



## CASE REPORT

# Inactivated COVID-19 vaccine-related herpes zoster and post-herpetic neuralgia: Three case reports

*İnaktif COVID-19 aşısı ile ilişkili herpes zoster ve postherpetik nevralji: 3 olgu raporu*

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## Summary

Vaccination programs against COVID-19 have been implemented all over the world since December 2020. Beside the common side effects of vaccines, there are also increasing reports of herpes zoster (HZ) activation. In this report, we describe three cases of HZ, one of them with post-herpetic neuralgia (PHN) after receiving inactivated COVID-19 vaccine. The first two patients developed HZ 8 and 10 days after vaccination, respectively. When pain could not be controlled with paracetamol and non-steroidal anti-inflammatories, the patients received weak opioid codeine. In addition, the first patient received gabapentin, and the second patient was applied erector spinae plane block. The third patient was admitted 4 months after the diagnosis of HZ and considered to have PHN and pain palliation was provided with tramadol. Although the exact cause has not yet been fully resolved, increased reports of HZ after vaccination suggests a link between vaccines and HZ. Considering that receiving COVID-19 vaccines will going on, HZ and PHN cases will continue to be seen. More epidemiological studies are needed to further evaluate the relationship between COVID-19 vaccines and HZ.

Keywords: COVID-19 disease; post-herpetic neuralgia; vaccination; herpes zoster.

## Özet

Aralık 2020 tarihinden bu yana tüm dünyada koronavirüs hastalığına (COVID-19) karşı aşı programları uygulanmaktadır. Aşıların yaygın yan etkilerinin yanı sıra herpes zoster aktivasyonu ile ilgili de artan olgu raporları bildirilmektedir. Bu olgu raporunda, inaktif COVID-19 aşısı olduktan sonra biri postherpetik nevralji gelişen üç herpes zoster olgusunu tanımlıyoruz. İlk iki hasta, aşılamadan sırasıyla sekiz ve on gün sonra herpes zoster gelişen hastaydı. Ağrı parasetamol ve nonsteroid antiinflamatuar ilaçlarla kontrol edilemeyince hastalara zayıf opioid olarak kodein verildi. Buna ek olarak, birinci hastaya gabapentin başlandı, ikinci hastaya ise erektor spina plan bloku uygulandı. Üçüncü hasta herpes zoster tanısından dört ay sonra başvuran hastaydı ve postherpetik nevralji olarak değerlendirildi. Tramadol ile ağrı palyasyonu sağlandı. Kesin neden henüz tam olarak belirlenmemiş olsa da aşılamadan sonra artan herpes zoster raporları, aşilar ile herpes zoster gelişimi arasında bir bağlantı olduğunu düşündürmektedir. COVID-19 aşılanmasının devam edeceği düşünüldüğünde, herpes zoster ve postherpetik nevralji olguları da görülmeye devam edecektir. COVID-19 aşıları ile herpes zoster arasındaki ilişkiyi daha fazla değerlendirmek için daha fazla epidemiyolojik çalışmaya ihtiyaç vardır.

Anahtar sözcükler: COVID-19; postherpetik nevralji; aşılanma; herpes zoster.

## Introduction

Vaccination programs against COVID-19 have been implemented all over the world since December 2020 and continue to be implemented worldwide. Various vaccines such as DNA/RNA-based vaccines, non-replicating viral vector vaccines, and inactivated vaccines have been developed to prevent viral transmission related to COVID-19 and reduce morbidity and mortality.<sup>[1]</sup> The use of COVID-19 vaccines is authorized in many countries. In Türkiye, inactivated vaccines and mRNA vac-

cines are authorized in January 2021 and in April 2021, respectively, with the priority of the elderly, along with health-care workers. Common vaccine-related side effects are pain and swelling at the injection site, fever, chills, headache, nausea, vomiting, rash, fatigue, etc.<sup>[2,3]</sup> In addition to mild and moderate vaccine-related side effects, rare side effects such as herpes zoster (HZ) have been reported. In this report, we describe three cases of HZ, one of them with post-herpetic neuralgia (PHN) after receiving inactivated COVID-19 vaccine.

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## Case Reports

**Case 1** – A 78-year-old male patient with a history of hypothyroidism, hypertension (HT), coronary artery disease (CAD), and previous cerebrovascular disease developed pain, itching, and vesicular eruptions in the left arm deltoid muscle, 8 days after receiving the first dose of inactivated COVID-19 vaccine on February 01, 2021. The patient was referred to the dermatology clinic and was diagnosed with HZ. As an antiviral medication, he received brivudine 75 mg once a day and additionally vitamin B12 once a day, topical fusidic acid for local application 3 times a day, and paracetamol 500 mg 3 times a day were prescribed. On March 17, 2021, after the lesions subsided, the patient consulted to the pain clinic with complaints of pain in the left arm deltoid region with a Numerical Rating Scale (NRS) score of 9, itching, burning, and his muscle strength in the left thumb was 4/5. In the cervical magnetic resonance imaging (MRI) on March 12, 2021, there were no features other than extensive osteophytic degenerations at the C3-T1 vertebral disc levels, narrowing of the anterior subarachnoid spaces. In the cranial MRI angiography, there was no pathological finding except that the right vertebral artery was in fine calibration.

The patient was commenced on gabapentin 600 mg twice daily, paracetamol+codeine combination 300/30 mg 3 times daily, and topical lidocaine 5% 3 times daily. After 3 weeks, there was a decrease in the complaint of pain, with an NRS score of 3. In the follow-up period, the patient stated that he had received the second dose of the inactivated vaccine on June 08, 2021, and the mRNA vaccine on August 10, 2021, without any complications.

**Case 2** – An 83-year-old male patient without any comorbidity attended to the dermatology clinic with vesicular eruptions due to HZ on the right T8-T12 dermatomal area, 10 days after receiving the first dose of inactivated vaccine on March 04, 2021. He was prescribed brivudine 75 mg once daily as antiviral medication, vitamin B12 once daily, topical fusidic acid thrice a day, and dexamethasone 25 mg twice a day. After a week, despite the subsidence in rashes, the patient was admitted to the pain clinic due to the persistence of severe pain, itching, burning, and numbness at the right T8-T12 dermatomal area. The patient was prescribed paracetamol+codeine com-

ination 300/30 mg 3 times a day, topical nimesulide 1%+lidocaine 5% 3 times a day, and dexamethasone 25 mg once daily. When the patient's complaints did not subside at the follow-up visit 1 week later, a total of 20 mL solution was prepared using 40-mg triamcinolone+8 mL saline+10 mL 0.5% bupivacaine and erector spinae plane block was applied at the level corresponding to the right T8-T12 dermatomal area. In the follow-up examination 2 weeks later, the NRS score of the patient decreased from 7 to 2. In the subsequent follow-ups, the patient stated that he received the second dose of inactivated vaccine on April 09, 2021, and the third dose on July 16, 2021, without experience any complications.

**Case 3** – A 94-year-old female patient with the diagnosis of HT, diabetes mellitus, CAD, chronic heart failure, dementia, and no previous vaccination history at any time in her life, was referred to her family doctor with vesicular eruptions in the left T6-T10 dermatomal area, 15 days after the first dose of inactivated vaccine on May 20, 2021. The patient was prescribed valacyclovir 500 mg twice daily and dexamethasone 25 mg twice daily. However, the patient was admitted to the pain clinic 4 months after the diagnosis of HZ with complaints of burning, numbness, and stabbing pain. Her NRS score was 8. The patient was diagnosed with PHN, and tramadol+paracetamol combination 37.5 mg/325 mg 2 times a day, topical naproxen sodium 10%+lidocaine 5% 3 times a day, and vitamin B12 once a day were prescribed. As the administration of medication, the patient's pain score regressed to an NRS score of 4.

## Discussion

Varicella-zoster virus (VZV) is a human neurotropic virus that usually causes varicella during childhood and adolescence. On the resolution of VZV infection, residual provirus segments travel by sensory nerves and stay dormant in the cranial or dorsal root ganglions. HZ is a common segmental vesicular eruption, pain, and sensorial symptoms caused by the reactivation of VZV. The average duration of the rash ranges from 7 to 10 days and is usually self-limited. However, neuropathic pain associated with HZ may continue after the acute period as post-herpetic neuralgia.<sup>[3]</sup> The incidence of HZ increases with age, trauma, immunosuppressive therapy, and comorbid conditions such as malignancy or chronic kidney or liver disease.<sup>[4]</sup>

In the literature, Walter et al.<sup>[5]</sup> reported three HZ reactivations after hepatitis A, inactivated influenza and rabies with Japanese encephalitis vaccines and, Ruder et al.<sup>[6]</sup> showed reduced allogeneic reactivity after the hepatitis B vaccine.

Although the occurrence of HZ after vaccination may be coincidental, many case reports of post-vaccination VZV reactivation have been published recently. From Türkiye, Bostan et al.<sup>[7]</sup> reported that HZ lesions developed in a 78-year-old patient after receiving an inactivated vaccine, Aksu et al.<sup>[8]</sup> reported HZ in a 68-year-old patient, and also from India, Arora et al.<sup>[9]</sup> reported HZ in a 60-year-old patient. Several case reports have been described regarding COVID-19 vaccination and HZ relation, furthermore. While most of the HZ patients are at an advanced age, there are also patients who developed HZ at young ages. Rodriguez et al.<sup>[10]</sup> described five young, healthy adults without risk factors who developed HZ reactivation and Özdemir et al.<sup>[11]</sup> reported HZ after vaccination in two young healthy adults. Development of HZ was observed not only after inactivated COVID-19 vaccines, also observed after mRNA vaccines. Tessa et al.<sup>[12]</sup> reported a 44-year-old health-care provider developed HZ after his first dose injection of the mRNA COVID-19 vaccine. Eid et al.<sup>[13]</sup> described a 79-year-old man referred with HZ after receiving an mRNA COVID-19 vaccine. Furer et al.<sup>[14]</sup> also mentioned HZ cases that developed after mRNA vaccination in six patients with autoimmune disease.

Since cellular immunity is of great importance in protecting against HZ reactivation, reduction, and dysfunction in T lymphocytes can reactivate VZV.<sup>[15]</sup> Lymphopenia occurs in more than 70% of COVID-19 patients, and a great decrease occurs in CD4+ and CD8+ lymphocytes.<sup>[16]</sup> As with COVID-19 infection, a decrease in cellular immunity was observed after receiving both inactive and mRNA COVID-19 vaccines. The decrease in T lymphocytes occurs in the 1<sup>st</sup> days after vaccination and returns to normal 6–8 days later.<sup>[17]</sup> The reason why the majority of HZ patients are in advanced age may be the decrease in cellular immunity with age. The most important risk factor of our patients was advanced age, and they did not mention any immunosuppressive drug use, radiation exposure, or physical trauma. The first patient had no comorbid disease except HT and CAD. Despite his advanced age, the second patient did

not have any comorbidity. The third patient was of advanced age and had serious comorbidities. In all three patients, despite the regression of HZ lesions, medication was commenced and invasive procedures were applied for ongoing neuropathic pain.

## Conclusion

Although the exact cause has not yet been fully resolved, the short time interval between the development of HZ and vaccination, increased case reports of HZ after vaccination suggests a link between vaccines and VZV reactivation. Considering that receiving COVID-19 vaccines will go on, it can be predicted that HZ and PHN cases will continue to be seen, especially in elderly individuals. In this context, more comprehensive epidemiological studies are needed to further evaluate the risk factors and possible mechanisms and prevent the relationship between COVID-19 vaccines and HZ.

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