



# Presumed oculomotor nerve palsy following COVID-19 vaccination

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## Abstract

We herein report the case of an 84-year-old female who presented to the outpatient clinic one day following her first dose of the Pfizer-BioNTech COVID-19 vaccine with mydriasis, ptosis, and a “down and out” gaze. She was subsequently diagnosed with oculomotor nerve palsy, and treated with corticosteroids and valacyclovir for a total of 7 days, with no clear improvement. On subsequent visits, ophthalmic examination improved steadily and showed complete resolution after 8 weeks. This article aims to report this unusual incidence that occurred following vaccination with the Pfizer-BioNTech COVID-19 vaccine. It is important for physicians to identify and report abnormal occurrences which may potentially be related to the COVID-19 vaccines, in order to reach a complete understanding of their possible side effects.

## Keywords

Covid-19, Vaccine, Oculomotor nerve palsy, Adverse event, Infectious diseases, Ophthalmology

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## Introduction

The Pfizer-BioNTech COVID-19 vaccine, which is considered safe and effective, has been recommended by the Centers for Disease Control and Prevention (CDC) for people aged 5 years and older.<sup>1</sup> Common side effects include pain, redness, and swelling at the site of injection, along with tiredness, headache, muscle pain, chills, fever, and nausea.<sup>2</sup>

In the Pfizer-BioNTech COVID-19 vaccine clinical trial, the only neurological adverse event cited was Bell’s Palsy. This condition was reported by four vaccine participants and none in the placebo group. This is consistent with the rate in the general population, which makes the casual relationship less certain and requires surveillance in larger populations.<sup>3</sup> However, oculomotor nerve palsy was not reported.

Oculomotor nerve palsy is one of the most common cranial nerve palsies reported to the Vaccine Adverse Event Reporting System (VAERS) after routine vaccination.<sup>4</sup> The association between vaccine administration and the onset of oculomotor nerve palsy has been previously reported with the inactivated Influenza Vaccine,<sup>5</sup> and the Measles Mumps Rubella vaccine.<sup>6</sup> So far, there are no reports of oculomotor nerve palsy in the literature since the deployment of any type of COVID-19 vaccine into the general population. Multiple neuro-ophthalmic conditions have however been reported

following COVID-19 infections, including cranial nerve palsies (III, VI, and VII), ocular myasthenia gravis, and ptosis as part of Guillain-Barré syndrome (GBS).<sup>7</sup>

We present a case of complete oculomotor palsy after the vaccination with the Pfizer-BioNTech COVID-19 vaccine in an 84-year-old woman.

## Case presentation

An 84-year-old female patient presented to our clinic with a complaint of sudden onset blurry vision with complete ptosis one day after she received the first dose of the Pfizer-BioNTech COVID-19 vaccine. She had no ocular pain, headache, fever, or weight loss.

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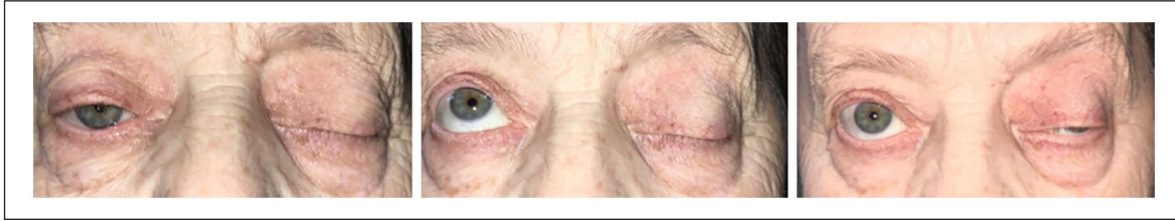
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**Figure 1.** Ophthalmic examination at presentation, 1 day after vaccination.

She had a medical history of well-controlled diabetes and hypertension. She had no history of dyslipidemia, smoking, obesity, systemic vasculitis, headache, neurological or thyroid disease. She had no significant family history of neurological disorders. The patient reported no history of head or eye trauma and no signs of giant cell arteritis (headache, jaw or tongue claudication, polymyalgia rheumatica, visual loss).

Her daily medications were metformin, gliclazide, pioglitazone, telmisartan and hydrochlorothiazide, rosuvastatin, clopidogrel, and bisoprolol.

On a general physical examination, her blood pressure was 132/67.

On ophthalmological examination, the patient presented mydriasis with severe ptosis in her left eye, compromising the visual axis. Pupillary light reflex showed an unreactive left pupil to the illumination of both eyes. On external examination, there was no exophthalmia, and the patient presented a spontaneous abduction and slight depression of the left eye, resulting in the characteristic “down and out” gaze (Figure 1). Her visual acuity was 20/20 in her right eye, and 19/20 in her left eye. Extraocular motility examination showed limitation of adduction (left medial rectus muscle), elevation (left superior rectus muscle), and depression (left inferior rectus muscle). Intraocular pressure was normal in both eyes. On slit-lamp examination, the conjunctiva was white and quiet, the cornea was clear and showed no signs of keratitis, the anterior chamber was quiet and showed no signs of uveitis. The lenses were clear with no signs of cataract, and the anterior vitreous was unremarkable in both eyes. Fundoscopy was unremarkable and showed no signs of diabetic retinopathy, venous or arterial occlusions, and no optic nerve pallor or thinning.

There were no signs of myasthenia gravis disease, as sustained upward gaze (fatigue test) did not increase ptosis, and the application of an ice pack to the left upper eyelid did not improve ptosis.

On neurological examination, the patient was alert, oriented, and cooperative, and her speech was clear and fluent. A comprehensive examination of cranial nerves was unremarkable. Facial sensation and corneal responses were intact, her face was symmetric, and she had normal hearing and symmetric elevation of the palate. Phonation was normal, head-turning and shoulder shrug were intact, and her tongue was midline with normal movements and no atrophy.

On motor examination, there was no pronator drift of outstretched arms. Muscle bulk, tone, and symmetry were normal. Strength was 5/5 bilaterally. Reflexes were 2/4 and symmetric at the biceps, triceps, knees, and ankles, and plantar responses were flexor. The patient presented normal sensitivity in fingers and toes to light touch, pinprick, position sense, and vibration sense. Coordination was intact, as there was no dysmetria on finger-to-nose and heel-knee-shin, and rapid alternating and fine finger movements were intact. The Romberg test was negative, and posture was normal. Gait was steady, and the patient walked normally on toes and heels and had a normal tandem gait when closing one of her eyes.

On blood work, her complete blood count (CBC), comprehensive metabolic panel, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), liver function tests, and lipid panel were unremarkable. Her hemoglobin A1c (HbA1c) was at 6.79%. Her thyroid-stimulating hormone was normal (0.88 mUI/L), thyroid peroxidase antibodies (anti-TPO) negative and cervical ultrasound unremarkable. COVID-19 testing by polymerase chain reaction was done to rule out COVID-19 infection and was negative.

Although her presentation was not typical of ocular myasthenia gravis, the diagnosis was ruled out with negative acetylcholine receptor (AChR) antibodies and electromyography (EMG), and a thoracic computed tomography (CT) scanner was unremarkable. Serum protein electrophoresis was unremarkable and antinuclear antibodies (ANA) were negative.

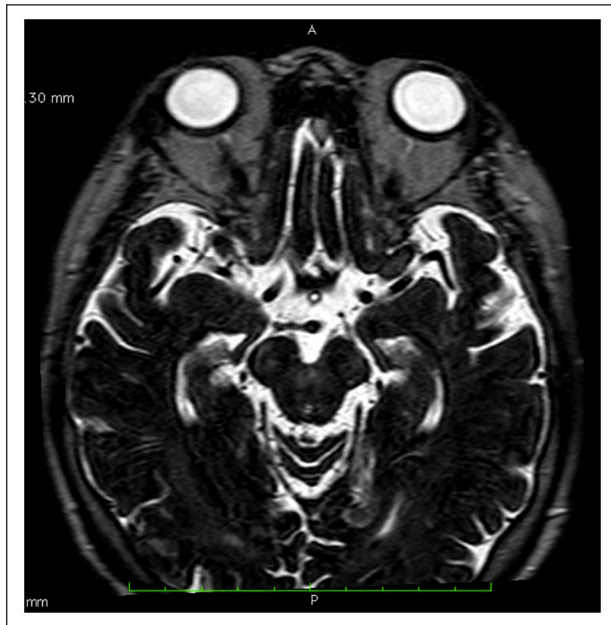
Imaging of the brain that included CT of the head without contrast, magnetic resonance imaging (MRI) of the brain with and without intravenous (IV) contrast showed no sign of ischemic stroke or hemorrhage and no anomaly of the third cranial nerve along its path between the oculomotor nucleus in the midbrain and the extraocular muscles within the orbit. Unfortunately, magnetic resonance angiography (MRA), computed tomographic angiography (CTA), or cerebral angiography were not obtained to rule out the possibility of a cerebral aneurysm; however, no aneurysms were seen on MRI. Orbital MRI did not show enhancement of the left oculomotor nerve and was unremarkable (Figure 2).

The patient did not have any accompanying meningeal signs, that is, no headache or neck stiffness, and no other cranial nerve involvement, so we did not perform a lumbar puncture.

She was treated with prednisone 40 mg daily for 5 days, followed by valacyclovir 500 mg twice daily for 7 days, with no improvement.

Her SARS-COV-2 IgG was positive (10.93 AU/mL) 50 days after the first dose of the vaccine. She did not receive the second dose.

On subsequent visits, ophthalmic examination showed steady improvement (Figure 3), and 2 months after her first visit, her symptoms had completely resolved (Figure 4).



**Figure 2.** Magnetic resonance imaging (MRI) showing a normal left third cranial nerve.

## Discussion

Most adverse reactions to vaccines are triggered by excessive immune responses and inflammatory damage. Although clinical trials undergo rigorous safety monitoring and assessment prior to the authorization of a vaccine, some serious adverse events may not be identified in trials, especially if rare, because of the limited follow-up duration, the small sample size, overly restrictive eligibility criteria, and the selection of participants who may not represent the general population. In particular, COVID-19 vaccines, which are notably the first mRNA vaccines that are licensed for use, were fast-tracked through the usual development stages given the burden of the pandemic and its catastrophic death toll.<sup>8</sup> For these reasons, it is crucial to ensure rigorous and robust monitoring of adverse reactions to inform policy, ensure safety, and build public trust.

However, an absolute certainty of the causal role of a vaccine in the occurrence of a reaction is always challenging due to the complexity of the pathogenesis of adverse reactions. The World Health Organization (WHO) has established guidelines for the causality assessment of Adverse Events Following Immunization (AEFI) in a four-step algorithm.

The first step is to rule out any strong evidence for other causes that might explain the adverse event that would thus exclude the role of the vaccine. In our case, the compressive and vascular causes were ruled out by history, physical examination, blood tests, and imaging studies. Although this patient has a history of diabetes, it is well controlled with an HbA1c of 6.79%, and the oculomotor palsy seen in diabetes typically spares the pupil,<sup>9</sup> this patient however presented with unreactive mydriasis.



**Figure 3.** Ophthalmic examination showing improvement 4 weeks after vaccination.



**Figure 4.** Ophthalmic examination showing full resolution 8 weeks after vaccination.



The second step is to see if there is a known causal relationship with vaccination and to see if the AEFI occurred within a time frame that would suggest causality. In our case, oculomotor dysfunction occurred one day following the first dose of the Pfizer-BioNTech COVID-19 vaccine, which confirms the temporal compatibility. This condition has never been reported following any COVID-19 vaccine. However, several reports have demonstrated that cranial nerve palsies are a part of the neurologic spectrum of COVID-19 infection,<sup>10–14</sup> including oculomotor nerve palsy.<sup>10,11,15–18</sup> In these cases, it is suggested that viral infection with SARS-CoV-2 is triggering a misdirected immune reaction against myelin sheaths and surrounding axons, a mechanism similar to the one seen in GBS, acute disseminated encephalomyelitis (ADEM), transverse myelitis, and optic neuritis.

A recent review of cranial nerve palsies following COVID-19 infection showed that most cases resolved spontaneously in 2–6 weeks. In our case, although oculomotor palsy occurred after COVID-19 vaccination and not the infection itself, the time to resolution was more or less the same.

The WHO guidelines also suggest looking for any strong evidence against a causal association between oculomotor nerve palsy and the COVID-19 vaccine. A review of all published evidence in the literature since the beginning of the pandemic did not show any data that would reject a potential association between COVID-19 vaccine and this condition.

Based on all arguments presented above, although we cannot confirm the causal association between this condition and the vaccine, this relationship is considered plausible, and we may categorize it as “consistent” according to the final step of the WHO algorithm.

The pathological mechanism behind this potential rare side effect is uncertain. An analogy may be made with facial nerve palsy which has been previously implicated as an adverse event of other vaccines and was suggested to result from an immunomodulatory response occurring within the cells, damaging myelin sheaths and surrounding axons.<sup>19,20</sup> In theory, we may hypothesize that the immune response produced after COVID-19 vaccination may result in similar damage via either antigenic mimicry or bystander activation of autoreactive T cells. However, further studies are necessary to confirm the underlying pathophysiology because the Pfizer-BioNTech vaccine is an mRNA vaccine with novel vaccine technology and an entirely different mechanism.

## Conclusion

This article aims to report a case of complete oculomotor palsy after the vaccination with the Pfizer-BioNTech COVID-19 vaccine. The temporal compatibility and the absence of any other identifiable cause raise the possibility of a causal relationship between the vaccine and oculomotor nerve palsy which must be further investigated. Given the current COVID-19 pandemic and its burden on global health, most vaccines were fast-tracked through the usual

pre-licensing stages to avoid further casualties. This raises concerns on the safety of newly licensed COVID-19 vaccines, and rigorous post-marketing surveillance is essential to reach a complete understanding of their possible side effects.

## Author contributions

All authors listed have significantly contributed to the investigation, development, drafting of the article, revising it critically for important intellectual content, and the final approval of the version to be submitted.

## Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

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## Statement of ethics

The patient signed a written informed consent to publish her case, including images. The research in this article was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

## Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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