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Aseptic meningoencephalitis after COVID-19 vaccination: A case report



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<i>Keywords:</i>	Introduction: Several types of vaccine have been shown to significantly reduce the risk of severe coronavirus disease 2019 (COVID-19). This study aims to report the first case of meningoencephalitis after receiving the second dose of Pfizer COVID-19 vaccine.
COVID-19	<i>Case report:</i> A 62-year-old lady presented with headache, fever and rigor for 4 days. She had acute confessional state and inability to talk. She was conscious, disoriented, not obeying commands. Acyclovir vial IV 750 mg three times a day for 14 days were prescribed. She responded very well.
Meningoencephalitis	<i>Discussion:</i> Concern has been raised about the safety of vaccinations. The most common side effects of COVID-19 vaccinations are local responses at the injection site, followed by non-specific systemic symptoms such as headache, tiredness, myalgia, and fever. These may appear shortly after immunization and disappear in a short period of time.
Aseptic	<i>Conclusion:</i> Although extremely rare, aseptic meningoencephalitis could occur after COVID-19 vaccination. The patient could be managed conservatively with a good clinical outcome.

1. Introduction

Since its discovery in China in early December, coronavirus disease 2019 (COVID-19) has spread aggressively around the world [1]. The pathogen has been termed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2]. SARS-CoV-2 has a high affinity for the angiotensin-converting enzyme 2 (ACE2) receptor found in human glial cells, neurons, respiratory epithelial cells, and vascular endothelial cells [3]. COVID-19 mostly causes respiratory disease, with manifestations ranging from mild symptoms with myalgia, sore throat, cough, fever, anosmia, and diarrhea to more serious complications of acute respiratory distress syndrome, multi-organ failure, and death. COVID-19 infection has been linked to a number of neurological problems [4]. SARS-CoV-2 can induce autoimmune illnesses, which may result in intensive care unit (ICU) hospitalization and significant mortality in certain individuals. Involvement of the nervous system has a bad prognosis. The pathophysiological mechanism of the disease, as well as the connection between COVID-19 and central nervous system (CNS) involvement, remains unknown [5]. Massive immunization is a key global goal to decrease the load on healthcare systems [6].

SARS-CoV-2's impact on individuals with neurological disorders poses a serious public health threat. When weighing the risks and benefits of vaccination, it is essential to consider this group [7]. Several vaccinations have been shown to significantly reduce the risk of severe COVID-19 infection, with a tolerable safety profile and an outstanding benefit/risk ratio [8]. A total of more than 5 billion vaccine doses have been administered globally as of September 5, 2021 [9]. Within days, the surveillance system revealed a suspicious cluster of significant neurologic adverse outcomes following vaccination among first-dose recipients [10].

However, development of meningoencephalitis after receiving COVID-19 vaccinations is an extremely rare condition. This study aims to report the first case of meningoencephalitis following receiving the second dose of Pfizer COVID-19 vaccine. The report has been arranged in line with SCARE 2020 guidelines with a brief literature review [11].

2. Case report

Patient's information: A-62-year-old lady presented with headache, fever and rigor for 4 days. The symptoms developed following

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Case Report

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receiving the second dose of COVID-19 Pfeizer vaccine before five days. She presented to the neurologic clinic with acute confessional state and inability to talk. Past history was unremarkable. She was a known case of ceftriaxone allergy.

Clinical findings: On examination: the patient was conscious, disoriented, and he did not obey commands. There was no aphasia. Dysarthria could not be evaluated. Positive meningeal irritation signs were observed. The pupils were isocor bilaterally, light reaction was positive also. There was no evidence of ophthalmoplegia. Babinski sign was negative. The patient was not able to stand up and walk. She was on wheelchair. Body temperature elevated.

Vital signs: temp. 38C, SPO2 98%, Pulse rate: 105 bpm, Blood pressure: 125/80 mmHg.

Diagnostic intervention: complete blood count showed mild leukocytosis (13000) and agranulocytosis. C reactive protein (CRP) elevated (12.9). There was ormal serum electrolyte with normal renal and liver function tests. Random blood sugar was 185mg/dl. Brain CT scan was normal. After 12 hours, brain MRI performed and showed normal brain parenchyma. Lumbar puncture was clear CSF macroscopically, and microscopically showed lymphocytic pleocytosis of 170 cells, Protein (802mg/dl), Glucose (71mg/dl), Lactate (19,61mg/dl) and negative gram stain. Viral polymerase chain reaction (PCR) for Herpes simplex virus both type 1 and 2 were negative.

Therapeutic intervention: Before neurological presentation, meropenem IV 1 gm twice daily started with Dexamethasone IV 4 mg once daily. As we suspected viral meningitis, we started Acyclovir vial IV 750 mg three times daily for 14 days.

Follow up: Patient responded very well to the acyclovir, she became conscious again and oriented within two days and 14 days later, she was discharged from the hospital without any focal neurological deficit.

3. Discussion

The COVID-19 outbreak had a catastrophic impact on public health, social life, and global economy [12]. It is well-known for affecting the nervous system and causing polyneuropathy, encephalopathy, and aortic ischemic stroke [13]. It had and continues to have a significant influence on people's life, both individually and sociologically, resulting in psychological problems and changes in the health behavior [14]. The pandemic is evolving fast, requiring novel strategies to maintain clinical preventative services, including vaccination, in order to avoid overburdening health-care systems and their eventual collapse [14]. The development of a vaccine has been demonstrated to be the sole effective option in combating the pandemic. Vaccines protect against severe disease caused by SARS-COV-2 infection [14]. The production and administration of COVID-19 vaccinations aid in the prevention of the illness; however, it is unknown how long the immunity created by the vaccines lasts until additional time has passed after patients were initially vaccinated [15]. For the COVID-19 vaccines, four primary vaccination mechanisms have been investigated: DNA-based vaccines, mRNA-based vaccines, protein-based vaccines, and inactivated virus. Using viral vectors, DNA-based vaccinations deliver the DNA coding for the SARS-CoV-2 spike protein into the cells, prompting cells to make spike proteins. mRNA vaccines work in a similar way, introducing mRNA into cells via a lipid nanoparticles. Protein vaccines are based on the spike protein or portions of it. Finally, some vaccines use inactivated SARS-CoV-2 virus [16]. The objective of the vaccination is to generate antibodies that can neutralize infections or mark them for destruction by the immune system [17].

COVID-19 vaccines have been tested in large, randomized controlled trials. Across all demographics, the vaccinations have been demonstrated great effectiveness and safety. However, as with all other vaccinations, they can cause a variety of adverse effects. COVID-19 vaccinations may cause neurological adverse effects. However, their frequency, has not yet been thoroughly investigated [18]. The Pfizer-BioNTech mRNA COVID-19 vaccine has been proven to be 95% effective in preventing infection [19]. Concerns have been raised about the safety of vaccinations since they were first introduced. The most common side effects of COVID-19 vaccinations are local responses at the injection site, followed by non-specific systemic symptoms such as headache, tiredness, myalgia, and fever. These symptoms may appear shortly after immunization and disappear in a short period of time [12]. Severe neurological consequences such as cerebrovascular accident, Guillain-Barré syndrome (GBS), Bell's palsy, transverse myelitis, and acute disseminated encephalomyelitis were also reported [20]. As more patients obtain access to COVID-19 vaccinations, neurologists are now facing questions about potential neurological consequences [16].

There have been reports of neurological adverse events following vaccination, such as cerebral venous sinus thrombosis and demyelinating episodes [21]. Only isolated cases of neurological events were reported in the clinical trials of major SARS-CoV-2 vaccines [22]. Finsterer et al. reported several cases with neurological problems, and it seemed possible that the neurological problems were caused by a recent SARS-CoV-2 vaccine. Seven hours after the first dosage of an mRNA-based vaccine, an ischemic stroke occurred in an old aged woman, but it was unclear if there was a true causal relationship between the vaccine and the stroke. An ischemic cerebellar stroke occurred four days after the first dose of a vector-based SARS-CoV-2 vaccination in a 29-year-old woman. A relapsed GBS experienced in a 32-year-old man eight days after receiving the first dose of a vector-based SAR-S-CoV-2 vaccination [22]. At least 19 patients with SARS-CoV-2 vaccination associated GBS have been reported as per the end of June 2021 [23]. According to data from the mRNA vaccine clinical trials, 7 out of 37,000 vaccination recipients got Bell's palsy [22]. Repajic et al. report a case with three previous bouts of Bell's Palsy developed left sided Bell's Palsy less than 36 hours after receiving the second dose of the Pfizer-BioNTech COVID-19 Vaccine [24]. An independent panel of neurological specialists determined three reported cases of transverse myelitis in trials for AstraZeneca's ChAdOx1 nCoV-19 vaccine, with two confirmed unrelated and one considered a potential connection [25]. These consequences have resulted in the temporary suspension of both vaccination trials and roll-out programs in several countries. In the absence of convincing proof of causative associations between the vaccination and adverse events, or the rarity of the complications, programs have been resumed [26].

Although the Pfizer-BioNTech's vaccine safety reports showed no suspected cases of meningoencephalitis, Saito et al. reported the first case of aseptic meningitis after the first dose of intramuscular injection of the BNT162b2 mRNA COVID-19 vaccine [27]. Aseptic meningitis has been recorded following vaccines against mumps, measles, rubella, and influenza. However, the specific etiology of meningitis following immunization is unknown [27]. There is a possibility that the molecular mimicry triggered by the protein generated by immunization will develop autoimmune meningitis. The autoimmune reaction or S1 protein generated by the vaccine itself may cause a breach of the blood-brain barrier, resulting in aseptic meningitis [27]. The current study reports the first case of meningoencephalitis after 5 days of receiving the second dose of Pfizer-BioNTech COVID-19 vaccination. Meningitis and encephalitis are infections of the meninges and the brain, respectively, and are important causes of death and long-term neurological consequences, particularly in children in the developing countries. Because these diseases are difficult to detect clinically, they are frequently combined under the umbrella term acute meningoencephalitis [28]. There are four different types of meningoencephalitis, affecting the meninges, gray matter, white matter, or both in a localized or diffuse form [29]. The viral agents that cause meningitis and encephalitis differ considerably between countries, with herpes viruses being the most common cause in western countries and vector-borne infections being the most common in tropical developing countries [30]. The current case was put on acyclovir and responded well to the treatment and discharged from the hospital after 14 days.

In conclusion, Although extremely rare, aseptic maningoencephalitis

could occur after COVID-19 vaccination. The patient could be managed conservatively with a good outcome.

Ethical approval

Approval is not necessary for case report in our locality.

Source of funding

None is found.

Registration of Research Studies

According to the previous recommendation, registration is not required for case report.

Consent

Consent has been taken from the patient and the family of the patient

Author contribution

Shwan A. Ahmad: neurologist diagnosing the case, follow up the patient, and final approval of the manuscript. Bestoon Kh. Salih, Krokh H. Salih, Tomas M. Mikael, Fahmi H. Kakamad, Abdulwahid M. Salih: literature review, writing the manuscript, final approval of the manuscript.

Guarantor

Fahmi Hussein Kakamad is the Guarantor of submission.

Declaration of competing interest

None to be declared.

References

- F.H. Kakamad, S.O. Mahmood, H.M. Rahim, B.A. Abdulla, H.O. Abdullah, S. Othman, et al., Post covid-19 invasive pulmonary Aspergillosis: a case report, Int. J. Surg. Case Rep. 82 (2021) 105865.
- [2] H.M. Abdullah, H.H. Hama-Ali, S.N. Ahmed, K.M. Ali, K.A. Karadakhy, S. O. Mahmood, et al., Severe refractory COVID-19 patients responding to convalescent plasma; A case series, Ann. Med. Surg. 56 (1) (2020) 125–127.
- [3] S.A. Ahmad, K.H. Salih, S.F. Ahmed, F.H. Kakamad, A.M. Salh, M.N. Hassan, et al., Post COVID-19 transverse myelitis; a case report with review of literature, Ann. Med. Surg. (2021) 102749.
- [4] A. Baram, F.H. Kakamad, H.M. Abdullah, D.H. Mohammed-Saeed, D.A. Hussein, S. H. Mohammed, et al., Large vessel thrombosis in patient with COVID-19, a case series, Ann. Med. Surg. 60 (1) (2020) 526–530.
- [5] A.A. Amin, A.H. Awakhti, L.A. Hussein, F.H. Fattah, H.O. Baba, F.H. Kakamad, et al., Survived COVID-19 patient presented with death on arrival: a case report, Int. J. Surg. Case Rep. 81 (1) (2021) 1–3.
- [6] L. Dogan, D. Kaya, T. Sarikaya, R. Zengin, A. Dincer, I.O. Akinci, et al., Plasmapheresis treatment in COVID-19–related autoimmune meningoencephalitis: case series, Brain Behav. Immun. 87 (2020) 155–158.

- [7] L. Dogan, D. Kaya, T. Sarikaya, R. Zengin, A. Dincer, I.O. Akinci, et al., Plasmapheresis treatment in COVID-19–related autoimmune meningoencephalitis: case series, Brain Behav. Immun. 87 (2020) 155–158.
- [8] D. Leys, M. Edwards, K. Vonck, P. Taba, E. Moro, A. Chan, et al., SARS-COV2 Vaccine-related Neurological Complications Need Large Collaborative Studies, Not Single Case Reports or Small Descriptive Series, 2021, 00:1–1.
- [9] World Health Organization, Accessed on September 5, https://covid19.who.int/, 2021.
- [10] M. García-Grimshaw, L.E. Hernández-Vanegas, I. Núñez, N. Hernández-Valdivia, D. A. Carrillo-García, A. Michel-Chávez, et al., Neurologic adverse events among 704,003 first-dose recipients of the BNT162b2 mRNA COVID-19 vaccine in Mexico: a nationwide descriptive study, Clin. Immunol. (2021), 108786.
- [11] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, A. Thoma, et al., The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) guidelines, Int. J. Surg. 84 (2020) 226–230.
- [12] M. Sharifian-Dorche, M. Bahmanyar, A. Sharifian-Dorche, P. Mohammadi, M. Nomovi, A. Mowla, Vaccine-induced immune thrombotic thrombocytopenia and cerebral venous sinus thrombosis post COVID-19 vaccination; a systematic review, J. Neurol. Sci. (2021) 117607.
- [13] M. Al-Olama, A. Rashid, D. Garozzo, COVID-19-associated meningoencephalitis complicated with intracranial hemorrhage: a case report, Acta Neurochir. 162 (7) (2020) 1495–1499.
- [14] A.F. Hernández, D. Calina, K. Poulas, A.O. Docea, A.M. Tsatsakis, Safety of COVID-19 vaccines administered in the EU: should we be concerned? Toxicol. Rep. 8 (2021) 871–879.
- [15] M. Neagu, D. Calina, A.O. Docea, C. Constantin, T. Filippini, M. Vinceti, et al., Back to basics in COVID-19: antigens and antibodies—completing the puzzle, J. Cell Mol. Med. 25 (10) (2021) 4523–4533.
- [16] A.L. Goss, R.D. Samudralwar, R.R. Das, A. Nath, ANA investigates: neurological complications of COVID-19 vaccines, Ann. Neurol. 89 (5) (2021) 856.
- [17] L. Lu, W. Xiong, J. Mu, Q. Zhang, H. Zhang, L. Zou, et al., The potential neurological effect of the COVID-19 vaccines: a review, Acta Neurol. Scand. (2021).
- [18] A.S. Matarneh, A.H. Al-battah, K. Farooqui, M. Ghamoodi, M. Alhatou, COVID-19 vaccine causing Guillain-Barre syndrome, a rare potential side effect, Clin. Case Rep. 9 (9) (2021), e04756.
- [19] F.P. Polack, S.J. Thomas, N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, et al., Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine, N. Engl. J. Med. (2020).
- [20] E. Khan, A.K. Shrestha, M.A. Colantonio, R.N. Liberio, S. Sriwastava, Acute transverse myelitis following SARS-CoV-2 vaccination: a case report and review of literature, J. Neurol. (2021) 1–2.
- [21] M. Butler, A. Tamborska, G.K. Wood, M. Ellul, R.H. Thomas, I. Galea, et al., Considerations for causality assessment of neurological and neuropsychiatric complications of SARS-CoV-2 vaccines: from cerebral venous sinus thrombosis to functional neurological disorder, J. Neurol. Neurosurg. Psychiatr. (2021).
- [22] J. Finsterer, F.A. Scorza, SARS-CoV-2 vaccines are not free of neurological side effects, Acta Neurol. Scand. 144 (1) (2021) 109.
- [23] J. Finsterer, SARS-CoV-2 vaccinations are unsafe for those experiencing postvaccination Guillain-Barre syndrome, Ann. Med. Surg. (2021).
- [24] M. Repajic, X.L. Lai, P. Xu, A. Liu, Bell's Palsy after second dose of Pfizer COVID-19 vaccination in a patient with history of recurrent Bell's palsy, Brain, Behav. Immun. Health 13 (2021) 100217.
- [25] M. Voysey, S.A. Clemens, S.A. Madhi, L.Y. Weckx, P.M. Folegatti, P.K. Aley, et al., Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK, Lancet 397 (10269) (2021) 99–111.
- [26] E. Mahase, Covid-19: WHO says rollout of AstraZeneca vaccine should continue, as Europe divides over safety 372 (2021) 728.
- [27] K. Saito, T. Shimizu, K. Suzuki-Inoue, T. Ishida, Y. Wada, Aseptic meningitis after vaccination of the BNT162b2 mRNA COVID-19 vaccine, Neurol. Sci. (2021) 1–3.
- [28] P.F. Horwood, V. Duong, D. Laurent, C. Mey, H. Sothy, K. Santy, et al., Aetiology of acute meningoencephalitis in Cambodian children, Emerg. Microb. Infect. 6 (1) (2017) 1–8, 2010–2013.
- [29] I. Steiner, H. Budka, A. Chaudhuri, M. Koskiniemi, K. Sainio, O. Salonen, et al., Viral meningoencephalitis: a review of diagnostic methods and guidelines for management, Eur. J. Neurol. 17 (8) (2010), 999-e57.
- [30] R.J. Whitley, J.W. Gnann, Viral encephalitis: familiar infections and emerging pathogens, Lancet 359 (9305) (2002) 507–513.