Neurological Sciences (2023) 44:1155–1157
https://doi.org/10.1007/s10072-022-06556-0

COVID-19

Bilateral anterior ischemic optic neuropathy after COVID-vaccination

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Received: 10 September 2022 / Accepted: 7 December 2022 / Published online: 9 January 2023

Abbreviations

MRI	Magnetic resonance imaging
CSF	Cerebrospinal fluid
AQP4-Ab	Antibodies to aquaporin-4
MOG	Myelin oligodendrocyte glycoprotein
VEPs	Visual evoked potentials
RRMS	Relapsing-remitting multiple sclerosis
NMOSD	Neuromyelitis optica spectrum disorder
MS	Multiple sclerosis
IV	Intravenous

Dear Editor,

Large-scale immunization due to Coronavirus disease 2019 (Covid-19) has made it possible to highlight several adverse reactions due to the interaction of the immunogenic particles with the human immune system.

The BNT162b2 vaccine (BioNTech/Pfizer), a modified RNA encoding the SARS-CoV-2 spike protein vehiculated by a lipid nucleoside, received marketing authorization given its positive benefit-risk ratio against Covid-19. Since its approval, tens of millions of subjects have been inoculated with the vaccine, side effects of which have been reported particularly in older adults and included fever, muscle and joint pain, fatigue, headache, vomiting, diarrhea, and long-lasting central nervous system effects, similar to those recently recognized as part of the LONG-COVID syndrome [1–3].

Here, we describe the case of an 85-year-old male patient, who developed acute bilateral optic neuropathy 2 weeks after the administration of the BNT162b2 vaccine.

The gentleman came to the out-patient clinic 10 days after receiving the first dose of the vaccine, complaining of bilateral complete loss of vision from the previous 24 h, that firstly involved his right eye and progressively spread to the contralateral eye within the following 2 days. Although he did not complain of ocular pain, he was unable to distinguish colors and shapes. No other relevant ocular symptoms were reported. His past medical history included mild diabetes with obesity, blood hypertension, and hypothyroidism for which he reported regular use of Repaglinide and Metformine, Olmesartan, and Levotiroxine. Before vaccination, this patient was fully independent in basic life activities and regularly practiced physical activity.

The remaining objective neurological assessment was unremarkable for systemic signs. The results of routine laboratory and autoantibody testing for the autoimmune disease were all normal. He underwent an MRI examination of the brain and whole spine, which showed several areas of gliosis without enhancement of the optic nerve on fat-suppressed T1-weighted MRI after intravenous gadolinium, devoid of signal intensity alteration at the diffusion-weighted imaging sequence that could point towards recent embolization and/or focal ischemia at the cerebral parenchyma level. Transthoracic echocardiography did not reveal signs of pathology at the cardiac level. The transcranial doppler with bubble study noticed only 7 microembolic signals under Valsalva's maneuver that did not justify the vision problems. Lumbar puncture demonstrated normal results in cerebrospinal fluids (CSF) analysis. Serum Aquaporin-4 (AQP4)-IgG and myelin oligodendrocyte glycoprotein (MOG)-IgG were negative.

To rule out diabetic retinopathy, he performed an ophthalmological evaluation: the funduscopic examination revealed diffused bilateral disc edema and optic nerve swelling, ocular/retinal computed tomography and electroretinogram resulted normal. The ophthalmic examination was integrated with the visual evoked potentials recording (VEP) that showed a N75-P100 amplitude decrease and a P100 latency great increase (Table 1).

The patient first practiced oral steroid therapy and then 5 days of IV Methylprednisolone sodium succinate at 1 g/day dose. After that, the patient experienced only little benefit in the following 3 days, mostly represented by slowly gradual

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Table 1 Summary scheme of the medical examinations performed by the patient

	Right eye	Left eye	Interpretation
Optical coherence tomography	Infra-red (IR) 30° (8.7 mm) ART 70) Q: 41 HS	IR 30° 30° (8.9 mm) ART (70) Q: 41 HS	Normal
Eye tonometry	14 mmHg	14 mmHg	Normal
Funduscopy	No signs of diabetic retinopathy. Pale optic disk with edema	No signs of diabetic retinopathy. Pale optic disk with vasal schlerosis	Optic neuropathy
Visual evoked potentials p100	144.5 ms	144.0 ms	Delayed latencies
Visual evoked potentials n75—p100 amplitude	2.2 µV	2.4 µV	Reduced amplitude
Flicker electroretinography 10 Hz	38.6 µV	42.7 µV	Normal
Flicker electroretinograpfy 20 Hz	36.8 µV	42.8 µV	Normal
Flicker electroretinograpfy 30 Hz	53.1 µV	48.1 µV	Normal
Brain magnetic resonance imaging: Isolated gliosis without enhancement of the optic nerve involvement after fat-suppressed T1-weighted MRI and infusion of intravenous gadolinium; Diffusion-Weighted Imaging sequence was negative			
Liquor AQP4-IgG and MOG-IgG: Not detected			
CSF analysis: Protein 30 mg/dl; glucose 68 mmol/L; 0 cells; oligoclonal IgG bands absent			

improvement of vision that remained otherwise limited to the partial perception of light and dark, while no shape and contrast difference or other improvements functionally useful for everyday life were noticed. Both the patient and his family rejected the second dose of the vaccine.

While mechanisms of these acute symptoms still remain unclear, this patient had several predisposing factors for vision impairment such as age, polypharmacy, and diabetes, and we consider that this vaccine-induced side effect could be ascribed to an ischemic optic neuropathy.

Non-arteritic anterior ischemic optic neuropathy results from ischemic damage to the anterior portion of the optic nerve due to small vessel circulatory insufficiency, but the mechanism of ischemia remains uncertain. It is usually characterized by acute unilateral visual loss, without pain in eye movements and optic disc swelling.

To our knowledge, 3 other cases of vaccine-associated bilateral optic neuropathies have been reported thus far. Helmchen and coll. [4] described the case of a 40-year-old female with a 21-year history of RRMS who developed binocular blindness 48 h after a vector-based vaccination against SARS-CoV-2 (AstraZeneca) and, after 2 weeks, she developed longitudinal extensive transverse myelitis compatible with NMOSD. In this case, Authors considered the vaccine as a trigger of the severe relapse of multiple sclerosis.

Arnao et al. [5] described a middle-aged healthy female who developed bilateral decreased vision and painful eye movements 2 weeks after receiving the first dose of inactivated virus vaccine (Oxford/AstraZeneca ChAdOx1). In this case, brain and spinal MRI showed an increased signal of the left optic nerve while the right one was normal. As in our case, no lab abnormalities, including antibodies panel, were detected and symptoms greatly improved after treatment with intravenous Methylprednisolone (1 g once daily for 5 days).

Sawala et al. [6] reported a bilateral neuritis in a 44-year-old man who had developed the symptom about 10 days after taking vaccines. In this case, the visual disturbance was associated with increased production of anti-MOG antibodies.

Several other cases of optic neuritis have been reported after taking various types of vaccines for COVID [7] but in such cases, an autoimmune mechanism was more clearly ruled out.

Compared to the above-mentioned reports of bilateral neuritis, in our case, no association with any autoimmune disease was found, neither the neuro-imaging nor the laboratory examinations were able to identify signs of possible optic neuro-myelitis. In addition, a poor response to corticosteroid therapy seemed to reinforce the extraneousness of dysimmune etiology. At present, we were unable to identify any particular predisposing condition or risk factors and the adverse event appears to be casual.

Massive COVID-19 vaccination is among the widest and fastest campaigns in medical history, extraordinarily succeeding in reducing mortality due to severe SARS-COV-2. Complications from COVID-19 vaccines are rare, and many aspects of adverse effects still remain obscure for the medical community, and it is highly important to promptly reported them. Defining a possible association between the administration of the first dose of BNT162b2 and the acute blindness is challenging, but it is important for physicians to consider acute ischemic optic neuropathy among possible COVID-19 vaccine-related side effects.

Data Availability The authors declare that all the data are available upon personal request.

Declarations

Ethical approval None.

Conflict of interest The authors declare no competing interests.

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