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Stevens-Johnson syndrome post second dose of Pfizer COVID-19 vaccine: a case report

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Coronavirus disease 2019 (COVID-19) began in December 2019 and has affected millions of people all over the world. Respiratory illness in the form of severe pneumonia, in addition to multiorgan failure and death, is the clinical spectrum of COVID-19. Although there are no specific therapeutic agents for COVID-19 infection, the COVID-19 vaccine reduces morbidity and mortality associated with COVID-19 infection and is generally well tolerated. We report one potential complication of the Pfizer COVID-19 vaccine: a known case of Stevens-Johnson syndrome (SJS) that occurred after the second dose of the Pfizer COVID-19 vaccine alone without exposure to any other drug. Despite the initial severe adverse reaction, the patient showed a full recovery. Although SJS can be associated with COVID-19 vaccination, it is rare, and the benefits of receiving the vaccination outweigh the potential harms. (Oral Surg Oral Med Oral Pathol Oral Radiol 2021;132:e139–e142)

Stevens-Johnson syndrome (SJS) is an acute hypersensitivity reaction that causes extensive necrosis of the mucous membrane and skin. SJS results from a cytotoxic immune reaction in keratinocytes, which leads to widespread keratinocyte apoptosis.¹

Although bacterial and viral infections are considered causative factors in the syndrome, medications also are thought to be a major cause.²

According to earlier studies, the prevalence of SJS is fewer than 1 to 2 cases per 100 million people per year.³

SJS and toxic epidermal necrolysis (TEN) are 2 severe cutaneous adverse reactions, mainly caused by drugs, that are usually associated with a high morbidity and mortality rate.⁴ The most common drugs associated with the development of SJS-TEN include phenytoin, phenobarbital, carbamazepine, nevirapine, lamotrigine, nonsteroidal anti-inflammatory drugs, cotrimoxazole, allopurinol, homeopathic medicines, and fluconazole.⁵

The Chinese Center for Disease Control and Prevention announced the identification of a new strain of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on January 8, 2020, as the causative pathogen of the global COVID-19 pandemic.⁶ The information available about the main clinical manifestations produced by SARS-CoV-2 such as fever, dry cough, diarrhea, and difficulty with respiratory tract function is extensive and detailed; however, information is growing on the most recently reported symptoms, present at an earlier stage of infection, such as

skin lesions and alterations in smell, whereas reports of oral manifestations are rare.⁷

The impact of COVID-19 on oral health is primarily determined by the immune system of the patient, the drug therapy the patient receives, and the pathogenesis of the virus. It has been suggested that the oral cavity is a perfect habitat for invasion by SARS-CoV-2 owing to the special affinity the virus has for cells with receptors of the angiotensin-converting enzyme 2 found in the respiratory tract, oral mucosa, tongue, and salivary glands.⁸

BNT162b1 (BioNTech, FosunPharma, Pfizer) is an enhanced mRNA vaccine by coding for SARS-CoV-2 receptor-binding domain (RBD). The vaccine provides an increase in immunity against COVID-19 infection, depending on the new technology used for mRNA and nano-delivery technology. Clinical trials revealed elevated RBD-specific IgG antibody levels with a geometric mean concentration of 8 to 46.3 times that of convalescent serum. Mild and transient local reactions and systemic events were observed with no adverse effects. However, analysis of the data did not evaluate the safety and immunologic responses 2 weeks after the administration of the second dose.⁹

Rare cases of SJS have been linked with some vaccines, including the smallpox vaccine,¹⁰ varicella and measles, mumps, and rubella immunization,¹¹ and influenza vaccination.¹²

SJS diagnosis is essentially dependent on clinical diagnosis. Constitutional symptoms such as sore throat, fever, malaise, and arthralgia are usually recorded in the patient history. Skin manifestations present as erythematous macules that coalesce together forming large patches.⁵ Ninety percent of the cases show oral manifestations of the disease,¹³ which are present as painful erythematous crusts and erosions with a grayish-white membrane.¹²

Recently, various serum markers have been studied, which can detect an early case of TEN and signal the progression of early morbilliform drug rash to a full-blown case of TEN. Some of them include soluble Fas

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ligand, granzyme B, soluble CD40 ligand, granulysin, serum high mobility group protein B1, serum lactate dehydrogenase level, alpha-defensins 1-3 in the blister, Bcl-2 expression in the dermal infiltrate, thymus, and activation-regulated chemokine, and glutathione-S transferase-pi expression.¹⁴

CASE PRESENTATION

A middle-aged female patient came to the College of Dentistry, Taibah University, Kingdom of Saudi Arabia, 5 days after the second dose of the COVID-19 Pfizer vaccine, complaining of large, red-colored bullae about 3 cm × 1.5 cm in diameter at the left retromolar area (Figure 1) that ruptured and refilled. The patient also had whitish-yellow patches all over the tongue dorsal surface and upper and lower lips (Figure 2), in addition to multiple large ulcers found at the buccal mucosa, labial mucosa, tongue, and palate (Figure 3). No adverse reactions were reported after the first dose of vaccine exposure.

A detailed medical history was taken from the patient. The patient was medically free of disease with no history of previous drug allergy. The patient reported that she had taken the second dose of the BNT162b1 SARS-CoV-2 vaccine 5 days previously. The patient reported that she had a mild fever and general weakness. A D-dimer test was done to detect the possibility of blood clots. Laboratory examination of

the D-dimer test showed a slight elevation with 0.63 mg/L.

Oral prednisolone (30 mg/d) was prescribed for the patient. Oral corticosteroids in the form of a mouth-wash that was prepared by the addition of 40 mg of triamcinolone acetonide to 100 mL of sterile saline was also given to the patient. The patient was instructed to take fluids with minerals and to avoid sharp and hard food.

DISCUSSION

SJS incidence is 1 to 3 reported cases per million people, which is considered a rare occurrence.¹⁵ Over 200 different medications have been identified as a causative factor of SJS. These drugs stimulate immune cells such as cytotoxic T cells and natural killer cells that secrete granulysin, which destroys cells in the skin and mucous membrane by dysregulation of specific trans-membrane protein pathways.¹⁶

Oral manifestations of SJS are described as polymorphic, erosive, ampullary, and erythematous lesions. SJS occurs mostly in adults between 20 and 40 years old¹⁷ with similar manifestations to those reported in this case of multiple ulcerations, erythema, and bullae.

SJS is extremely rare with vaccination. Only a few cases have been reported with SJS after vaccinations. Six cases of SJS or TEN were reported after vaccination without other obvious triggers in a survey

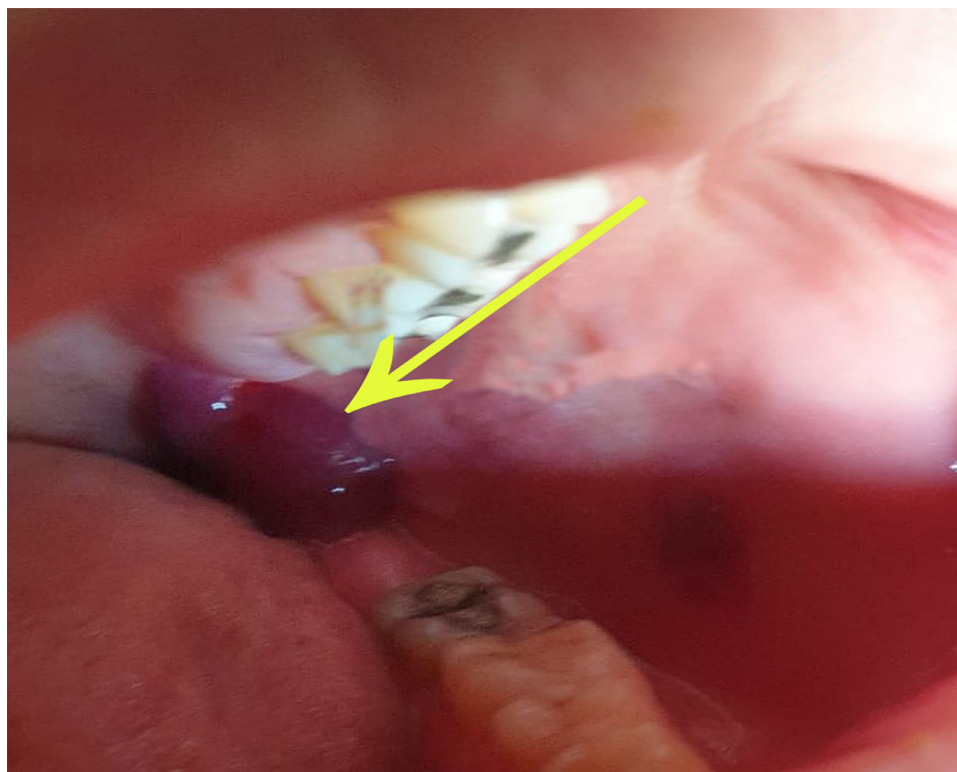


Fig. 1. Large, deep-red bullae at retromolar area.



Fig. 2. Large oral ulcerations at labial mucosa with yellow crust at lower lip.



Fig. 3. Multiple large oral ulcerations at buccal mucosa.

conducted by Ball et al.¹⁵ Also, 89 reports of SJS, 6 reports of SJS/TEN, and 7 reports of TEN from 466 027 reports were received by the Vaccine Adverse Event Reporting System in the United States during 1999-2017 after childhood vaccines (e.g., combined measles, mumps, and rubella vaccine) and the smallpox vaccine among people aged 19 to 49 years.¹⁸ Another case report of SJS was in a 19-year-old male military reservist who had been immunized recently with smallpox, anthrax, and tetanus vaccines.¹⁹

SJS has been associated with influenza vaccination alone, which supports the possibility that it can result solely from the influenza vaccine. The second case of SJS related to the influenza vaccine was reported by Tong and Chan,²⁰ with an oral manifestation of multiple ulcerations at the labial mucosa, whereas the first reported case of SJS after influenza vaccination was reported by Ball et al.¹⁵

A 2-dose regimen of BNT162b2 vaccine conferred 95% protection against COVID-19 in persons 16 years of age or older.²¹ Four related serious adverse events were reported among BNT162b2 recipients including shoulder injury related to vaccine administration, right axillary lymphadenopathy, paroxysmal ventricular arrhythmia, and right leg paresthesia.²¹ No cases were reported with SJS, which makes this case the first known case report of SJS after COVID-19 vaccination with BNT162b2.

Although the presence of such an SJS case associated with COVID-19 vaccination is considered to be the first case, SJS is also considered to be a very rare sequela. This does not diminish the importance and necessity of vaccination against COVID-19 to effectively control this pandemic.

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