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Acute abducens nerve palsy following COVID-19 vaccination

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We report the case of a healthy 59-year-old woman who presented with an acute abducens nerve palsy 2 days after receiving the Pfizer-BioNTech COVID-19 vaccine. In adults, such palsies are typically caused by microvascular disease or compressive tumors, although they have also been described after routine vaccinations. Given the temporal relationship between vaccination and the onset of symptoms, the lack of preexisting medical conditions, and unremarkable magnetic resonance imaging, the patient's abducens nerve palsy was felt to be related to her vaccination. This case highlights the importance of recognizing the potential of a COVID-19 vaccine to have neurologic sequelae similar to those that as have been reported with the virus itself as well as with other vaccines.

Case Report

A previously healthy 59-year-old woman presented emergently to the Bascom Palmer Eye Institute with acute binocular and painless, horizontal diplopia 2 days after receiving the Pfizer-BioNTech COVID-19 vaccine. She reported 1 day of fever; however, the remainder of her review of systems was unremarkable, and there were no other neurologic symptoms, including facial or generalized weakness, gait abnormality, paresthesias, and anosmia. At presentation, her best-corrected visual acuity was 20/25 in each eye. Intraocular pressure in each eye was within normal limits, and there was no afferent pupillary defect. On sensorimotor examination, the patient had a new right esotropia of 25^{Δ} in primary gaze, 30^{Δ} in right gaze, and 10^{Δ} in left gaze as well as a severe abduction deficit of the right eye (Figure 1). Pictures taken before these ocular motor findings developed demonstrated no prior eye misalignment. Slit-lamp and fundus examination were unremarkable. The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were both mildly elevated, at 42 mm/hr and 0.8 mg/dL, respectively. Magnetic resonance imaging (MRI) of the brain and orbits with and without gadolinium at time of presentation showed no abnormal signal, enhancement, mass lesion or mass effect. The patient was diagnosed with an abducens nerve palsy with a likely association to the COVID-19 vaccine, given the temporal relationship. Although her fever resolved, her sensorimotor examination remained unchanged at the most recent follow-up.

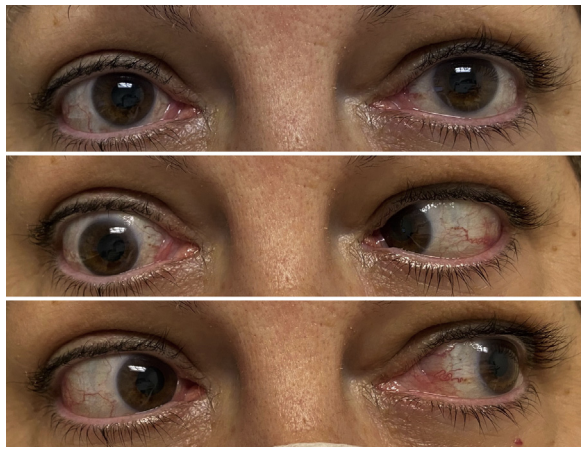

FIG 1. External photographs demonstrating an esotropia and limitation to abduction of the right eye consistent with an abducens nerve palsy.

Discussion

Abducens nerve palsy is the most frequent isolated ocular motor nerve palsy, with an annual incidence of 11.3/100,000.[1,2] In children, abducens nerve palsies are often associated with trauma, elevated intracranial pressure, neoplasm, or viral infections.[3] In adults, they are more commonly caused by microvascular disease or tumors.[1]

Though rare, vaccination-induced ocular motor nerve palsies have also been reported. Excluding facial nerve palsies, abducens nerve palsies are the most frequent after routine immunization, followed by oculomotor and trochlear nerve palsies.[4] Abducens nerve palsies after immunization were first reported in 1983 by Werner and colleagues,[5] with 2 of 4 children having abducens nerve palsies that following immunizations for diptheria-pertussis-tetanus and rubeolla-mumps-rubella virus. Abducens nerve palsies have also been reported in measles-mumps-rubella, hepatitis B, and annual influenza vaccines, with onset ranging from 2 days to 3 weeks from time of vaccination.[6-8] Postimmunization abducens nerve palsies typically

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resolve spontaneously within 6 months, but they can be recurrent.[5-7]

Although the pathophysiology behind postimmunization ocular nerve palsies remains unknown, it is hypothesized to be related to immune-mediated damage resulting in demyelination or localized vasculitis.[4-8] Isolated case reports of abducens nerve palsies have been described in setting of COVID-19 infection. Falcone and colleagues[9] reported an acute abducens nerve palsy in a healthy 32-year-old man 3 days after developing respiratory symptoms and subsequently testing positive for COVID-19. MRI 5 weeks after symptom onset showed ipsilateral atrophy and hyperintensity of the lateral rectus muscle, consistent with denervation of the abducens nerve as described in previous reports. Similarly, Greer and colleagues[10] reported 2 cases of isolated abducens nerve palsies following a febrile period 3 days after COVID-19 symptom onset. Various mechanisms of COVID-19 mediated cranial nerve palsies have been proposed, including direct invasion of endothelial cells by the virus and indirect injury through proinflammatory mechanisms incited by infected leukocytes, although the exact pathophysiology remains uncertain.[10]

Our patient developed an acute right abducens nerve palsy following a febrile illness 2 days after receiving the Pfizer-BioNTech mRNA COVID-19 vaccine. Her lack of vascular risk factors, negative review of systems, normal optic nerves, and unremarkable MRI make microvascular or neoplastic etiologies unlikely. Given the patient's mild elevation in ESR and CRP, we hypothesize that this patient developed a viral-like inflammatory reaction to the vaccine, inciting an immune-mediated indirect insult along the abducens nerve. Although less likely in this patient, given the normal MRI, it is also important to consider vaccine-related thrombotic events as a possible etiology. The differential diagnosis incudes Duane syndrome, orbit fibrosis, myasthenia gravis, and even temporal arteritis, but all of these are unlikely, given the preexisting photographic evidence, lab findings, scan, and clinical course. Our finding has been reported to the CDC and FDA via the Vaccine Adverse Event Reporting System as well as to the manufacturer (Pfizer, New York, NY).

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Ocular manifestations of Beckwith-Wiedemann syndrome

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Beckwith-Wiedemann syndrome (BWS; OMIM #130650) is a pediatric overgrowth disorder with few known ocular manifestations. We retrospectively reviewed the medical records of patients with BWS evaluated at Bascom Palmer Eye Institute over a 10-year period and identified 5 patients, of whom 4 presented with ocular misalignment and 1 with eye rubbing. Three patients were noted to have strabismus, and 1 patient manifested with significant astigmatism. No patients received surgical intervention.

Beckwith-Wiedemann syndrome (BWS; OMIM #130650) is a pediatric overgrowth disorder caused by mutation or deletion of imprinted genes in the chromosome 11p15.4-5 region or hypomethylation of genes in this region.[1,2] It was first described in the early 1960s, and over 500 cases have been reported, with an estimated incidence of about 1 in

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