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Autoimmune/Inflammatory syndrome induced by adjuvants (ASIA): Neuromyelitis optica spectrum disorder after BBIBP-Cor-V vaccine, case report

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ABSTRACT

Background: Recently the term Autoimmune/Inflammatory Syndrome induced by Adjuvants has been proposed to describe different clinical conditions, among them post-vaccinal phenomena like demyelinating diseases.
Objective: We aim to add knowledge on the possible association of vaccines and the development of demyelinating diseases.
Case report: We present the case of a 38-year-old female that developed a brainstem syndrome after vaccination with COVID-19 BBIBP-CorV Sinopharm Vaccine. The final diagnosis after extensive work-out was Neuromyelitis Optica spectrum disorder with positive Aquaporin 4 positive antibodies; and long-term treatment with Rituximab was initiated.
Conclusion: Since we are facing a large-scale vaccination, professionals should be aware of the presence of demyelinating diseases as adverse events for COVID-19 vaccine.

Introduction

Autoimmune/Inflammatory Syndrome induced by Adjuvants (ASIA syndrome) establishes a temporal relationship between vaccine adjuvants and different autoimmune diseases, that included central nervous system (CNS) demyelinating diseases. (Guimarães et al., 2015 Oct) Since the development of severe acute respiratory syndrome-related to COVID-19 infection (SARS-CorV) in late December 2019, 5'592,266 deaths have been reported. (WHO Coronavirus 2022) The strongest strategy to end to this pandemic is vaccination, therefore COVID-19 vaccines have been rapidly developed through unprecedented efforts. (Reichard et al., 2020 Jul, Watad et al., 2021 Apr 29) Hence, there is much concern about the efficacy and safety of the vaccines being developed. (Vishnevetsky et al., 2021 Apr) This report aims to add knowledge on the development of NMOSD after the COVID-19 BBIBP-CorV Sinopharm vaccine. Written informed consent was obtained from the patient.

Case report

A 38-year-old female with history of SARS-CorV infection eight months before. After receiving the first dose of BBIBP-CorV vaccine, she developed persistent headache, and numbness in the left upper extremity that spontaneously resolved within hours; probably an immunization stress-related response. Two weeks later she started with unbalance and instability, left lateralization upon gait, and difficulty urinating. The next day, she developed vertigo, tinnitus, left hemiparesis and vomiting, therefore she was admitted in our institution. On examination, she was alert, oriented, left hemi hypoesthesia, left hemiparesis (4/5 MRC), and generalized hyperreflexia. After two days, diplopia, dysphagia and urinary retention was developed. On examination, a right VI nerve palsy, left dysmetria, ataxia and left hemiparesis (3/5 MRC) was observed.

Routine blood count, biochemistry and metabolic test were between normal ranges. A vitamin D deficiency was observed (12.46 ng/ml,

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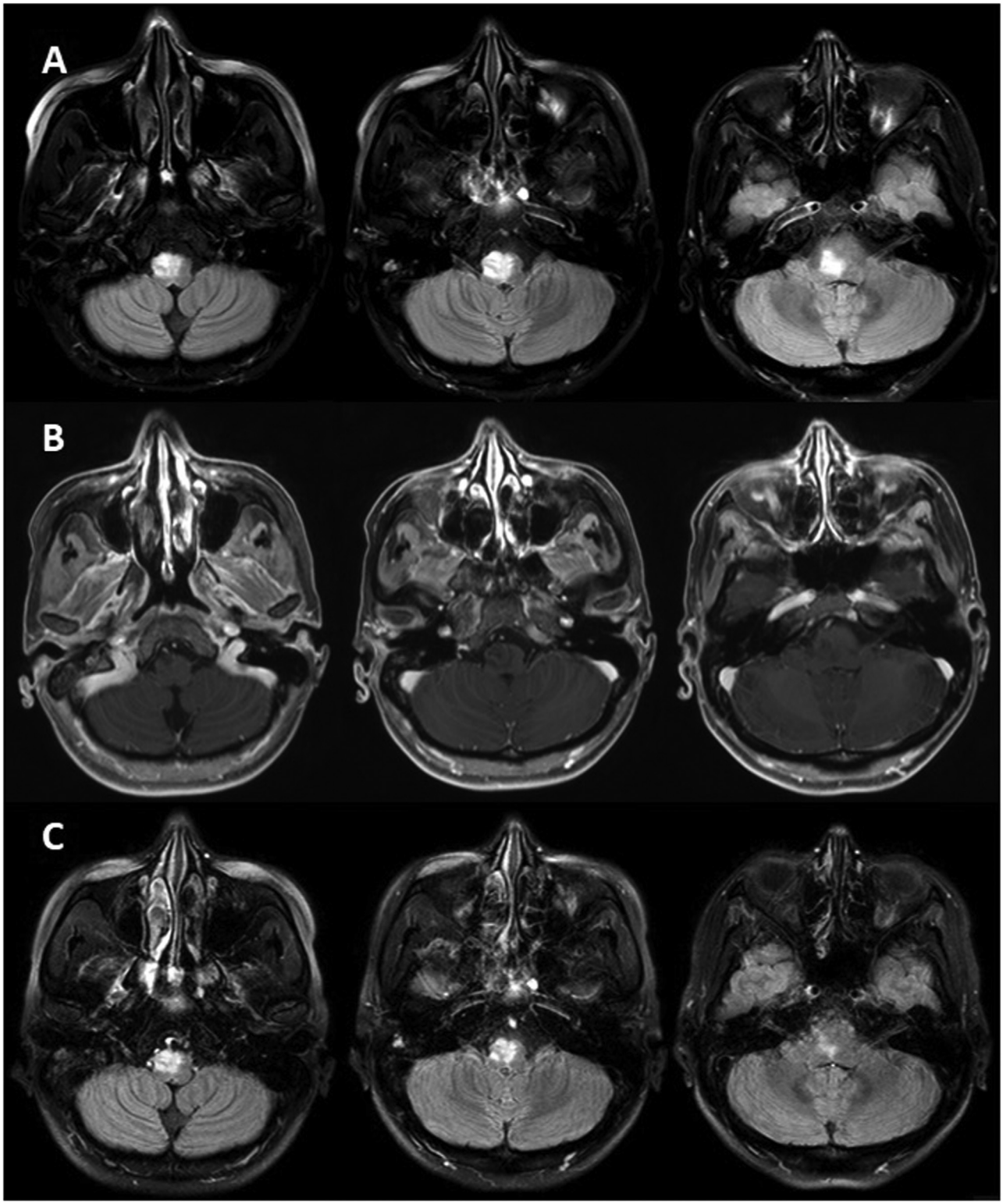

Fig. 1. Brain MRI of the patient. A. Fluid attenuated inversion recovery (FLAIR) sequence showing a demyelinating lesion in the brainstem. B. T1 post-contrast sequence showing gadolinium enhancement. C. Follow-up brain MRI after methylprednisolone.

normal range >30 ng/ml). COVID-19 PCR and serology was negative. CSF investigation showed 64 mononuclear cells, elevated protein level (0.77 g/L) and normal glucose level. Brain MRI showed a hyperintense T2 and fluid-attenuated inversion recovery (FLAIR) lesion in the medulla oblongata with faint gadolinium enhancement (Fig. 1). We propose an inflammatory etiology and run a panel of neuronal surface, AQP4 and myelin oligodendrocyte glycoprotein (MOG) antibodies.

We initiated two courses of methylprednisolone 1g/day for 5 consecutive days with three days apart. After the second course there were almost full resolution of symptoms. AQP4 antibodies were positive and long-term Rituximab treatment was initiated.

Discussion

We present the case of a young woman that developed a brainstem demyelinating event with AQP4 positive antibodies two weeks after receiving the COVID-19 vaccine. Our patient fulfilled the NMOSD diagnostic criteria (Wingerchuk et al., 2015 Jul 14), since she has one core clinical characteristic, acute brainstem syndrome, and AQP4 positive antibodies. Besides, she also fulfilled ASIA criteria (Perricone et al., 2013 Dec), with two major criteria: 1) previous exposure to an external stimulus, BBIBP-CorV vaccine; and 2) typical neurological manifestation, acute demyelinating brainstem syndrome; and one minor criteria: 1) evolvement of an autoimmune disease, NMOSD AQP4 positive.

There have been reported only seldom NMOSD cases after vaccination, especially presenting as a brainstem syndrome. Secondly, ASIA case reports associated with COVID-19 vaccines are scarce. Our case is the first report in the literature with the association between NMOSD and a BBIBP-CorV vaccine. There are also reports in the literature that demonstrate the association between viral vector and inactivated vaccines and the development of NMOSD. (Anamnart et al., 2022, Chen et al., 2021)

Vaccines can trigger autoimmune diseases by different mechanisms, one of them being adjuvants. Aluminum salts are adjuvants present in human vaccines, such as BBIBP-CorV, which contain aluminum hydroxide. (Xia et al., 2021) Aluminum can cause immune-mediated diseases by boosting the activation of receptors of pathogen-associated molecular patterns in the innate immune system, enhancing immune activity. (Perricone et al., 2013, Toussirot & Bereau, 2015) Producing different adverse neurologic and neuropsychiatric symptoms since aluminum particles can cross the blood-brain barrier and initiate an inflammatory response in neural tissues. (Guimarães et al., 2015)

By the way, the time intervals between vaccination and CNS demyelinating event can range from 5 to 28 days. (Principi & Esposito, 2020) It has been reported that the time interval between COVID-19 vaccine and immune-mediated disease flares or new-onset disease was 4 days (range 1 to 25 days) after the first dose; and 4 days (range 1 to 7 days) after the second dose of the vaccine. Most of the cases (77.8%) ocurred after the first dose of the vaccine. (Watad et al., 2021) In our case, symptom onset is between those ranges, and the symptoms developed after the first dose of the vaccine.

It has been reported the development of autoimmune neurological disorders after BNT162b2 vaccine. Watad A. et al. (Watad et al., 2021), reported 4 autoimmune neurological disorders, two Myasthenia Gravis cases, one case of Multiple Sclerosis, one case of Neurosarcoidosis and small fiber neuropathy. Nevertheless, our case is the first description of CNS autoimmunity related to the BBIBP-CorV vaccine to our knowledge.

The recognition of ASIA syndrome represents an important step toward a better comprehension of adjuvants as triggers of autoimmune diseases and in understanding adverse reactions after vaccination. (Pellegrino et al., 2015) Giving the massive vaccination against COVID-19 globally, it's very important to raise awareness upon the development of demyelinating diseases. Our case contributes to future research on COVID-19 vaccine safety, and the association between vaccine, adjuvants, and autoimmunity.

Conclusion

We present here the first case of CNS autoimmunity after the BBIBP-CorV Sinopharm vaccine. Since we are facing a large-scale vaccination, professionals should be aware of the presence of demyelinating diseases as adverse events for COVID-19 vaccine. Even though its occurrence is low, the association doesn't imply causality.

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Declaration of Competing Interest

The authors declare no conflicts of interest.

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