Unusual Case of Painful Glossitis and Xerostomia Following Vaccination with Pfizer-BioNTech SARS-CoV-2 (BNT162b2)

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Financial support: None declared

Conflict of interest: None declared

Patient: Female, 60-year-old

Final Diagnosis: Adverse effects following immunisation

Symptoms: Dry mouth • painful tongue

Medication: —

Clinical Procedure: —

Specialty: Immunology

Objective: Unusual clinical course

Background: Adverse events following immunization (AEFIs) remain under recognized, particularly when the symptoms experienced are uncommon and mimic natural disease. In the context of the worldwide effort to provide protection against SARS-CoV-2 using multiple doses of vaccination and with the availability of multiple vaccines, the early recognition and prompt treatment of AEFIs has increased importance, as does the ability to carefully select an alternative after an AEFI occurs.

Case Report: A 60-year-old woman presented for clinical immunology review with a 9-month history of glossitis and xerostomia. Onset of symptoms occurred following her first vaccination with a COVID-19 vaccine (BNT162b2). After partial interval improvement, her symptoms progressively worsened after a second vaccination and third booster vaccination with BNT162b2. While undergoing reviews from multiple specialists for possible underlying connective tissue disease, and with other causes of her symptoms being excluded, the patient’s symptoms progressed, with worsening tongue swelling with new fissuring and xerostomia. The patient experienced an unintentional weight loss of 8 kg due to oral discomfort. It was only after this time that an AEFI was considered the cause of her presentation, after all other diagnostic considerations were considered unlikely. Targeted, symptomatic, localized treatment with topical oral corticosteroids was initiated, followed by a gradual tapering regimen, with excellent response.

Conclusions: This case highlights the need to consider AEFIs early in the differential diagnosis of unusual presentations and the importance of considering a trial of targeted symptomatic treatment for patients, even if diagnostic uncertainty remains.

Keywords: BNT162 Vaccine • COVID-19 Vaccine • Glossitis • mRNA Vaccine

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/937212

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

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Background

With any vaccine there are multiple reports of associated adverse events following immunization (AEFI), which can be defined as an unfavourable or unintended sign, abnormal laboratory finding, symptom, or disease following immunization [1]. An AEFI can be coincidental, meaning that the event is caused by something other than the vaccine [1]. In other cases, a causal association can be identified when no other factors are implicated in the process and the vaccine is biologically plausibly linked to the adverse event [1]. This report describes the case of a patient with an unusual AEFI manifesting with glossitis and xerostomia.

In December 2019, an outbreak SARS-CoV-2 in Wuhan, China, rapidly led to a global pandemic [2], prompting the development of multiple vaccines [3]. The Pfizer-BioNTech COVID-19 vaccine (BNT162b2) is a modified ribonucleic acid vaccine encoding the SARS-CoV2 full-length spike protein delivered in a lipid nanoparticle, which has demonstrated significant vaccine efficacy [4]. BNT162b2 has now been incorporated into vaccination regimens worldwide. Common reported AEFIs of BNT162b2 include injection site pain, fatigue, headache, myalgias, and arthralgias [3], as well as pericarditis and myocarditis [5]. However, there are only a few reports of oral adverse effects following COVID-19 vaccination. Differentiating between causal and coincidental AEFIs is a challenge during population rollout of a new vaccine, such as in the current situation. Spontaneous occurrence of new illnesses and symptoms being coincidentally attributed to the vaccine are both likely. On the contrary, uncommon AEFIs can easily be under reported and under recognized initially, as highlighted in the present case.

We report a case of a patient who developed debilitating glossitis and xerostomia. The onset of these symptoms occurred after her first vaccination with BNT162b2 and progressively worsened after each dose, with partial interval improvement. This resulted in her seeking multiple specialist medical reviews for management of the symptoms and to explore the postulated diagnosis of Sjogren syndrome. An AEFI was considered as a differential diagnosis 9 months later, and targeted therapy was initiated for symptomatic management.

Case Report

A 60-year-old woman received her first BNT162b2 vaccination and 3 days later developed oral symptoms of glossitis with new fissuring, stomatitis, and xerostomia. There was partial resolution of the oral symptoms prior to her receiving her second BNT162b2 vaccination 3 weeks later. Over the next few months, symptoms improved gradually but not completely. After receiving her BNT162b2 booster 6 months after the second vaccination, there was significant worsening, particularly of her oral manifestations (Figure 1A, 1B), resulting in an overall 8-kg weight loss due to reduced oral intake, secondary to oral pain.

Her background history included visual impairment since childhood, hypercholesterolemia, and uterine fibroids. Regular medications were stable throughout this time and included rosuvastatin and oral vitamin B12, vitamin D, and folate supplementation. She reported an allergy to Bactrim (trimethoprim/sulfamethoxazole). No new medications were commenced prior to the onset of symptoms.

Blood tests requested by the patient’s primary physician revealed a positive anti-nuclear antibody (ANA titre ≥1:640; homogenous pattern) and mildly elevated erythrocyte...
sode, the entirety of the patient’s history did not support this. The B12 level was within the reference range. An oral swab was negative for human papillomavirus high-risk genotypes. She was subsequently referred to outpatient Rheumatology services for suspected Sjogren syndrome.

Further laboratory findings included normal full blood count, renal function, and liver function tests, with no proteinuria on urinalysis. The C-reactive protein level was normal. Further autoimmune serology demonstrated negative rheumatoid factor and anti-cyclic citrullinated peptide, negative anti-dsDNA, and negative anti-extractable nuclear antigen panel (anti-Ro, La, RNP/Sm, Jo-1, Scl 70). The complement C3 level was normal, while the C4 level was mildly elevated (69 mg/dL; reference range: 10-50 mg/dL).

The new-onset persistent xerostomia prompted her primary physician to appropriately consider the diagnosis of Sjogren syndrome, which most commonly presents in middle-aged females, with 95% citing sicca symptoms (dry mouth and dry eyes) at diagnosis [6]. Oral features of sore mouth and dysphagia are reported [6], and can include glossitis, angular cheilitis, and recurrent ulcerations or fissuring in severe cases [7]. Arthralgias and myalgias are reported in more than half of patients [6]. However, on a subsequent rheumatologist review, clinical findings and serology were not entirely supportive of Sjogren syndrome, nor of any other connective tissue disease, such as lupus. As outlined above, the patient’s autoimmune serology was unremarkable. Up to 25% of patients with Sjogren syndrome have an elevated erythrocyte sedimentation rate at diagnosis, and 30% have cytopenia [6]. Anti-Ro/SSA antibodies are found in two-thirds of patients, often associated with anti-La/SSB antibodies [8]. Approximately 50% have a positive rheumatoid factor [8]. Conversely, ANA positivity is seen in the absence of autoimmune disease, with increasing age and female sex being risk factors across several populations [9,10].

Oral symptoms are not a common adverse event associated with COVID-19 vaccination, and therefore an AEFI was not considered initially. A subsequent review of the timeline of history and medications, including vaccinations, identified a clear relationship between the exacerbation of oral symptoms after each BNT162b2 vaccination, raising the possibility that this represented an AEFI with causality attributable to the vaccine. The other possibility was that this was a coincidental AEFI; for example, in which the patient may have developed a new illness spontaneously or had exacerbation of a pre-existing illness that was not previously recognized. The patient did not exhibit other symptoms that might be attributable to SARS-CoV2 infection at any time and was therefore not tested for infection. While atypical presentation of infection can be a plausible differential diagnosis for a single episode, the entirety of the patient’s history did not support this.

Prior to clinical immunology review, the patient had been reviewed by a local dental clinic for the oral symptoms after her second BNT162b2 vaccination, where she was prescribed an oral topical clonazepam preparation for burning mouth syndrome, without significant improvement. Her symptoms progressed; therefore, her primary physician prescribed oral prednisolone 30 mg per day for 2 weeks, which resulted in 60% improvement in symptoms; however, this was ceased after 5 days due to significant abdominal discomfort.

Following clinical immunology review, the differential diagnosis of an AEFI was considered most likely. Management focused on addressing the oral symptoms, which were causing the most discomfort and resulting weight loss. Given the localized symptoms and her inability to tolerate systemic corticosteroids, she was commenced on a topical oral preparation of 5 mg prednisolone dissolved in 10 to 20 mL water 3 times per day, as described by the Charles Clifford Dental Hospital (National Health Service, United Kingdom) [11].

After 2 weeks, the prednisolone frequency was reduced to twice daily for 2 weeks, then once daily for 2 weeks before ceasing. The tongue fissures and stomatitis gradually resolved completely, with associated improvement in xerostomia (Figure 2). She was able to resume a normal diet, and at the last follow-up, had not had recurrence of disease.
Discussion

A variety of oral symptoms have been described in patients after COVID-19 vaccination. Case reports of oral lesions following vaccination is not a novel phenomenon and has been described following influenza [12] and hepatitis B vaccination [13], and xerostomia has been described after vaccination against human papillomavirus [14]. However, only a few cases have been reported specific to COVID-19 vaccines. Azzi et al (2021) reported on a 31-year-old woman who developed oral mucositis 3 days after her first ChAdOx1 COVID-19 vaccine, which was treated with topical corticosteroids [15]. Manfredi et al (2021) reported a case of a 34-year-old woman who presented with diffuse oral ulcerations, swelling of the lips and gingiva, and mild angular cheilitis 2 days after BNT162b2 vaccination. Following a treatment with topical antibiotics, the mucosa was completely healed by day 15 [16]. Thongprasom et al (2021) described the case of a 38-year-old woman who was diagnosed with oral pemphigus based on examination and direct immunofluorescence on mucosal biopsy, with onset of mucosal desquamation and ulceration 1 week following ChAdOx1 vaccination [17]. One week of topical steroid therapy resulted in improvement. Sayare et al (2021) reported petechial lesions developing at the injection site and palatal area in a 21-year-old man within days of the first dose of the ChAdOx1 vaccine [18]. He was found to have mild thrombocytopenia (140 000 platelets/μL blood), and the lesions self-resolved after 5 days. These cases are all reported only in the oral health literature, likely contributing to the limited widespread recognition of these AEFI.

Riad et al (2021) reported a broad overview of oral adverse events after BNT162b2 vaccination among 877 health care workers in the Czech Republic [19], of which, 114 (13%) reported at least 1 oral adverse reaction, including blisters (36%), ulcers (14%), bleeding gingiva (11.4%), angular cheilitis (4.4%), taste disturbance (3.5%), swollen lips (3.5%), and xerostomia (2.6%). The majority (28.6%) reported onset within 1 week of vaccination. Of those with oral involvement, the tongue was involved in 13%. Despite various case reports, no definitive association between oral lesions and COVID-19 vaccines has been formally established [16]. Of those with oral involvement, the tongue was involved in 13%.

Based on World Health Organization guidelines, with the available evidence in this case, we could conclude that the most likely causality classification of this AEFI was type B1 (indeterminate), whereby a temporal relationship was consistent, but there was insufficient definitive evidence for the vaccine causing the event [1]. There was no strong evidence for another cause, and there was a strong temporal relationship between onset and exacerbation of symptoms following each vaccination. There is, however, no definitively established causal relationship in the literature between any of the COVID-19 vaccines and oral adverse events.

Conclusions

This case demonstrates that oral symptoms can be associated with BNT162b2 vaccination, which is likely under recognized by practitioners outside the field of oral health. It is evident in the limited case reports encompassing oral AEFI after COVID-19 vaccination that topical oral corticosteroids appear to be a useful treatment approach. It is important to consider medication and vaccination-induced adverse events in the differential diagnosis of any presentation, as these may rarely be implicated.

Additionally, this case highlights that in some patients a clear unifying diagnosis may not always be possible. When the diagnosis is not clear, a symptom-based approach can still be applied based on the clinical features to provide the most benefit to the patient, particularly when symptoms significantly affect quality of life. In this case, for instance, addressing our patient’s main concern of glossitis with a localized therapy aiming to reduce inflammation resulted in resolution of symptoms, and most importantly reversed her unintended weight loss and restored her quality of life.

Declaration of Figures’ Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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