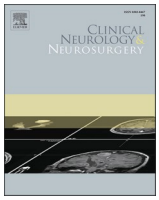
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Clinical Neurology and Neurosurgery 224 (2023) 107578

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro



Case Report

Complex regional pain syndrome after mRNA-based COVID-19 vaccination

Shiro Horisawa *, Tamon Ando, Takakazu Kawamata, Takaomi Taira

Department of Neurosurgery, Tokyo Women's Medical University, Tokyo, Japan

ARTICLE INFO

Keywords:
COVID-19
CRPS
Pain
Movement disorder
Vaccination

ABSTRACT

We describe the case of a 17-year-old woman diagnosed with complex regional pain syndrome (CRPS) at a pain clinic after the second dose of the COVID-19 vaccine. She was referred to our department for surgical treatment of movement disorder seven months after the second inoculation. Baclofen (50 μg), administered intrathecally, improved the involuntary movements of her right hand. After administration of zolpidem (5 mg), involuntary movements of the right index finger almost disappeared. However, neither zolpidem nor intrathecal baclofen improved the limited range of motion of the first joint of the left-hand finger. Despite various reports on CRPS development after vaccination, only one case post COVID-19 vaccination has been reported. Therefore, healthcare providers should keep in mind that CRPS can appear after the COVID-19 vaccination.

1. Introduction

Complex regional pain syndrome (CRPS) is a difficult disease to treat, with various symptoms including severe pain and swelling in the extremities following surgery or trauma, limited joint range of motion and involuntary movements, and autonomic nervous system symptoms such as skin temperature changes. While several cases of CRPS have been reported after vaccination, the causal relationship between the two is unknown. Currently, 66.8 % of the global population has received at least one dose of the COVID-19 vaccine, and 12.2 billion doses have been administered worldwide (https://ourworldindata.org/covid-vaccinations). However, only one case of CRPS after the COVID-19 vaccine administration has been reported [1]. Here, we report a case of CRPS that occurred after the COVID-19 vaccination.

2. Case report

A 17-year-old woman with no specific medical history received the first dose of coronavirus mRNA vaccine (Pfizer and BioNTech COVID-19 vaccine) on her left upper arm, which caused mild swelling at the site of vaccination and resolved quickly. Three weeks later, the second dose of the vaccine was administered to her left upper arm, and she developed a fever of 37.8 °C, which resolved within a few hours. Two days later, a bruise appeared on the back of her left hand and spread to the entire left hand, which became edematous and caused severe pain (Fig. 1A). Five days later, the bruise gradually moved proximally to the upper arm (Fig. 1B, C), and even the slightest touch caused severe pain. The time course of bruise development is shown in Fig. 2. Two weeks after the second inoculation, the bruise gradually began to resolve and disappeared almost completely three weeks later; however, severe pain and swelling persisted. Six weeks later, the patient visited a pain clinic, where CRPS was diagnosed, and a stellate ganglion block was performed. Two months after the second inoculation, numbness and involuntary flexion of the right hand and fingers began to appear. Though pain and swelling in the left hand decreased three months later, and the patient was able to move the hand, the distal interphalangeal of the left hand remained in a flexed position. Subsequently, four months later, involuntary movements with pain in the index finger of the right hand appeared (Video 1). She was prescribed trihexyphenidyl for involuntary movements, however, there was no improvement. She was referred to our department for surgical treatment of this movement disorder seven months after the second inoculation. On examination, there was no swelling of the left hand, and the patient had difficulty extending the distal interphalangeal joints of the fingers, but the range of motion at other joints was restricted (Video 2). An injection of 50 μg baclofen was administered intrathecally, which resulted in a definite improvement of involuntary movements of the right hand. After administration of 5 mg of zolpidem, the involuntary movements of the index finger of the right hand almost disappeared, and the patient did not experience drowsiness. Neither zolpidem nor intrathecal baclofen improved the limited range of motion of the first joint of the left-hand finger.

* Correspondence to: Department of Neurosurgery, Neurological Institute, Tokyo Women's Medical University, Shinjuku-ku, Kawada-cho, 8-1, Tokyo 162-8666, Japan.

E-mail address: neurosurgery21@yahoo.co.jp (S. Horisawa).

https://doi.org/10.1016/j.clineuro.2022.107578
Received 12 August 2022; Received in revised form 15 November 2022; Accepted 26 December 2022
Available online 28 December 2022

Supplementary material related to this article can be found online at doi:10.1016/j.clineuro.2022.107578.

3. Discussion

There have been various reports of CRPS after vaccination, including the hepatitis B, influenza, rubella, and human papillomavirus vaccines. Only one case of CRPS occurring after COVID-19 vaccination has been reported (with no mention of the name of the vaccine manufacturer) [1]. A 33-year-old woman received the first dose in the left upper arm. Two days after vaccination, she developed dyshidrosis, increased skin temperature, swelling of the entire left hand extending from the vaccination site, and decreased range of motion of the joints. Two months after inoculation, edema and burning pain were reduced, and motor function of the left hand improved to some extent but did not resolve completely. In a report of four patients who developed CRSP after hepatitis B vaccination, all reported complete improvement of CRPS symptoms within four months [2]. In our case, pain and swelling in the left upper extremity had almost completely resolved four months after onset, which is consistent with previous reports. However, the limited range of motion of the first joint of the left index finger did not improve, and it is questionable whether the involuntary movements that appeared in the index finger of the right hand should be considered as CRPS-associated symptoms. However, it has been reported that some of the CRPS patients develop movement disorders including dystonia, tremor, and myoclonus in both hands [3]. Therefore, it is possible that involuntary movements in the right hand in our case may be associated with CRPS in the left hand. Additionally, a previous study has reported the combination of dystonia and tremor or dystonia and myoclonus, which is consistent with the observation in the present case [3].

Possible mechanisms of CRPS after vaccination include injection trauma, hypersensitivity reaction to vaccine component, nerve damage by either direct invasion of the virus or secondary immune hyperactivity. So far, an increased risk of CRPS with vaccination has not been reported [4]. Jastaniah et al. reported that induction of CRPS may result from injection trauma or may be an allergic response to a vaccine constituent [2]. They administered antihistamines prior to vaccination to avoid any possible allergic reactions, but this did not prevent the development of CRPS. There were no findings suggestive of allergy in the post-vaccination CRPS described above including in our case. However, generally, viruses including that causing COVID, can cause damage to nerves and can also damage nerves by secondary immune hyperactivity. Although an increased risk of Bell's palsy, encephalomyelitis, and Guillain-Barré syndrome in persons after SARS-CoV-2 infection has been reported, but Li et al. have reported no increase in risk with vaccination [5]. Considering these factors, it is highly likely that CRPS was caused by injection trauma in our case.

Healthcare providers should keep in mind that CRPS can occur after the COVID-19 vaccination.

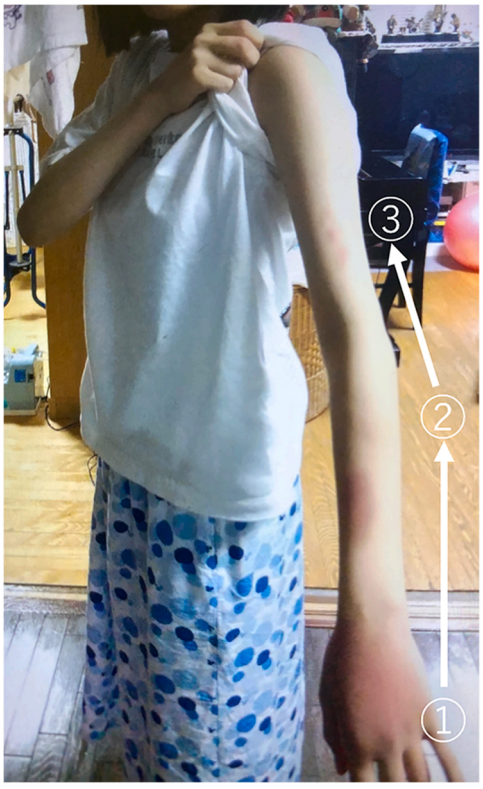


Fig. 2. The bruise ascended from the left hand to the left upper arm as indicated by the arrow. ① The bruise and swelling appeared on the left hand 2 days later. ② Five days later, a bruise appeared from the left forearm to the elbow. ③ Ten days later, a bruise appeared on the left upper arm.

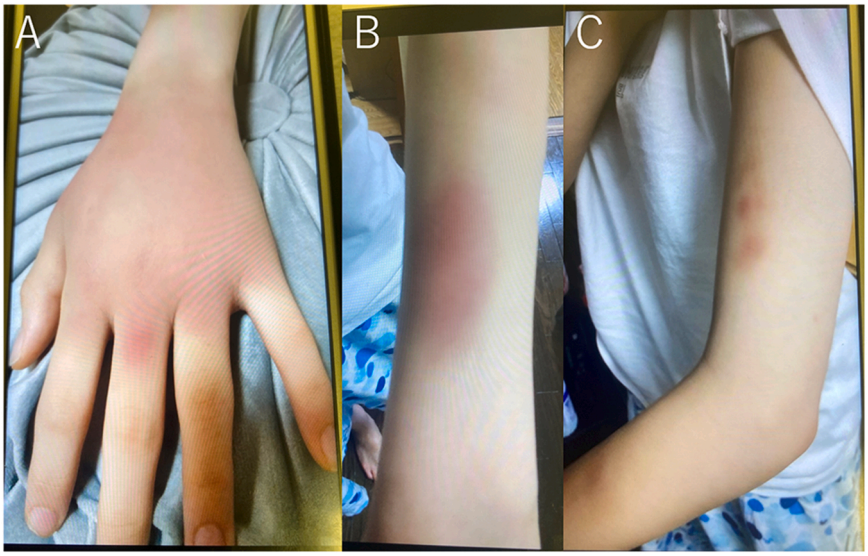


Fig. 1. Bruised and edematous left hand. (A) Swollen left hand. (B) Left elbow. (C) Left upper arm.

Funding

This work was supported by JSPS KAKENHI Grant no. JP21K09113.

Informed consent and ethical approval

The authors confirm that the approval of an institutional review board was not required for this work. Written and verbal informed consent from the patient was obtained. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Declarations of interest

None.

References

[1] P. Raman, Complex regional pain syndrome post COVID-19 vaccine shot: an autobiographical case report, Cureus 13 (2021), e20257, https://doi.org/10.7759/cureus.20257.

[2] W.A. Jastaniah, S. Dobson, J.G. Lugsdin, R.E. Petty, Complex regional pain syndrome after hepatitis B vaccine, J. Pediatr. 143 (2003) 802–804, https://doi.org/10.1067/S0022-3476(03)00536-5.

[3] J.J. Van Hilten, Movement disorders in complex regional pain syndrome, Pain Med. 11 (2010) 1274–1277.

[4] A. Hviid, N.M. Thorsen, P. Valentiner-Branth, M. Frisch, K. Mølbak, Association between quadrivalent human papillomavirus vaccination and selected syndromes with autonomic dysfunction in Danish females: population based, self-controlled, case series analysis, BMJ 370 (2020) m2930, https://doi.org/10.1136/bmj.m2930.

[5] X. Li, B. Raventós, E. Roel, A. Pistillo, E. Martinez-Hernandez, A. Delmestri, C. Reyes, V. Strauss, D. Prieto-Alhambra, E. Burn, T. Duarte-Salles, Association between covid-19 vaccination, SARS-CoV-2 infection, and risk of immune mediated neurological events: population based cohort and self-controlled case series analysis, BMJ 376 (2022), e068373, https://doi.org/10.1136/bmj-2021-068373.