



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

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

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The introduction and approval of vaccines against COVID-19 is a pivotal step in the quest to break the global pandemic. Unprecedented vaccination programs have been initiated worldwide with the ultimate goal to achieve herd immunity (Wouters et al., 2021). Various vaccines based on different technologies are currently in use (Wouters et al., 2021, Bogdanov et al., 2021): viral vector (AstraZeneca, J&J, Gamaleya), mRNA (Moderna, Biontech/Pfizer) and inactivated SARS-CoV-2 virus (Sinopharm). According the latest studies, the safety, tolerability and efficacy profiles of all vaccines appears to be favorable (Wu et al., 2021). Limited local reactions at the injection site are most commonly reported after the vaccine administration followed by mild systemic discomfort like headache and flu-like symptoms (Wu et al., 2021). Severe adverse events (e.g. thrombosis, thrombocytopenia, myocarditis) rarely reported (0.1%) (Wu et al., 2021).

While the vaccination programs are progressing, more knowledge about possible vaccination side effects is surfacing. It is difficult to establish causative associations between conspicuous (possibly rare) clinical findings and COVID vaccine administration and findings have to be interpreted with care (Anaya-Saavedra, 2021). However, in the endeavor to improve the understanding of the underlying immunologic mechanisms of action of the current and future vaccines, a meticulous surveillance of possible side effects is warranted.

Cutaneous and mucosal side effects (allergic and non-allergic) in the wake of vaccinations (in general) are well described (Rosenblatt & Stein, 2015). A rare vaccination-associated event is the onset of lichen planus (LP) or lichenoid reactions (Lai & Yew, 2017). A review published in 2017 found a total of 33 cases of LP arising after various vaccinations (Lai & Yew, 2017). Most cases of LP (very rarely with oral manifestations) or lichenoid reactions were observed within a fortnight following a Hepatitis B, Influenza or Herpes zoster vaccination (inactivated/attenuated virus vaccinations) (Lai & Yew, 2017, Tannock et al., 2020).

With the progress of the worldwide COVID vaccination campaign an increasing array of tentative vaccine associated (muco-)cutaneous side effects are recognized (Bogdanov et al., 2021). Recently published reports have associated COVID-19 vaccinations with the emergence of cutaneous LP or the exacerbation of oral manifestations of LP (Hiltun et al., 2021, Merhy et al., 2021, Kulkarni & Sollecito, 2021). LP and oral LP (OLP) are the clinical correlate of an autoimmunologic reaction of mainly CD8<sup>+</sup> cytotoxic T-cells against epidermal basal layer keratinocytes which induces keratinocyte apoptosis via different complex humoral or cytokine mediated mechanisms (Nogueira et al., 2015). This process is mainly maintained and promoted by the secretion of IL-2, TNF- $\alpha$  and IFN- $\gamma$  secreted by CD4<sup>+</sup> (Th1)

lymphocytes (Nogueira et al., 2015, Hiltun et al., 2021). The LP/OLP associated immune reaction is represented histologically by the accumulation of lymphocytic infiltrates in the basal epidermal layer (Müller, 2017).

An important and intended effect of all COVID-19 vaccines is the broad stimulation of the immune system inducing an intense T-cell driven response leading to B-cell activation and antibody production (Alter et al., 2021). Long-lasting and potentially increasing immunologic responses have been shown for the Ad26.COV2.S (Johnson&Johnson) vaccine (Alter et al., 2021, Barouch et al., 2021). These responses include elevated levels of proinflammatory cytokines, such as IL-2, TNF- $\alpha$  and IFN- $\gamma$  which are implicated in the development of LP and OLP.

While cases of initial onset of cutaneous LP and flares of preexisting OLP have been published (Hiltun et al., 2021, Merhy et al., 2021, Kulkarni & Sollecito, 2021), literature searches failed to reveal descriptions of COVID-19 vaccine associated initial manifestations of OLP without extraoral efflorescences. Thus, this may be the first report of OLP that developed in timely association with the COVID-19 vaccination (Ad26.COV2.S).

A 49 year old male patient presented with a 9 week history of oral mucosal discomfort, burning sensations, desquamation and signs of inflammation. Further exploration revealed that the symptoms had developed six days after the COVID-19 vaccination with Ad26.COV2.S (Johnson&Johnson). The patient had suffered from flu-like symptoms for three days immediately following the vaccination. The clinical examination showed the classical image of OLP with Wickham striae on the buccal mucosa and extensive plaque formation on the tongue (figures 1 and 2). The clinical diagnosis was confirmed by a surgical biopsy. The histological image showed the defining band-like accumulation of lymphocytes in the vicinity of the epidermal basal membrane with infiltration into the epidermis with signs of necrotic (apoptotic) keratinocytes (figure 3). The patient was treated with a four week course of topical clobetasol mouth irrigation solution (0.5mg/ml) which led to a significant improvement of the symptoms.

Newly arising OLP lesions have been recognized in patients suffering or convalescent from COVID-19 (Burgos-Blasco et al., 2021, Fidan et al., 2021). However, the onset of OLP has not been associated with COVID-19 vaccinations to date despite initial hints for the emergence of cutaneous LP after COVID-19 jabs. The reported LP cases evolved in patients who received mRNA based vaccines (Moderna, Biontech/Pfizer). In the present case report OLP manifested after vaccination with a vector based COVID-19 vaccination (Ad26.COV2.S, Johnson&Johnson). The induction of inflammatory cytokine release and T-

cell activation is one of the main steps of the vaccines independent of the underlying technology. It is plausible that this cytokine flare might be implicated in vaccination associated (cutaneous) side effects such as LP and OLP the pathophysiology of which is based on the infiltration of activated T-cells infiltration epidermal layers (Nogueira et al., 2015). Oral mucosal disorders might have been falsely associated with COVID-19 and its aftermath or COVID-19 vaccines and the limited clinical significance of single case reports must be highlighted (Anaya-Saavedra, 2021). However, in an emerging knowledge base concerning COVID vaccine associated side effects, even rare events should be recognized and communicated in order to increase the understanding of the vaccine mechanism of action.

### Figure legends

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

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

**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)

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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)

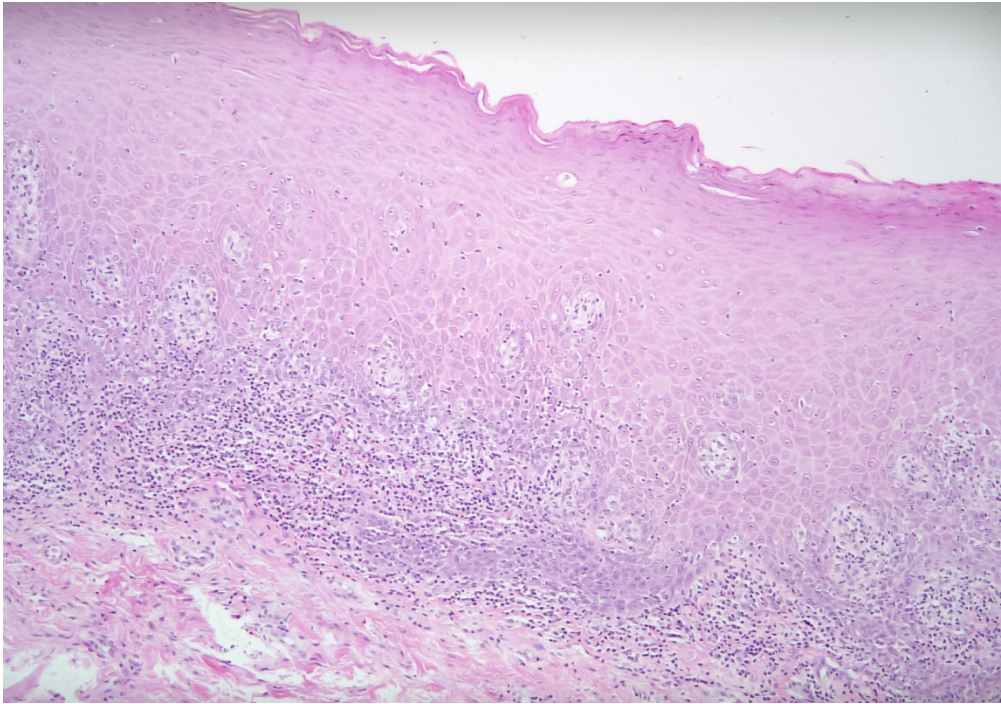


Figure 3: Histological image of the biopsy of the buccal mucosae with the linear accumulation of lymphocytes along the basal epidermal membrane with intraepidermal lymphocytic infiltrates and single necrotic keratinocytes (hematoxylin-eosin stain, magnification: 5x)

562x394mm (72 x 72 DPI)