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.

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Received 7 May 2021
Accepted 20 July 2021
Available online 9 August 2021

https://doi.org/10.1016/j.neurol.2021.07.013

Steroid-responsive aseptic meningitis after BNT162b2 SARS-CoV-2 vaccine

Dear editor,

Aseptic meningitis (AM) is an inflammatory disorder of the meninges that can be of iatrogenic origin. Non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics or intravenous immunoglobulin (IVIg) can cause AM [1]. There is also an associated risk with certain attenuated virus vaccines, including polio, measles-mumps-rubella, and yellow fever [2]. New nucleoside-modifier messenger RNA (mRNA) vaccines against SARS-CoV-2 were recently introduced. Their safety profile is not fully understood.

A 62-year-old woman presented to the emergency department with fatigue, difficulties concentrating, dizziness, myalgia, unstable gait, and mild headache, all worsened in orthostatism. She had no fever or systemic complaints. Symptoms started the day after the first SARS-CoV-2 vaccine [BNT162b2-Pfizer®] and progressed for two weeks (she was medicated with paracetamol but not NSAIDs for her symptoms). There was no evidence of prior COVID-19 infection. Her medical history included long-term controlled dyslipidemia and anxiety. She had the vaccination schedule completed without vaccine-related adverse events. Neurological examination was unremarkable, including for higher nervous functions and meningeal irritation. Active standing revealed symptomatic postural tachycardia (supine 59 bpm, 3-minute-standing 93 bpm, 10-minute-standing 88 bpm) without blood pressure changes.

Blood analysis revealed mild lymphopenia, and cerebrospinal fluid (CSF) showed lymphocytic pleocytosis with high protein count and normal glucose (Table 1). Systemic (Sjögren's syndrome, systemic erythematous lupus, Beçhet's disease, sarcoidosis) and neurological inflammatory disorders, antineuronal disease, autoimmune encephalitis, human

Table 1 – Blood (B) and cerebrospinal fluid (CSF) results.

Laboratory tests (reference values)	Results (first LP)	Results (second LP)	Results (third LP)
Lymphocytes (B, 1.10–4.40 G/L)	1.05	0.96	1.02
Leukocytes (< 3/mm^3)	101	301	145
Erythrocytes (< 3 mg/dL)	856	75	24.000
Proteins (15–40 mg/dL)	154	208	128
Glucose (40–70 mg/dL)	54	61	53
Pressure opening	–	8 cm H_2O	–
PCR virus (CSF)	Negative		Negative
CSF immunophenotyping	–	100% lymphocytes with normal phenotype, 73% T-lymphocytes: 52% CD4 (37% activated) and 44% CD8 (39% activated)	–

Lumbar punctures (LPs) were performed 16 days (1st), 25 days (2nd) and 36 days (3rd) after vaccine. 1st and 3rd LP were traumatic. The 3rd LP was performed 10 days after dexamethasone onset. CSF clearance was observed in all samples after centrifugation.

immunodeficiency virus, other neurotropic viruses, mycobacteria, and fungal infection were excluded. Bacterial cultures on CSF were negative. Serum SARS-CoV-2 antibody titers were 1357.5 U/mL (25 days after vaccination, vaccine reactivity reference > 50 U/mL). SARS-CoV-2 was not detected in the CSF. Electroencephalography and brain magnetic resonance imaging were unremarkable. The patient started intravenous dexamethasone 5 mg every 8 hours with complete clinical improvement the following day. Lymphocyte and protein count in CSF decreased (Table 1). There was no clinical relapse after suspension of corticosteroid therapy, and the patient remained asymptomatic after three months. She decided not to take the second dose of the SARS-CoV-2 vaccine.

Immune-mediated mechanisms are a possible cause of AM after vaccination, and, in our case, some points support this association. First, the temporal profile and the combined presentation with postural orthostatic tachycardia. This latter is another vaccine-induced immune syndrome that has already been reported after mRNA vaccines [3,4]. Also, low blood lymphocyte count and CSF pure lymphocytic pleocytosis can be related to the immunogenic pathophysiology. Transient mild lymphopenia after BNT162 has been described [5]. This process is attributed to a redistribution of lymphocytes to lymphoid tissues after innate immune system stimulation. In the present case, blood lymphopenia persisted for several weeks following the vaccine, and we hypothesized that an abnormal shift of lymphocytes to the subarachnoid space occurred.

In terms of primary etiology for the AM, vaccine adjuvants, which have been recently implied in an autoimmune/inflammatory syndrome (ASIA), are a plausible explanation [6]. The BNT162b2 vaccine's adjuvant is a nanoparticle-based polyethylene glycol (PEG) stabilizer that has been implied as a trigger of ASIA syndrome in other organs [7]. AM is well-established as a non-specific reaction to certain drugs (e.g. NSAIDs, IVIg) and, along with ASIA, is frequently associated with systemic immune disorders [6,8]. However, a recent case of AM after the COVID-19 mRNA vaccine did not find serum anti-PEG antibodies, making this relationship merely elusive [9]. The link between vaccination and remote adverse events is challenging to prove and, in most cases, remains not definitive.

Funding

This work did not receive any additional funding.

Disclosure of interest

The authors declare that they have no competing interest.

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Received 7 October 2021
Accepted 14 October 2021
Available online 4 November 2021

https://doi.org/10.1016/j.neurol.2021.10.002