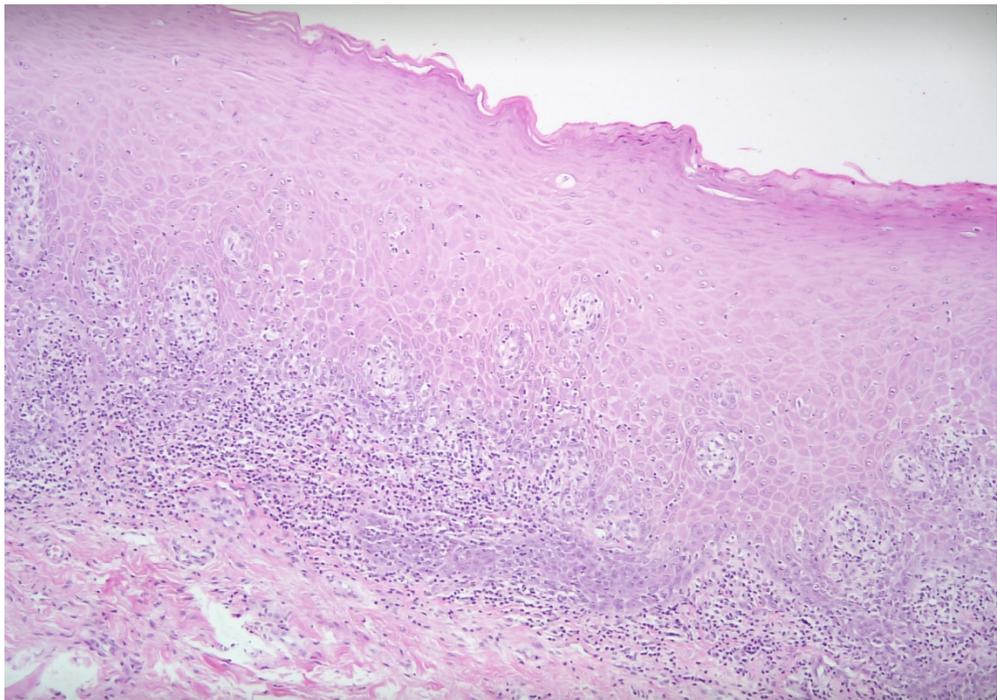


Figure 3: Histological image of the biopsy of the buccal mucosae with the linear accumulation of lymphocytes along the basal epidermal membrane with intraepidermal lymphocytic infiltrates and single necrotic keratinocytes (hematoxylin-eosin stain, magnification: 5x)

562x394mm (72 x 72 DPI)