Case series: Atypical optic neuritis after COVID-19 vaccination

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The global impact of the COVID-19 pandemic has led to the development of the highly efficacious Pfizer and Moderna vaccines. Because these mRNA vaccines are novel, there is limited knowledge about their potential adverse effects. Optic neuritis is an immune-mediated disorder characterized by subacute onset painful vision loss, commonly associated with demyelinating conditions of the central nervous system, which may occur following infection or vaccination, and is usually steroid-responsive.1 In this case series, we describe two patients who developed atypical optic neuritis following COVID-19 vaccination.

Case 1: A 65-year-old woman with a history of medullary thyroid cancer status post total thyroidectomy on levothyroxine, vitamin D deficiency on supplementation, pre-diabetes mellitus, and hyperlipidemia received her first dose of the Pfizer COVID-19 mRNA vaccine. Within hours following vaccination, she experienced a headache. Five days later, she developed right-sided vision loss and pain with eye movements. She presented with light perception only vision and an afferent pupillary defect in her right eye, with 360-degree optic disc swelling associated with cotton wool spots and flame hemorrhages (Figure 1). Her ophthalmologic and neurologic examinations were otherwise normal. MRI orbits showed evidence of right optic neuritis (Figure 2). MRI brain, cervical and thoracic spine showed no demyelinating lesions. COVID-19 polymerase chain reaction (PCR) was negative. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were within normal limits. Antinuclear antibody (ANA), antineutrophil cytoplasmic antibodies (ANCA), and angiotensin-converting enzyme (ACE) were negative. Serum myelin oligodendrocyte glycoprotein (MOG) IgG and aquaporin-4 IgG were negative. She was treated with a 5-day course of methylprednisolone 1 g IV every 24 hours and
intravenous immunoglobulin (IVIG) 2 g/kg administered over 3 days. Five weeks later, visual acuity improved to 20/100 in her right eye, but she perceived minimal recovery in central vision.

Case 2: A 67-year-old man with a history of pre-diabetes mellitus, hyperlipidemia, glaucoma, and episcleritis received his second dose of the Moderna COVID-19 mRNA vaccine. The next day, he developed bilateral eye redness and chemosis with blurred vision. Hours later, he noted rapidly progressive vision loss in the left eye associated with pain with eye movements along with ocular surface irritation. He denied deep orbital or boring pain. He presented with visual acuity of 20/40 in the right eye, no light perception in the left eye, and a left afferent pupillary defect. He also had temporal chemosis and injection in both eyes that improved but did not completely blanch with phenylephrine. His ocular ductions were full, and ophthalmologic and neurologic examinations were otherwise normal. MRI orbits showed evidence of left optic neuritis (Figure 2). MRI brain was normal, COVID-19 PCR was negative. ESR was within normal limits. CRP was elevated to 57.2 mg/L. ANA, ANCA, and rheumatoid factor were negative. Serum MOG IgG and aquaporin-4 IgG were negative. Thyroid stimulating hormone (TSH) and thyroid antibodies were normal. He was given a 5-day course of methylprednisolone 1 g IV every 24 hours. Six weeks later, visual acuity improved to 20/20 in the right eye with a normal visual field, but he continued to have no light perception in the left eye.

These two patients developed optic neuritis within the first week of COVID-19 mRNA vaccination in the absence of MOG or aquaporin-4 antibodies. Both patients were older than the typical age of presentation for optic neuritis, usually in the 3rd to 5th decades of life², and neither had rapid improvement in visual acuity with steroids.
Optic neuritis has been reported in patients with COVID-19 infection, including cases of MOG seropositivity\textsuperscript{3-4}. Optic neuritis has also occurred following vaccinations against influenza, measles-mumps-rubella, hepatitis A and B, and rabies\textsuperscript{1}. There is a case report of a patient who developed anti-MOG antibody positive bilateral optic neuritis and thyroiditis after vaccination with Sinovac’s inactivated COVID-19 vaccine.\textsuperscript{5} There is also a published case of a patient with multiple sclerosis who developed chiasmal optic neuritis and longitudinally extensive transverse myelitis following vaccination with the vector-based Astra Zeneca COVID-19 vaccine.\textsuperscript{6} Multiple mechanisms have been proposed to explain such autoimmune phenomena, including molecular mimicry, epitope spreading, bystander activation, direct inflammatory damage, formation of immune complexes, and genetic predisposition to autoimmunity\textsuperscript{1}. To the best of our knowledge, this is the first report of optic neuritis following COVID-19 mRNA vaccination.

This case series is limited in that it cannot determine if the association between COVID-19 immunization and optic neuritis is causal or merely temporal. The development of optic neuritis in the days to weeks after vaccination is a rare event, and a case control study of 91 individuals who developed optic neuritis following vaccination between 2007 and 2012 found no increased risk of vaccine exposure when comparing patients with an initial episode of optic neuritis to their age-, sex-, and vaccine-matched controls.\textsuperscript{7}

The Pfizer and Moderna COVID-19 mRNA vaccines have shown an excellent safety record and are anticipated to greatly reduce morbidity and mortality during the COVID-19 pandemic. Thus, the benefits of vaccination will outweigh the risks in most people. However, as large-scale vaccination against COVID-19 continues, it is important for medical providers to be aware of the
potential association between these mRNA vaccines and atypical optic neuritis. These two cases illustrate the need to study large datasets to determine the frequency and mechanisms by which mRNA vaccines may trigger immune-mediated reactions.
References:


Figure Legends

Figure 1. Optic discs on fundoscopic examination

Panel A. The right optic disc is pale and edematous with flame hemorrhages and obscuration of the major vessels.
Panel B. The left optic disc is normal in color with sharp margins and well-defined retinal vessels.
Figure 2. MRI orbits with and without contrast showing evidence of optic neuritis

Axial T2-weighted sequence (A) shows an enlarged right optic nerve (long arrow) and axial T1-weighted post-contrast image (B) demonstrates contrast enhancement of the right optic nerve (arrowhead) in a 65-year-old woman who received the Pfizer COVID-19 vaccine. Axial (C) and coronal (D) T1-weighted post-contrast sequences with fat saturation show enhancement of the left optic nerve (arrowhead) and bilateral retrobulbar fat (short arrows) in a 67-year-old man who received the Moderna COVID-19 vaccine.
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