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Vaccine 41 (2023) 1003–1008

Contents lists available at ScienceDirect

Vaccine

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

Short communication

CNS demyelinating disease following inactivated or viral vector SARS-CoV-2 vaccines: A case series

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ARTICLE INFO

Article history:
Received 17 June 2022
Received in revised form 28 August 2022
Accepted 3 January 2023
Available online 6 January 2023

Keywords:
COVID-19 vaccine
Vaccination
Demyelinating disease
Multiple sclerosis
Neuromyelitis Optica spectrum disorders
NMOSD

ABSTRACT

Background: Several reports have been documented in possible association with the administration of different severe acute respiratory coronavirus 2 (SARS-CoV-2) vaccines and central nervous system (CNS)demyelinating disorders, specifically post mRNA vaccines. We report twelve cases of developing Multiple sclerosis (MS) or Neuromyelitis Optica spectrum disorders (NMOSD) following neither the first nor second dose of inactivated or viral vector COVID-19 vaccine.

Methods: We retrospectively compiled twelve patients' medical information with a new onset of MS or NMOSD in their first six weeks following a COVID-19 vaccine.

Results: We report twelve cases of MS (n = 9), clinically isolated syndrome (CIS)(n = 1), and NMOSD (n = 2) following COVID-19 inactivated vaccines (n = 11) or viral vector vaccines (n = 1), within some days following either the first (n = 3), second dose (n = 8), or third dose (n = 1). Their median age was 33.3 years, ranging from 19 to 53 years. Ten were women (83 %). All patients fully (n = 5) or partially (n = 2) recovered after receiving 3 doses of Corticosteroids. Common medications were Natalizumab, Teriflunomide, Dimethyl fumarate, and Rituximab. Also, Interferon beta 1-a was administered to one patient with severe symptoms of numbness.

Conclusion: Our case series identifies the Sinopharm BBIBP-CorV and the AstraZeneca AZD1222 vaccines as potential triggers for CNS demyelinating diseases. Vaccine administration routines are not affected by these rare and coincidental events. However, these manifestations are not deniable and require serious attention. Further investigations are needed to clarify the actual mechanisms and real associations.

1. Introduction

The new coronavirus, known as severe acute respiratory coronavirus 2 (SARS-CoV-2), caused an epidemic that started in December 2019 in Wuhan, China [1]. Besides respiratory complications, this novel coronavirus has been found to cause neurological damage to the central nervous system, as well as the peripheral nervous system. Some of these neurological complications are headache, seizure, faintness, dizziness, ataxia, ischemic stroke, Guillain-Barré syndrome, encephalitis, and demyelinating diseases like Neuromyelitis Optica spectrum disorders (NMOSD) and multiple sclerosis(MS) [2–4]. It is clear that mass immunization with COVID-19 vaccines is the best way to combat this disease, and vaccines have proven to be highly effective and safe [5]. However, there is also some concern regarding safety and adverse effects, including post-vaccination neurological complications, which require immediate medical attention. Paresthesia, myalgia, headache, dizziness, Guillain-Barre syndrome, transverse myelitis, Bell's palsy, and MS are some of these neural manifestations [6]. There are some reports of post-COVID-19 vaccination demyelinating diseases, including MS and NMOSD [7–10]. In this report, we describe the clinical features of twelve patients who received COVID-19 inactivated vaccines (n = 11) or viral vector vaccines (n = 1) and, within some days following either the first (n = 3), second dose (n = 8), or third dose (n = 1), presented with new neurological manifestations consistent with a new-onset central nervous system (CNS) demyelination disorder (MS, n = 9, clinically isolated syndrome (CIS), n = 1, NMO, n = 2). All patients responded to corticosteroids and showed a range of partial to full recovery Table 1.

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https://doi.org/10.1016/j.vaccine.2023.01.003
0264-410X/

Table 1
Demographic characteristics and clinical findings of the cases.

Case number	Sex	Age	Comorbidities	Family history of autoimmune disease	Vaccine platform, name, dose	Immediate post-injection symptoms	Primary demyelinating symptoms	Days between vaccine and demyelinating symptoms	Diagnosis	Initial EDSS	Disease modifying therapy	Follow up Outcome
1	Male	24	Headache	No	Inactivated virus vaccines, BBIBP-CorV, 2nd	1st: Fatigue, weakness 2nd: local pain	Balance disturbance	14	MS	3	Natalizumab	5 months Stable
2	Female	46	OCD, IDA, Depression	No	Inactivated virus vaccines, BBIBP-CorV, 2nd	1st: Headache, Lethargy, Weakness, Fatigue 2nd: Headache, Lethargy, Weakness, Fatigue	Right hand paresthesia	3	MS	2.5	Teriflunomide	4 months Stable
3	Female	42	Hyperthyroidism, Hypertension, Asthma	No	Inactivated virus vaccines, BBIBP-CorV, 1st	1st: Lethargy, Fatigue, Numbness	Diplopia	20	MS	2.5	Teriflunomide	6 months Stable
4	Female	21	IDA	Yes Mother (MS) Cousin (MS)	Inactivated virus vaccines, BBIBP-CorV, 2nd	1st: Fever, Dizziness, Irregular menstruation 2nd: None	Left hand paresthesia	2	MS	2	Dimethyl fumarate	5 months Stable
5	Female	20	None	No	Inactivated virus vaccines, BBIBP-CorV, 2nd	1st: None 2nd: None	Left hand paresthesia	60	MS	NA	Dimethyl fumarate	1.5 months Stable
6	Female	23	None	Yes Sister (MS)	Inactivated virus vaccines, BBIBP-CorV, 1st	1st: None	Left hand paresthesia, Lhermitte sign	10	MS	2.5	Rituximab	2 months Stable
7	Female	19	IDA, Hypothyroidism, OCD	No	Inactivated virus vaccines, BBIBP-CorV, 2nd	1st: Fever, Myalgia, Fatigue 2nd: None	Right-sided facial paresthesia	10	MS	1.5	Teriflunomide	6 months Stable
8	Female	50	OCD	No	Adenovirus vaccine platform, AZD1222, 2nd	1st: None 2nd: None	left-sided numbness	11	MS	1.5	Teriflunomide	3 months Stable
9	Female	30	None	No	Inactivated virus vaccines, BBIBP-CorV, 3rd	1st: None 2nd: None 3rd: None	Numbness in left hand and foot	6	MS	2.5	Teriflunomide	3 months Stable
10	Female	40	IDA	Yes, Sister (NMOSD) Uncle (Lupus) Uncle (MS)	Inactivated virus vaccines, BBIBP-CorV, 2nd	1st: None 2nd: Myalgia	Paresthesia	1	NMOSD	3.5	Rituximab	4 months Stable
11	Female	32	None	No	Inactivated virus vaccines, BBIBP-CorV, 1st	1st: Injection site pain	Left-sided Paresthesia	3	CIS	2	Interferon beta-1a	4 months Stable
12	Male	53	None	No	Inactivated virus vaccines, BBIBP-CorV, 2nd	1st: None 2nd: None	Severe paresthesia in lower extremities	4	NMOSD	5.5	Rituximab	NA

NA: Not available, MS: Multiple sclerosis, CIS: Clinically isolated syndrome, NMOSD: Neuromyelitis Optica spectrum disorder, EDSS: Expanded disability status scale, OCD: Obsessive-Compulsive Disorder, IDA: Iron Deficiency Anemia.

2. Case presentation

2.1. Case 1

A 24-year-old male, who smoked one pack-year and a body mass index (BMI) of 26.73, had a history of headaches but no other disease. He got the first dosage of the Sinopharm Beijing Bio-Institute of BBIBP-CorV on October 1, 2021. After the initial dosage, fatigue and weakness persisted for two days. The second dosage was administered on October 30, 2021. The second dosage just caused injection pain that went away after 24 h. Fourteen days after getting the second dosage of the COVID-19 vaccination, he suffered a sudden onset of blackout and loss of balance, which caused him to fall and split his lips owing to the intensity of the impact. This prompted him to seek medical attention, and he was diagnosed with MS as a result. The patient's parents were not blood-related, and he had no family history of MS, NMO, or any other autoimmune illnesses. He only had surgery for a pilar cyst two years ago under local anesthesia. His initial expanded disability status scale (EDSS) was 3, and he was treated with three doses of Methylprednisolone (1000 mg in 1000 ml normal saline) with marked improvement in his primary symptoms. Then after, Natalizumab was started for him as the main MS treatment. At the moment, after five months, his imbalance is entirely resolved, and he has no difficulty doing his daily tasks.

2.2. Case 2

A 46-year-old female with a history of obsessive–compulsive disorder (OCD), iron deficiency anemia (IDA), depression, and BMI of 19.2, developed right-side numbness (started from her right-hand fingers) three days after receiving her second dose of Sinopharm COVID-19 vaccine. Her post-injection symptoms were such that after the first dose, she felt numbness in her hands, lethargy, weakness, and fatigue, so she needed to take an Acetaminophen pill once, but after the second dose, her symptoms of fatigue and headache were milder. About one year ago, she felt neck pain, headache, pain, and paresthesia in her dominant (right) hand (because of her job), which made her undergo physiotherapy due to osteoarthritis, and these symptoms completely disappeared. No family history of autoimmune disease was reported. She received three doses of Corticosteroids (methylprednisolone 1000 mg in 1000 ml normal saline), and her initial EDSS was 2.5. Her current medication is Teriflunomide (Tebazio®). Forty-two days after her diagnosis, numbness was resolved, but she experienced frequent urination and urinary incontinence one to three times a week. After a four-month follow-up, she said that her urinary dysfunctions were no longer an issue and that she was seldom bothered by them.

2.3. Case 3

A 42-year-old female with two children and two abortions developed diplopia, blurred vision, imbalance, and severe nausea 20 days after her first dose of Sinopharm COVID-19 vaccine, and was diagnosed with MS based on her Magnetic resonance imaging (MRI) and her initial symptoms. She has had a medical history of hyperthyroidism and hypertension for 20 years and her BMI is 24.09. The patient was diagnosed with mild asthma seven years ago, which was triggered by a detergent allergy and detergent gas poisoning. She doesn't smoke cigarettes but has smoked hookah twice in the last two years, re-taking asthma medications under a doctor's supervision. About two years ago, she experienced dizziness and a middle ear infection, was visited by an ear, nose and throat (ENT) specialist, and her symptoms resolved. Once in August 2020, she got infected with COVID-19 which was confirmed by a positive PCR test. Her COVID-19 symptoms were as follow: runny nose, fatigue, body aches, fever, chills, and slight dizziness, however, there was no lung infection. Her infection was self-limiting and after a few days, her symptoms improved. Her symptoms after receiving the first dose of the COVID-19 vaccine (October 2021) included lethargy, fatigue, numbness, and lower extremities weakness for a few days. She assumed them to be normal and took painkillers, which relieved her symptoms. However, twenty days after her injection, when symptoms such as diplopia, hazy vision, imbalance in movement, and extreme nausea persisted, she decided to visit a doctor; which resulted in the MS diagnosis for her. The patient had no family history of MS, NMO, or other autoimmune diseases, and her parents were not blood relatives. She received three doses of Corticosteroids (Methylprednisolone 1000 mg in 1000 ml normal saline); also, her initial EDSS was 2.5, and her current medication is Teriflunomide (Tebazio®). Her symptoms are now gone, and she has no difficulty doing her daily chores, and the most recent EDSS, 173 days after her diagnosis, reported 1.5 owing to a neurologist evaluation.

2.4. Case 4

A 21-year-old woman with a BMI of 23.51 presented with a new onset of numbness in her left-hand fingers, worsening dizziness, and headache two days after receiving her second dose of Sinopharm BBIBP-CorV. Eight days later, her condition worsened to complete numbness on her left side and severe dizziness and headaches. She was diagnosed with MS based on MRI and her condition. The patient was right-handed and had both her vaccines shot in her left arm. She had no symptoms after her second dose, but experienced fever, dizziness, and irregular menstruation after her first dose. She had a medical history of IDA, no other underlying disease, and no exposure to COVID-19 infection in the last 2 years. According to her family history, MS was diagnosed in her mother and cousin when they were 29 and 30, respectively. The patient received three doses of Corticosteroids (Methylprednisolone 1000 mg in 1000 ml normal saline), her initial EDSS was 2, and her current medication is Dimethyl fumarate (Diphosel®). As the last follow-up, 5 months after her diagnosis, all symptoms are disappeared, and she has no difficulty with her daily routines.

2.5. Case 5

A 20-year-old female without any prior medical history received her first dose of the Sinopharm BBIBP-CorV on September 7, 2021, and her second dose on October 10, 2021, both with no immediate adverse reactions. About two months after her second vaccine dose (early December), she developed constant numbness and tingling in three fingers of her right hand and three fingers of her left hand. Also, by bending her neck, she experienced vibration in her back. These symptoms persisted for 15 days until she visited a doctor and was diagnosed with MS. Her BMI was 23.44, and she once underwent hormone replacement therapy due to her high testosterone level one year ago. By the confirmation of the PCR test, the patient got infected by COVID-19 once in 2020, with the only symptom of anosmia. She had no family history of MS, NMO, or other autoimmune diseases, and her parents were not blood-relatives. She started to be treated with Dimethyl fumarate (Zadiva®) after receiving three doses of Corticosteroids (Methylprednisolone 1000 mg in 1000 ml normal saline). She feels no numbness in her fingers anymore, but as she bends her neck, she still feels some trembling in her back.

2.6. Case 6

A 23-year-old healthy female with a BMI of 20.42 noticed tingling in her left hand and developed the Lhermitte sign, which passed down her neck and radiated through her toes 7 to 10 days after her first dose of Sinopharm BBIBP-CorV. The patient showed no special symptoms following vaccination and took no special drugs but B-complex supplements. Her parents were not blood-relatives, but her family medical history showed her sister being diagnosed with MS at 21. Her sister takes Interferon beta-1b (Actoferon®) as her current medication. Following a doctor's visit, the initial EDSS of our case was 2.5, and she was treated with three doses of Corticosteroids (Methylprednisolone 1000 mg in 1000 ml normal saline) and her medication followed by ordering Rituximab (Zytux®). After these two months, She still feels a slight electric shock passing down her neck, but her numbness and tingling have gone away.

2.7. Case 7

A 19-year-old female suffering from iron deficiency anemia, hypothyroidism, and OCD, experienced an acute onset of right-sided facial numbness and tingling in her right-hand fingers, 10 days after receiving her second dose of Sinopharm BBIBP-CorV. Her initial dose (38 days prior to the onset of symptoms) was followed by some symptoms such as fever, body aches, lethargy, and fatigue, which resolved after 2 or 3 days, but after her second dose, she experienced no adverse reactions following the vaccination. The patient had her first vaccine shot in her left hand but the second dose was injected in her right hand.

As we mentioned about her OCD, it needs to note that in order to cope with the stress of the entrance exam, she underwent a psychiatrist's supervision to start taking Citalopram but stopped it a while later without consulting her doctor, which caused her dizziness and balance problems. Later on, she resumed the medication under the supervision of her psychiatrist, so her symptoms resolved. There were no family medical histories of MS or NMO in her family. Her initial EDSS was 1.5, and she was treated with three doses of Corticosteroids (Methylprednisolone 1000 mg in 1000 ml normal saline), and her current medication is Teriflunomide (Giomide®). At present, after 6 months, all her symptoms like numbness or tingling are resolved.

2.8. Case 8

A 50-year-old single woman with a BMI of 21.01 was diagnosed with MS due to her symptoms 11 days after receiving her second dose of the AstraZeneca(AZD1222 COVID-19 vaccine (which caused her no special symptoms). Her symptoms began with left-sided facial numbness, which led to the numbness of her left leg in less than 24 h, and numbness of the left half of her body after 48 h. She only had a medical history of mild OCD. After receiving three doses of Corticosteroids (Methylprednisolone 1000 mg in 1000 ml normal saline), her numbness disappeared and she started taking Teriflunomide (Giomide) as her medication. The patient showed an improvement in her EDSS score from 1.5 to 0.

2.9. Case 9

A 30-year-old healthy, married woman with a BMI of 25.34 presented with the symptoms of numbness in her left hand (the injection site) fingers, and in less than 3 days, this feeling of numbness spread all over her body, especially in her hands and legs. Her symptoms started only 6 days after receiving her third dose of the Sinopharm COVID-19 vaccine. Nevertheless, neither of her past two injections resulted in post-vaccination adverse effects. She consulted a doctor and was diagnosed with MS. The patient had no family history of MS or NMO. After receiving three doses of Corticosteroids (Methylprednisolone 1000 mg in 1000 ml normal saline) and two weeks of taking Teriflunomide (Giomide), she only feels a slight numbness in her fingertips, and her EDSS score improved from 2.5 to 0.5 after 3 months.

2.10. Case 10

A 40-year-old female with a medical history of IDA, and a BMI of 22.66, received her first Sinopharm COVID-19 vaccine dose with no post-vaccination adverse effects. In less than 24 h after her second vaccine dose, she developed lethargy and numbness in her left leg. Over the next 6 h, her right leg started to show the same symptoms, and these feelings of numbness, stinging, and paresthesia moved up from her legs closer to her chest. These feelings persisted for about 48 h after the vaccine injection. Her symptoms progressed to vertigo and numbness in her abdomen and lower back simultaneously. No optic neuritis or upper limb numbness was reported, and there was no history of numbness or relapse in her medical records and history. Yet, her sister was diagnosed with NMO at 27, and one of her uncles was suffering from MS and lupus. Ultimately, 3 days following the vaccine injection, she was given a definitive diagnosis of definite seropositive NMOSD. Currently, after receiving 3 doses of Corticosteroids (Methylprednisolone 1000 mg in 1000 ml normal saline) and 2 doses of Rituximab (Zytux®), her symptoms of numbness have completely disappeared. Her EDSS has decreased from 3.5 to 2 since her last examination four months following her diagnosis.

2.11. Case 11

A 32-year-old healthy woman with 2 children, 2 abortions, and a BMI of 20.76 complained of a slight feeling of paresthesia in her left hand (injection site) 3 or 4 days after receiving her first dose of the Sinopharm COVID-19 vaccine. In less than 24 h her condition worsened so that she suffered from severe facial numbness and her entire left side started to become numb. She had these symptoms for about 3 days until she visited a doctor and got a diagnosis of the CIS. The patient had never had the feeling of numbness or tingling before. She had no family history of MS, NMOSD, or any other autoimmune diseases, and her parents were not blood-relatives. About a year ago, she got infected with the coronavirus, with the symptoms of severe body ache, fever, and rhinorrhea, which lasted only for 3 days, but she isolated herself for 14 days. Her initial EDSS was 2 and now after receiving 3 doses of Corticosteroids (Methylprednisolone 1000 mg in 1000 ml normal saline) and having one dose of Interferon beta-1a (Cinnovex®), it has improved to 0 for her EDSS.

2.12. Case 12

A 53-year-old healthy man, non-smoker, and without any previous medical history received his first BBIBP-CorV Sinopharm COVID-19 vaccine shot with no adverse reactions (not even arm pain). His BMI was 27.68 and he had no family history of MS, NMO, or other autoimmune diseases. According to the BBIBP-CorV injection protocol, the second dose was given one month following the first, and there were no adverse reactions on the first day. Four days after receiving his second dose, he experienced a severe general numbness in his lower extremities up his pelvis. This numbness was so severe that he was unable to sit, stand, or move. After several times of visiting orthopedists, he was finally diagnosed with definite seropositive NMOSD two weeks following his second vaccine shot. The patient received 5 doses of Corticos-

teroids (Methylprednisolone 1000 mg in 1000 ml normal saline), and at his last visit, his EDSS was 5.5 before taking rituximab.

3. Discussion

CNS demyelinating disorders are some conditions resulting in damage to the myelin sheath of the nerves in the brain, spinal cord, and optic nerves. These disorders represent a wide range of conditions varying in their clinical features and pathophysiology. Some of these disorders have significant overlap, which can result in misdiagnosis or uncertainty in diagnosis [11]. Demyelinating diseases of CNS like MS and NMOSD are caused by idiopathic inflammation of the CNS, which results in the selective degeneration of the myelin sheaths [12]. Gene-environment interactions play a role in both MS and NMOSD. Familial cases of MS make up 13 % of all cases and have so far identified more than 200 genes involved in MS pathogenesis, each of which has a small effect on the incidence of the disease, but together, they determine genetic susceptibility in individuals [13]. In addition, in terms of NMOSD prevalence, familial cases account for 3 %, which is considered a high frequency due to its rarity [14]. Also, autoimmunity plays an important role in their pathogenesis. (NMOSD as an anti-AQP4 (aquaporin 4) autoantibodies-mediated disease [15] and MS as a T lymphocyte (T-helper 1 and T-helper 17) cell-mediated autoimmune disorder [16].) Besides all these, infections can have a significant role in MS and NMOSD pathophysiology.

Possible mechanisms include altering the blood–brain barrier or BBB's permeability, causing antibodies to pass through, and molecular mimicry [17,18]. Epstein-Barr virus (EBV) and cytomegalovirus (CMV) are considered to trigger MS and NMOSD [19] . Also, cases of post-herpes simplex virus (HSV) and post-varicella-zoster virus (VZV) NMOSD have been reported [17]. Several inflammatory demyelinating disorders related to SARS-CoV-2 have been documented, including Guillain-Barré syndrome [20], MS [21], and NMOSD [22].

Vaccines are crucial for preventing a variety of infections; Studies showed by not getting vaccinated, people get at higher risk for contracting viral infections, which leads to worsening demyelinating diseases like MS and NMOSD [23,24]. Nevertheless, there have been several reports of CNS demyelinating conditions connected to immunization with different types of vaccines, e.g., influenza (most cases), hepatitis A and B, human papillomavirus or Human Papillomavirus (HPV), yellow fever, rabies, anthrax, tetanus, meningococcus, rubella, measles [25] and most recently COVID-19 [26]. This will require serious attention and evaluation.

Our understanding of the link between vaccination and demyelinating and autoimmune diseases is incomplete. However, it can be said that vaccines generally can trigger inflammatory or autoimmune conditions, by eliciting autoantibodies or by destroying the body's self-tolerance [27,28]. One of the main immunopathological mechanisms involved in post-vaccination CNS demyelination is the molecular similarity between virus proteins used in vaccines and self-antigens like myelin components [29]. The antibodies against SARS-CoV-2 cross-react with 21 human tissue antigens, triggering autoimmunity against connective tissues, cardiovascular, gastrointestinal, and nervous system, in those who contracted the COVID-19 virus or got SARS-CoV-2 vaccines [30]. Also, 22 proteins share common peptides in the nucleus ambigous, dorsal motor nucleus, jugular ganglion, nodose ganglion, and SARS-CoV-2, which are responsible for CNS complications [31].

Moreover, vaccines triggering a series of immune responses may cause overactivation of innate and acquired immunity specifically T lymphocytes that target self-antigens of myelin sheet [32].

Yehuda Shoenfeld coined the term ASIA syndrome as autoimmune syndromes in association with adjuvants, which shows adjuvants that are used in vaccines for enhancing the antigen-specific immune responses [33], can cause autoimmunity [29]. Sinopharm vaccine contains aluminum salt as an adjuvant, as do Pfizer and Moderna mRNA vaccines against COVID-19, which contain lipid or polymer-based nanoparticle adjuvants [34]. Furthermore, adjuvants shield antigens physically, allowing the immune system to be exposed to those antigens for a longer period of time and allowing for a more robust immune response of both B-cells and T-cells involving autoreactive lymphocytes; in our case, myelin-specific [25].

We have added to other recently published papers on MS and NMOSD after COVID-19 mRNA [8,9,26] and viral vector vaccines [35,36]. The mRNA vaccines work by exposing dendritic cells to this exogenous mRNA, thereby stimulating the growth of T and B cells [37]. So that in those cases reported, we see both old and new lesions meaning that this excessive immune response may contribute to the unmasking of these diseases following vaccination in those who already have a weakened immune system.

About AstraZeneca vaccine as a viral vector vaccine, causing autoimmunity, two hypotheses can be considered. First, this vaccine contains an oil-in-water emulsion called MF59® as its adjuvant, known for inducing inflammation through the release of cytokines e.g., IL-6 and IL-8 [38]. IL-6 malfunctions the T regulatory lymphocytes, and our lymphocytes are commonly controlled by peripheral tolerance mechanisms, which are mostly regulated by a Treg cell (CD4 + Foxp3 +) [39]. Hence, Treg suppression can lead to immune-mediated diseases like NMOSD and MS. Second, AstraZeneca contains only the spike protein, not a full virus particle. The SARS-CoV-2 spike can pass through the BBB and get to the brain parenchyma through Angiotensin-converting enzyme 2 (ACE-2) interaction or the olfactory bulb. This can somehow justify the neurodegenerative complications of COVID-19 vaccines [36].

Moreover, Chen et al, reported a middle-aged female patient developing NMOSD 3 days following the first dose of her Sinopharm vaccine (inactivated virus) with the signs and symptoms of unsteady gait and dizziness, treated with 500 mg intravenous Methylprednisolone (IVMP) for five days and a complete improvement. The authors denied molecular mimicry and hypothesized that the vaccine, in conjunction with a preexisting systemic immune response, overactivated the immune system, enhanced the production of AQP4-IgG antibodies, and caused NMOSD [40].

Here, we report twelve cases of CNS demyelinating disease (MS and NMOSD) following either inactivated COVID-19 vaccine (Wuhan Sinopharm n = 11) or viral vector COVID-19 vaccine (AstraZeneca n = 1). There were new neurologic complications in all patients, occurring less than a day to 40 days (mean 13 days) after injection, related to brain or spinal cord involvement, mostly including dizziness, imbalance, limb or face numbness, and limb weakness. Four patients had at least 1–3 previously diagnosed demyelinating or autoimmune diseases in their family (MS (n = 5), NMO (n = 1), lupus (n = 1)). The definitive diagnosis of these patients was new-onset MS (n = 10), or new-onset NMOSD (n = 2). We should note that the vaccination may have been the cause of the disease directly, especially in those with no related medical history, but it may have been an exacerbation of a latent clinical condition, in individuals with a familial background or a relevant medical history. Depression, anxiety, hypertension, hypercholesterolemia, and chronic lung disease are respectively the most predominant comorbidities related to MS [41]. In our report, relevant comorbidities were a woman with depression, a woman with hypertension and mild asthma, and a teenage girl who had suffered from anxiety. Neither do we calculate or prove that SARS-CoV-2 inactivated or viral vector vaccines cause CNS demyelinating or autoimmune disease. Overall, there is a relatively low risk of devel-

oping demyelinating disease after vaccination [25], and more studies or randomized controlled trials are required to determine if COVID-19 vaccines actually cause acute CNS demyelination.

4. Conclusion

Our case series identifies the Sinopharm BBIBP-CorV and the AstraZeneca AZD1222 vaccines as potential triggers for CNS demyelinating diseases. Vaccine administration routines are not affected by these rare and coincidental events. However, these manifestations are not deniable and require serious attention. Further investigations are needed to clarify the actual mechanisms and real associations.

5. Ethical considerations

Written informed consent was obtained from all participating patients.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability

No data was used for the research described in the article.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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