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CASE REPORT

Inflammatory Sixth Nerve Palsy Post-COVID-19 Vaccination: Magnetic Resonance Imaging Findings

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ABSTRACT

Sixth nerve palsy is the most common post-vaccination oculomotor palsy. It is generally transient with most patients making a complete recovery. We report the case of a 46-year-old healthy male patient who presented with a painless sixth nerve palsy after the second dose of the Pfizer BioNTech COVID-19 vaccine, which recovered over the course of the next month. We confirmed the lesion localisation by demonstrating enhancement of the root exit zone and the cisternal portion of the sixth nerve on sequential magnetic resonance imaging during the symptomatic period. Here, a temporal relationship between vaccine application and diplopia onset suggests an aetiologic relationship. Moreover, the lack of pre-existing medical conditions suggests a post-vaccination inflammatory process.

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Introduction

Coronavirus infection is by far the most serious public health problem of the 21st century due to its global impact and its high mortality and morbidity. Multiple organ damage principally relates to direct viral invasion, cytokine storm, hypercoagulable states, autoimmune-mediated post-infectious systemic pathology or a combination of all of these factors. Neuro-ophthalmological abnormalities have been subject of several reviews to date. The urgent search for prevention and treatment led to the development of COVID vaccines in record time. A number of vaccines were developed that utilised a viral vector or genetic sequencing (deoxyribonucleic acid [DNA] or messenger ribonucleic acid [mRNA]) with beneficial results well reflected in world statistics.[1]

Adverse ocular effects of the common vaccines have been reported,[2] however, rapid vaccine development to match epidemiological urgency of COVID-19, has meant that the side effects of these new vaccines are just now coming to light. This is particularly the case with the novel recombinant mRNA vaccines. While the beneficial effect of the vaccine far outweighs potential risk, awareness of side effects and their management, may lessen public vaccination hesitance and increase safety awareness among consumers.

We had the opportunity to evaluate a healthy patient who developed a left sixth nerve palsy after a second dose of the Pfizer BioNTech COVID-19 vaccine.

Case report

A 43-year-old man woke up with horizontal painless diplopia 4 days after a second dose of the Pfizer BioNTech COVID-19 vaccine. He denied a recent history of fever, malaise, cough, or anosmia. There was no personal history of migraine, arterial hypertension, diabetes, trauma, neurological, ophthalmological, or other systemic diseases. He had received the two Pfizer vaccine doses within 21 days of each other. He read the manuscript and gave consent for publication.

Neuro-ophthalmological examination showed the best corrected visual acuity was 20/20 (cylinder 0.25 × 170) for the right eye and 20/20 (sphere +0.25 dioptres [D]) for the left eye. The near vision was 20/20 (add sphere +1.50

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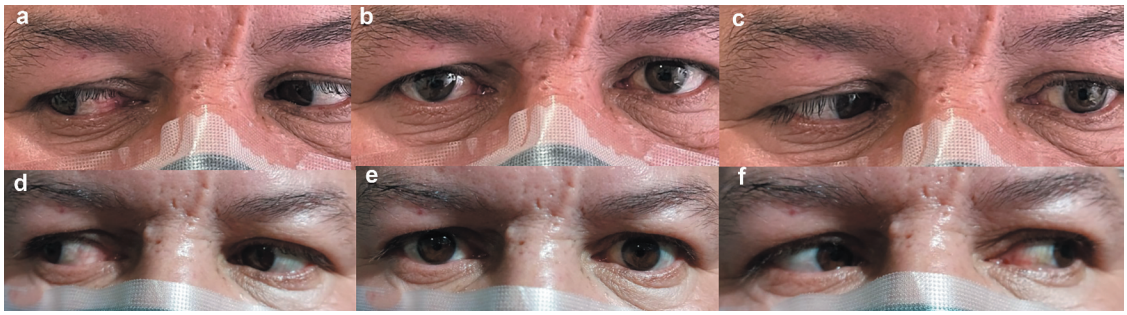

Figure 1. (a) Normal versions on right gaze. (b) Left eye esotropia in primary position. (c) Reduced abduction of the left eye on left gaze. After a month. (d) Normal versions on right gaze. (e) Orthotropia in primary gaze. (f) Normal versions on left gaze.

D). The Ishihara test, confrontation visual field, pupils, slit-lamp examination, intraocular pressure, corneal sensitivity, and funduscopic examination were all normal. Eye movement examination revealed a 10 $^{\Delta}$ left esotropia in primary gaze, which increased to 16 $^{\Delta}$ in left gaze and decreased to 6 $^{\Delta}$ in right gaze. Left eye abducting saccades were reduced and he had a compensatory left-head turn (Figure 1a–c). Forced ductions were negative. The facial nerve function and the remaining neurological examination was normal. Family album photographs did not document any previous eye deviation. We diagnosed an isolated sixth nerve palsy.

The laboratory tests (haematology, HbA1c, and complete chemistry) were normal. Sars-CoV-2 polymerase-chain reaction (PCR) test was negative. Orbital computer tomography scans were normal. Brain magnetic resonance imaging (MRI) obtained 10 days after symptom onset showed focal enlargement of the root exit zone and the cisternal portion of the left sixth nerve with post-gadolinium enhancement (Figure 2a,b). On follow–up, 2 weeks later, the sixth nerve palsy had begun to improve and it resolved within five weeks (Figure 1d–f). Parallel to the clinical improvement, further MRI 4 weeks after presentation showed decreased perineural contrast uptake (Figure 2c, d). Because of the steady, spontaneous improvement, we did not pursue additional investigation. Eight weeks later, the patient remained asymptomatic and contrast-enhance brain MRI showed residual minimal enhancement of the sixth nerve (Figure 2e,f).

Discussion

The most common oculomotor nerve affected by post-vaccination palsy is the sixth nerve followed by the third and fourth nerves in order of frequency.[3] Reported post-vaccination sixth nerve palsy has been reported to occur in association with influenza,[4] brucella,[5] measles-mumps-rubella,[6] varicella,[6,7] hepatitis B,[8] yellow fever,[9] and more recently, COVID-19 vaccines.[10–13]

Herein, we have reported a patient without systemic disease who developed a sixth nerve palsy 4 days after a second dose of the Pfizer BioNTech COVID-19 vaccine. A good temporal correlation between the timing of vaccination and clinical presentation is a strong argument for causation, however we cannot rule out a chance relationship.

Post-gadolinium MRI showed contrast enhancement of the pontine exit-root (transition from central to peripheral myelin) and an enlarged nerve with perineural enhancement. Gadolinium enhancement and cranial nerve thickening has been recently reported to occur in two patients following the first dose of the same Pfizer BioNTech COVID-19 vaccine. Interestingly, in one report the patient developed multiple cranial nerves palsies (second, fifth, sixth and seventh nerves),[12] and the second report featured Guillain-Barré syndrome (GBS).[14] Post-gadolinium MRI showed enhancement of several cranial nerves in the first report[12] and the lumbosacral roots in the second.[14] GBS after COVID vaccination tends to be progressive.[13,15,16] For this reason, we performed frequent clinical monitoring of our patient's motor function and deep tendon reflexes during his clinical course.

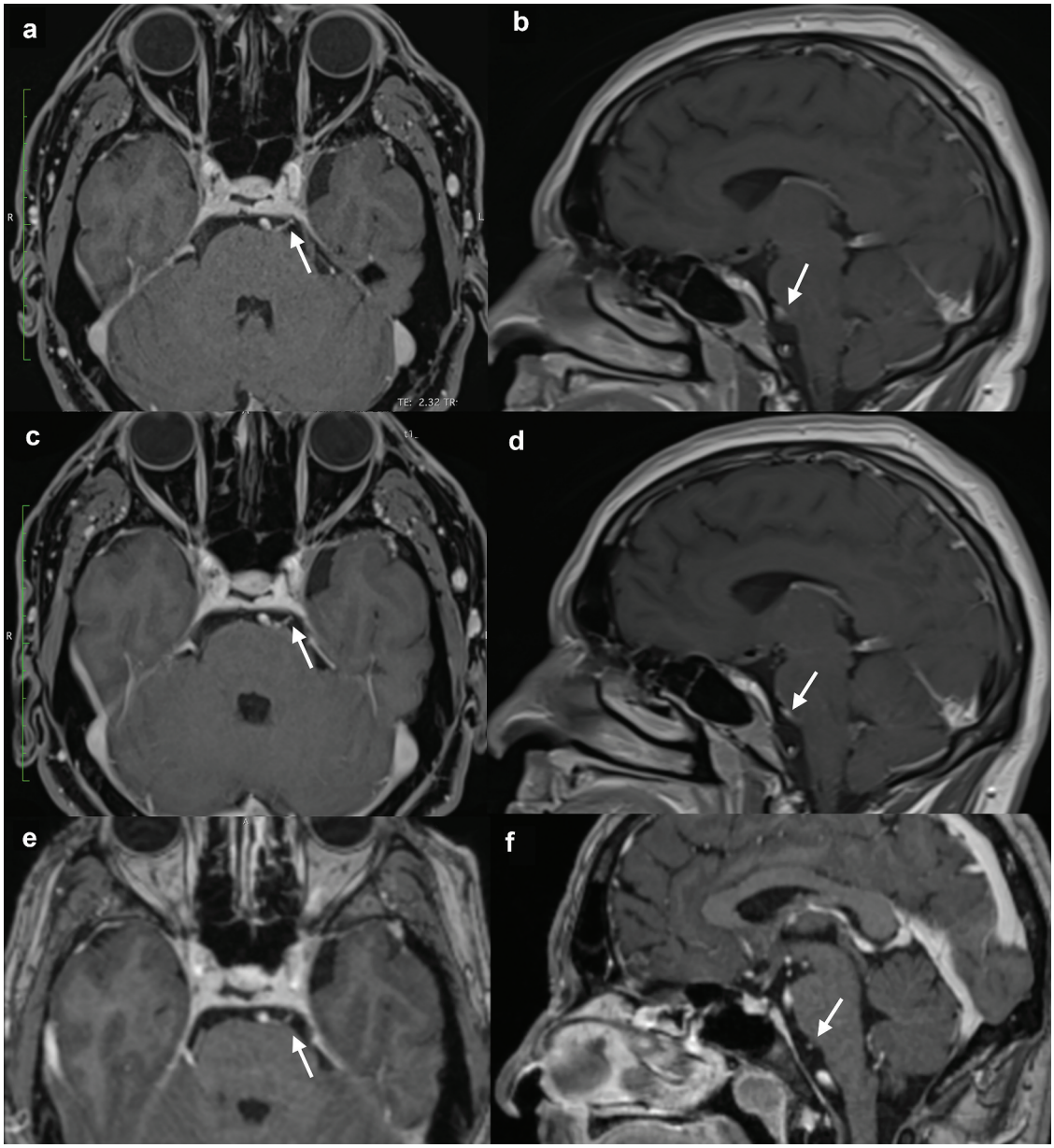

Figure 2. Post-gadolinium brain magnetic resonance imaging. (a) Axial and (b) sagittal views demonstrating enhancement of the cisternal segment of the left sixth nerve. After a month, (c) axial and (d) sagittal views showing diminution of the enhancement of the cisternal segment of the left sixth nerve. After 2 months, (e) axial and (f) sagittal views demonstrating minimal enhancement of the left sixth nerve.

Contrast enhancement is a marker of local inflammation, possibly triggered by an autoimmune reaction to either active disease or post-vaccination, which probably share a common mechanism, including GBS,[16,17] isolated ophthalmoplegia,[18] and post-COVID vaccination.[12,14]

We speculate that the mechanism involves an isolated autoimmune inflammatory peripheral demyelinating neuropathy as observed in patients with chronic inflammatory demyelinating polyradiculoneuropathy during symptomatic periods, or a GBS-like event. In either instance MRI often shows multiple cranial nerve enhancement.[12,14] Unlike other aetiologies of cranial neuropathies, our patient's ophthalmoplegia improved at a slow pace; in other instances the ophthalmoplegia resolves prior to the MRI findings.

It is important to remark that direct COVID-19 disease causes cranial nerve palsies with similar enhancement of the cranial nerves.[15] Our patient had no clinical manifestations of active COVID-19 and had a negative SARS-CoV2 PCR test.

The new technology of this gene sequencing vaccine involves insertion of encoded viral DNA and mRNA into recipient cells, which stimulates protective immunity through the host cell, thus, allowing host cells to produce protective immunity. The inherent risk is instability of the mRNA in the extracellular tissue,[2] as a potential trigger for an autoimmune response.

Post-vaccination cranial nerve palsies are uncommon. Facial nerve paralysis is the most frequent cause of non-ocular motor paralysis reported with the mRNA vaccines (Moderna and Pfizer) with spontaneous resolution.[19] Interestingly, post-vaccination nerve palsies previously reported with other vaccines have also had good outcomes.[3–13]

In conclusion, our main impetus in this report is to highlight out patient's recovery, particularly when one considers the large volume of vaccines administered worldwide. Oculomotor complications are not only infrequent but also benign.

Disclosure statement

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