American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2023; 24: e938667
DOI: 10.12659/AJCR.938667

Received: 2022.10.16
Accepted: 2022.12.22
Available online: 2022.12.29
Published: 2023.01.18

Herpes Zoster Following COVID-19 Vaccine Booster

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF Muhammad Shah Shahrudin
ACD Mohamed-Syarif Mohamed-Yassin
ABCDE Nik Munirah Nik Mohd Nasir

Department of Primary Care Medicine, Universiti Teknologi MARA, Batu Caves, Selangor, Malaysia

Corresponding Author: Mohamed-Syarif Mohamed-Yassin, e-mail: syarif8258@uitm.edu.my
Financial support: None declared
Conflict of interest: None declared

Patient: Male, 82-year-old
Final Diagnosis: Herpes zoster
Symptoms: Vesicular rash
Medication: —
Clinical Procedure: —
Specialty: Immunology • Infectious Diseases • Public Health

Objective: Unusual or unexpected effect of treatment

Background: Herpes zoster is a condition in which there is reactivation of varicella zoster virus (VZV), which is usually seen in the elderly and those with immunocompromised states. Recently, however, there have been many reports of herpes zoster after administration of COVID-19 vaccines, although initial trials showed that these vaccines have good safety and immunogenicity profiles. At the time of writing, about 5 billion people worldwide had received their full course of COVID-19 vaccination. This case report describes an elderly man who developed herpes zoster after receiving a booster dose of the Pfizer-BioNTech (BNT162b2) vaccine, with no adverse effects after the first and second dose.

Case Report: An 82-year-old man with underlying type 2 diabetes mellitus, hypertension, dyslipidemia, and cerebrovascular disease presented with left-sided chest and upper back pain. The pain was intermittent, burning in nature, and disturbed his sleep. A week prior to his presentation, he received a COVID-19 vaccine (BNT162b2) booster dose. Examination revealed multiple vesicles along his anterior and posterior T3 dermatome. He was diagnosed with herpes zoster and treated with a course of oral acyclovir. Upon review 7 days later, he had recovered well, with resolution of his vesicles and pain.

Conclusions: COVID-19 vaccination remains an important measure to prevent transmission of infection and to reduce the mortality and morbidity caused by it. However, healthcare practitioners should be aware of the possible association between COVID-19 vaccination and herpes zoster. Appropriate explanation and safety advice on the possible adverse events following COVID-19 vaccination, including herpes zoster infection, should be given to patients. This will facilitate early recognition and treatment of this condition.

Keywords: BNT162 Vaccine • COVID-19 • COVID-19 Vaccine Booster Shot • Herpes Zoster

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/938667

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

Background

Herpes zoster is caused by varicella zoster virus (VZV), which is an alpha-herpes virus. Initially, this virus causes varicella (chicken pox), which is a common childhood illness. Following a period of latency, the virus may then reactivate and cause herpes zoster among the elderly and those with immunocompromised states. Recently, however, there have been many reports of herpes zoster occurring after administration of COVID-19 vaccines [1-4]. A study conducted in Hong Kong found that the incidence of herpes zoster-related hospitalization following COVID-19 vaccination was 7.9 events per 1 million doses for the BNT162b2 vaccine and 7.1 events per 1 million doses for the CoronaVac® vaccine [5]. The presentation of herpes zoster following COVID-19 vaccination varies from asymptomatic vesicular lesions and mild symptoms of pruritus and pain [2] to life-threatening conditions involving the ophthalmic and nervous systems [5]. The occurrence of herpes zoster has been reported for almost all types of COVID-19 vaccines including the mRNA vaccines (BNT162b2 and mRNA-1273) [2,4,6], the adenovirus-based vaccine (AZD1222) [7,8], and the inactivated virus-based vaccines (CoronaVac® and BBV-152) [5,9]. These reports documented that herpes zoster occurrences after the first or second dose of COVID-19 vaccine [2,5,7-9]. To the best of our knowledge, there are no published cases of herpes zoster following a booster dose of a COVID-19 vaccine. This case report describes an elderly man who developed herpes zoster after receiving his booster dose of the BNT162b2 vaccine.

Case Report

An 82-year-old Chinese man with a background of type 2 diabetes mellitus, hypertension, dyslipidemia, and a cerebrovascular accident in October 2021 presented to our primary care clinic with left-sided chest and upper back pain of 1-week duration. His regular medications consisted of metformin extended-release 1 g nocte, gliclazide modified-release 30 mg once daily, amlodipine 5 mg once daily, atorvastatin 10 mg nocte, and aspirin 100 mg once daily. The pain was intermittent, burning in nature, rated as 7 out of 10 in severity, and disturbed his sleep. He did not have fever, cough, or shortness of breath, nor did he have palpitations, diaphoresis, or reduce effort tolerance. The pain did not get worse on physical exertion. He did not recall doing any heavy lifting or experiencing any trauma to the area preceding the onset of the pain. As he thought the pain was caused by muscle spasms, he only took paracetamol 1 g when he needed to, which slightly reduced the pain to 5 out of 10 in severity. As the pain did not resolve after 1 week, he decided to seek medical care. The only significant recent event was receiving his BNT162b2 vaccine booster dose 1 week before this pain started. He received his first and second doses of the same vaccine on 21 May 2021 and 11 June 2021, respectively. He had no recent direct contact with anyone with active shingles prior to development of his symptoms. He had no history of herpes zoster in the past and did not know if he had varicella zoster during childhood. He was not on any immunotherapy and had no risk factors for human immunodeficiency virus (HIV) infection.

On examination, he looked well and was not tachypneic. His temperature was 36.8°C, blood pressure was 125/66 mmHg, pulse rate was 70 beats per minute, and oxygen saturation was 98% on room air. Upon inspection of his chest wall, there were crops of erythematous vesicular lesions within the left T3 dermatome affecting the anterior and posterior regions (**Figures 1, 2**). These rashes were only detected during clinical examination and the patient did not notice them before this. There was no rash seen elsewhere on his body. On auscultation, there were normal first and second heart sounds. Vesicular breath sounds were heard equally on both lung fields.

He was diagnosed with herpes zoster affecting the left T3 region. No investigations were ordered as the diagnosis was made clinically. The latest blood investigation (taken a week prior to his booster vaccine for monitoring of his chronic medical conditions) showed that his HbA1c level was 7.3% (target level: <7.0%). Acyclovir 800 mg 5 times daily for 10 days and gabapentin 300 mg daily were prescribed for his condition and for pain relief, respectively. He presented for follow-up after 7 days. His pain score had decreased to 2 out of 10 and the vesicles had dried up (**Figures 3, 4**).

Discussion

We presented an interesting case of herpes zoster following a booster dose of the BNT162b2 vaccine. The potential limitation in our approach to this case is that a confirmatory test was not performed for the diagnosis of herpes zoster. However, the dermatomal rash distribution was classic for herpes zoster, so we did not pursue any further investigation.

The pathogenesis of herpes zoster starts following the primary infection of varicella (chicken pox), when the VZV becomes dormant in the neurons of the cranial nerve, dorsal root, and autonomic ganglia [10]. The reactivation of VZV after a period of latency causes herpes zoster and it usually appears when the immune system fails to contain the latent VZV replication [11]. There are multiple factors that can trigger reactivation of the virus. In particular, viral reactivation is more common in older people due to decreased cell-mediated immunity, a phenomenon known as immunosenescence [12]. Other triggering factors include immunosuppression conditions such as HIV or acquired immunodeficiency syndrome (AIDS) and malignancies, physical trauma, psychological stress, and underlying

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

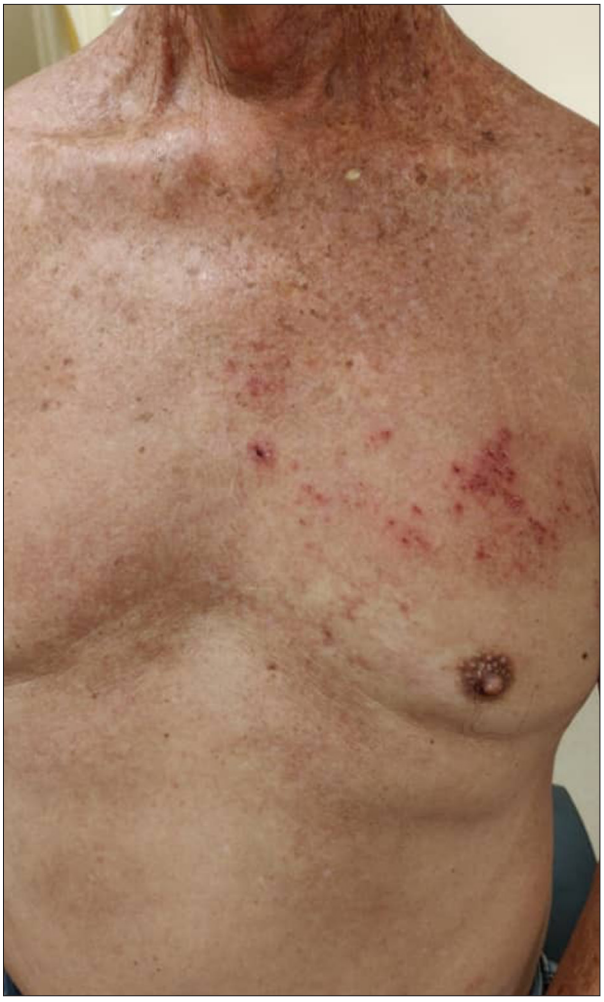

Figure 1. Vesicles on the left chest wall along the T3 dermatome during initial presentation.

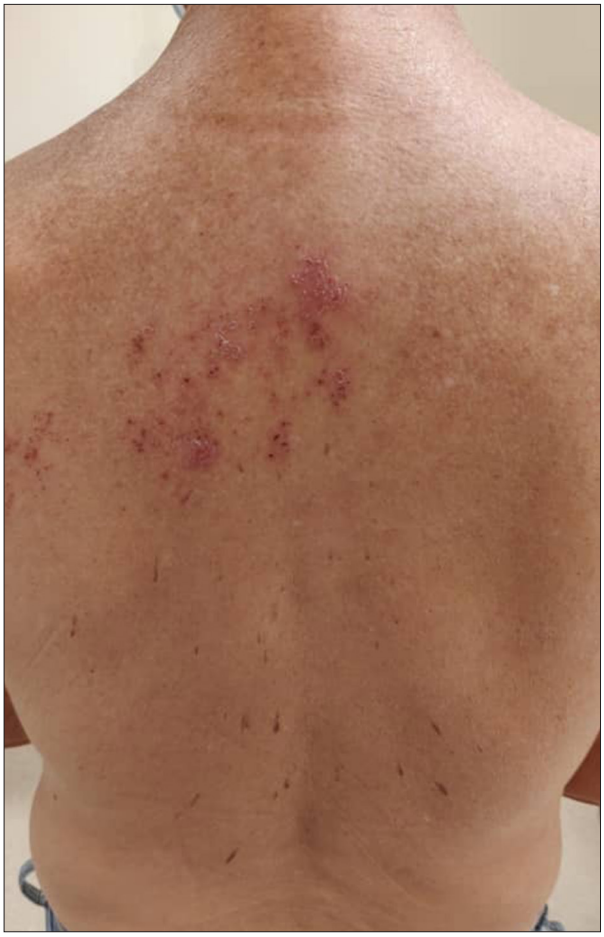

Figure 2. Vesicles on the left upper back along the T3 dermatome during initial presentation.

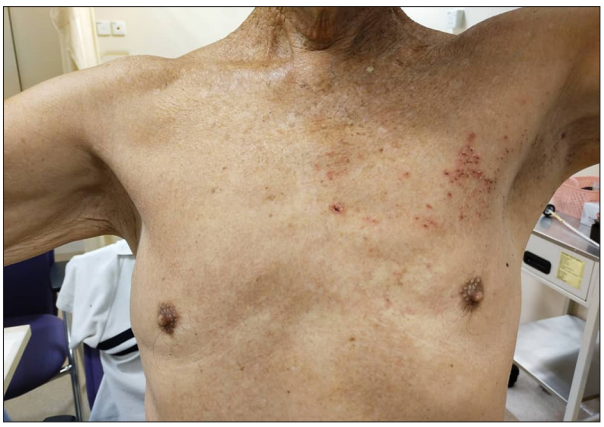

Figure 3. Healed lesions on the left chest wall along the T3 dermatome during follow-up.

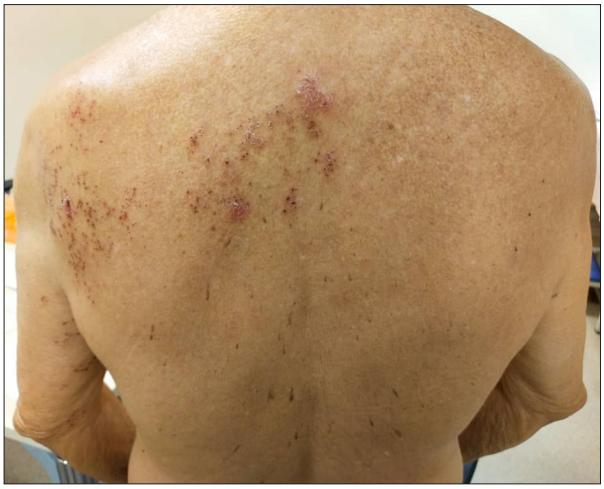

Figure 4. Healed lesions on the left upper back along the T3 dermatome during follow-up.

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

comorbidities such as chronic obstructive pulmonary disease and chronic renal failure [13].

At the time of writing, about 5 billion people worldwide had been fully vaccinated against the COVID-19 virus [14]. Full vaccination status refers to when a person has completed the primary series for a particular vaccine. For a 2-dose vaccine, a person is said to be fully vaccinated 2 to 4 weeks after receiving the second dose of the vaccine [15]. The vaccines that are currently available on the market have an established safety profile. However, a variety of mild to moderate adverse effects are experienced by some individuals receiving the vaccines [16]. Based on the initial clinical trials, there were no documented cases of herpes zoster from mRNA-based vaccines [17,18]. However, there are an increasing number of herpes zoster cases reported worldwide following COVID-19 vaccinations, especially those associated with mRNA-based vaccines.

According to the European EudraVigilance database, 15 887 cases of herpes zoster infection after BNT162b2 vaccination had been documented, accounting for 1.5% of total reported events following this vaccine [19]. On the other hand, there were 1257 reports of herpes zoster infection (0.5% of total reported events) following BNT162b2 vaccination according to the United States' Vaccine Adverse Event Report System (VAERS) [20]. Several published case reports also suggested a link between the BNT162b2 vaccine and herpes zoster infection [2,4,21].

A nationwide cross-sectional study conducted in Spain found that there was a greater number of herpes zoster cases following administration of mRNA vaccines (BNT162b2 and mRNA-1273) as compared to the the adenovirus-based vaccine (AZD1222) [7]. Of these 2 mRNA vaccines, BNT162b2 was found to be more strongly associated with herpes zoster than was mRNA-1273 [7,22]. Furthermore, a study in Hong Kong found that there were more events of herpes zoster-related hospitalization following the BNT162b2 vaccine as compared to the CoronaVac® vaccine [5].

Interestingly, our patient only developed herpes zoster infection following his booster dose but did not have any adverse effects from his first 2 BNT162b2 vaccine doses. Findings from the literature showed various patterns of onset for herpes zoster infection. A systematic review [8], including a case report in Spain and Israel, found that most of these infections occurred after receiving the first dose as compared to the second dose of COVID-19 vaccines [4,21]. On the other hand, a case report from Las Vegas, USA found similar numbers of herpes zoster cases after both the first and second doses of the BNT162b2 vaccine [2]. However, at the time of writing, there were no published cases of herpes zoster occurring after a booster dose of this COVID-19 vaccine.

A study on the safety and immunogenicity of the BNT162b2 vaccine found that there was a transient decrease in lymphocyte count following either the first or the second dose of the vaccine [23]. This reduction resolved 1 week after the vaccination [23]. The lymphopenia might be caused by an increase in the level of type 1 interferon, as hypothesize by Sahin et al [24]. This may also be due to the observation that mRNA vaccines can boost cytokines such as type 1 interferons via Toll-like receptor signalling [25]. Therefore, it is feasible that varicella zoster virus (VZV) reactivation occurs following immunization due to a brief phase of lymphopenia. In addition, the mRNA-based COVID-19 vaccines could potentially trigger herpes zoster infections, as these vaccines stimulate Toll-like receptor signalling, a pathway involved in the latency and reactivation of varicella zoster virus [25,26]. On the contrary, theoretically, vaccines trigger a CD8+ T cell response, which boosts the immune system. An increase in the response of CD4+ T cells and CD8+ T cells was observed after 2 doses of the BNT162b2 vaccine [24]. The possible explanation for this paradoxical phenomenon is that VZV-specific CD8+ cells are unable to maintain the VZV latent state following the massive shift of naive CD8+ cells during vaccination [7].

The occurrence of herpes zoster 7 days after receiving BNT162b2 vaccine, as in our case, supports the likelihood of a relationship between the infection and this vaccine. Studies have documented the onset of herpes zoster infection to be within 7 to 11 days [1,6,27]. Our case is consistent with a systematic review of the literature on 54 patients [28], as well as a review of 35 cases [22] of VZV reactivation after COVID-19 vaccination that were recorded in an international dermatology registry. In these 2 reviews, the median time to onset was 7 days.

Most cases of VZV reactivation following administration of the BNT162b2 vaccine occurred among those with immunocompromised conditions, including advanced age and autoimmune disease, and in those on immunosuppressants [11,21] and those with comorbidities such as hypertension and dyslipidemia [2,11]. Our patient also had multiple medical comorbidities. Rodriguez et al, however, reported that 5 individuals without any comorbidities developed herpes zoster after receiving the BNT162b2 vaccine [4]. Two other case reports also described herpes zoster infection after COVID-19 vaccination in individuals with no comorbidities [1,3]. A national study conducted in Israel found that irrespective of underlying comorbidities, there was an increased risk in herpes zoster infection of 15.8 events per 100 000 people for those receiving the BNT162b2 vaccine compared to non-vaccinated people [29].

Herpes zoster can affect any part of the body. The distribution of the herpes zoster in our patient was at the left T3 dermatome. A systematic review of case reports on VZV reactivation following COVID-19 vaccination found that the mammary

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

region was the most commonly affected anatomical site [8]. Our patient's presentation was consistent with this.

Herpes zoster infection following COVID-19 vaccination can also mimic hypersensitivity reactions. It is important to differentiate these 2, as their management differ. A meta-analysis reported that COVID-19 vaccines can cause hypersensitivity reactions ranging from mild allergic reaction to more severe forms of anaphylaxis reaction [30]. The symptoms vary from pruritus and urticarial rash to more severe symptoms of wheezing and shortness of breath [30]. These reported hypersensitivity reactions were seen after the first and second doses of COVID-19 vaccines [30]. The time interval between vaccine administration and the occurrence of the symptoms was from few minutes to a few days [30]. A case report from Brazil found that COVID-19 vaccines led other medical substituents to cause a hypersensitivity reaction [31]. That case report described several patients who had developed hypersensitivity reactions in the form of edema and induration around the application sites of their hyaluronic acid dermal fillers, after their COVID-19 vaccination [31].

In summary, COVID-19 vaccination is one of the important measures to prevent the transmission of the infection as well as to reduce the mortality and morbidity caused by it. Since there is increasing evidence suggesting a link between COVID-19 vaccinations, particularly the BNT162b2 vaccine, and herpes zoster, certain steps can be considered prior to vaccination to decrease the chances of developing it. Prophylactic antivirals had been proposed as an option prior to vaccination in those at high risk of VZV reactivation [8]. Another recommendation is to advise vaccination against shingles (zoster vaccine) prior to COVID-19 vaccination for those who are immunocompromised. This is in line with the Centers for Disease Control and Prevention of the United States (CDC)'s recommendation for routine vaccination against herpes zoster for people age 19 years and above with immunocompromised states [32]. In addition, health care providers should be vigilant for symptoms or signs suggestive of VZV infection after COVID-19 vaccination. Appropriate explanation and safety advice on the possible adverse events following COVID-19 vaccination, including herpes zoster infection, should be given to patients.

Conclusions

This case adds to the body of literature suggesting a link between COVID-19 vaccination, in particular the BNT162b2 vaccine, and herpes zoster infection. However, this must not deter the continuous effort for widespread COVID-19 vaccination, as the benefits of vaccination still outweigh the possible adverse effects. Instead, healthcare practitioners should be aware of this possible adverse effect to guide early recognition and treatment.

Acknowledgements

We would like to express our gratitude to the patient and his family members for sharing his photos and consenting for this case report to be published. We also would like to thank all the primary care doctors who were involved in managing this case.

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.

References:

1. Vallianou NG, Tsilingiris D, Karampela I, et al. Herpes zoster following COVID-19 vaccination in an immunocompetent and vaccinated for herpes zoster adult: A two-vaccine related event? Metabol Open. 2022;13:100171
2. Lee C, Cotter D, Basa J, Greenberg HL. 20 Post-COVID-19 vaccine-related shingles cases seen at the Las Vegas Dermatology clinic and sent to us via social media. J Cosmet Dermatol. 2021;20(7):1960-64
3. van Dam CS, Lede I, Schaar J, et al. Herpes zoster after COVID vaccination. Int J Infect Dis. 2021;111:169-71
4. Rodríguez-Jiménez P, Chicharro P, Cabrera L-M, et al. Varicella-zoster virus reactivation after SARS-CoV-2 BNT162b2 mRNA vaccination: Report of 5 cases. JAAD Case Reports. 2021;12:58-59
5. Wan EYF, Chui CSL, Wang Y, et al. Herpes zoster related hospitalization after inactivated (CoronaVac) and mRNA (BNT162b2) SARS-CoV-2 vaccination: A self-controlled case series and nested case-control study. Lancet Reg Health West Pac. 2022;21:100393
6. Lee T-J, Lu C-H, Hsieh S-C. Herpes zoster reactivation after mRNA-1273 vaccination in patients with rheumatic diseases. Ann Rheum Dis.2022;81(4):595-97
7. Català A, Muñoz-Santos C, Galván-Casas C, et al. Cutaneous reactions after SARS-CoV-2 vaccination: A cross-sectional Spanish nationwide study of 405 cases*. Br J Dermatol. 2022;186(1):142-52
8. Katsikas Triantafyllidis K, Giannos P, Mian IT, et al. Varicella zoster virus reactivation following COVID-19 vaccination: A systematic review of case reports. Vaccines. 2021;9(9):1013
9. Arora P, Sardana K, Mathachan SR, Malhotra P. Herpes zoster after inactivated COVID-19 vaccine: A cutaneous adverse effect of the vaccine. J Cosmet Dermatol. 2021;20(11):3389-90
10. Patil A, Goldust M, Wollina U. Herpes zoster: A review of clinical manifestations and management. Viruses. 2022;14(2):192
11. Psichogiou M, Samarkos M, Mikos N, Hatzakis A. Reactivation of varicella zoster virus after vaccination for SARS-CoV-2. Vaccines. 2021;9(6):572
12. Palacios-Pedrero MÁ, Osterhaus ADME, Becker T, et al. Aging and options to halt declining immunity to virus infections. Front Immunol. 2021;12:681449
13. Marra F, Parhar K, Huang B, Vadlamudi N. Risk factors for herpes zoster infection: A meta-analysis. Open Forum Infect Dis. 2020;7(1):ofaa005
14. World Health Organization. WHO Coronavirus (COVID-19) Dashboard. World Health Organization; 2022, March 29 [2022, September 13]; Available from: https://covid19.who.int/?mapFilter=vaccinations
15. World Health Organization. Coronavirus disease (COVID-19): Vaccines. World Health Organization; 2022, May 17 [2022, September 13]; Available from: https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-(covid-19)-vaccines

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

16. Pormohammad A, Zarei M, Ghorbani S, et al. Efficacy and safety of COVID-19 vaccines: A systematic review and meta-analysis of randomized clinical trials. Vaccines. 2021;9(5):467
17. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med. 2021;384(5):403-16
18. Thomas SJ, Moreira ED Jr., Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine through 6 months. N Engl J Med. 2021;385(19):1761-73
19. European Medicines Agency. European database of suspected adverse drug reaction reports. European Medicines Agency; 2012, May 31 [2022, July 28]; Available from: https://www.adrreports.eu/
20. Centers for Disease Control and Prevention. The United States Vaccine Adverse Event Report System (VAERS). Centers for Disease Control and Prevention; 2022, April 27 [2022, July 28]; Available from: https://wonder.cdc.gov/vaers.html
21. Furer V, Zisman D, Kibari A, et al. Herpes zoster following BNT162b2 mRNA COVID-19 vaccination in patients with autoimmune inflammatory rheumatic diseases: A case series. Rheumatology (Oxford). 2021;60(Si):Si90-95
22. Fathy RA, McMahon DE, Lee C, et al. Varicella-zoster and herpes simplex virus reactivation post-COVID-19 vaccination: A review of 40 cases in an International Dermatology Registry. J Eur Acad Dermatol Venereol. 2022;36(1):e6-e9
23. Walsh EE, Frenck RW, Falsey AR, et al. Safety and immunogenicity of two RNA-based COVID-19 vaccine candidates. N Engl J Med. 2020;383(25):2439-50
24. Sahin U, Muik A, Derhovanessian E, et al. COVID-19 vaccine BNT162b1 elicits human antibody and TH1 T cell responses. Nature. 2020;586(7830):594-99
25. Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines – a new era in vaccinology. Nat Rev Drug Discov. 2018;17(4):261-79
26. West JA, Gregory SM, Damania B. Toll-like receptor sensing of human herpesvirus infection. Front Cell Infect Microbiol. 2012;2:122
27. Préta LH, Contejean A, Salvo F, Treluyer JM, et al. Association study between herpes zoster reporting and mRNA COVID-19 vaccines (BNT162b2 and mRNA-1273). Br J Clin Pharmacol. 2022;88(7):3529-34
28. Desai H, Sharma K, Shah A, et al. Can SARS-CoV-2 vaccine increase the risk of reactivation of Varicella zoster? A systematic review. J Cosmet Dermatol. 2021;20:3350-61
29. Barda N, Dagan N, Ben-Shlomo Y, et al. Safety of the BNT162b2 mRNA COVID-19 vaccine in a nationwide setting. N Engl J Med. 2021;385(12):1078-90
30. Alhumaid S, Al Mutair A, Al Alawi Z, et al. Anaphylactic and nonanaphylactic reactions to SARS-CoV-2 vaccines: A systematic review and meta-analysis. Allergy Asthma Clin Immunol. 2021;17(1):109
31. Ortigosa LCM, Lenzoni FC, Suárez MV, et al. Hypersensitivity reaction to hyaluronic acid dermal filler after COVID-19 vaccination: A series of cases in São Paulo, Brazil. Int J Infect Dis. 2022;116:268-70
32. Anderson TC, Masters NB, Guo A, et al. Use of recombinant zoster vaccine in immunocompromised adults aged ≥19 years: Recommendations of the Advisory Committee on Immunization Practices – United States, 2022. MMWR Morb Mortal Wkly Rep. 2022;71(3):80-84

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