Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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LETTER TO THE EDITOR

Isolated abducens nerve palsy following Covid-19 vaccine

Paralysie isolée du nerf abducens suite au vaccin Covid-19

Since emergence of Covid-19 infection, neuro-ophthalmic manifestations of Covid-19 virus have been reported in literature. Previously, isolated six nerve palsy has been documented as a presenting symptom or during the course of Covid-19 disease [1—6]. Reyes-Capo et al reported a woman who presented with an acute abducens nerve palsy 2 days after receiving the PfizerBioNTech Covid-19 vaccine [7]. Herein, we describe a 40-year-old man patient with isolated abducens nerve palsy occurred following Covid-19 (Bharat BioTech Covid-19 vaccine) vaccination.

A 40-year-old Caucasian none-smoker man was referred to Poostchi Eye clinic (affiliated to Shiraz University of Medical Sciences) with complaint of sudden onset painless horizontal diplopia worsening at right lateral gaze. Past medical history was unremarkable and there was no history of diabetes mellitus, hypertension or cerebrovascular disorders. Also he had not any previous history of head trauma or ocular diseases. On physical examination, patient had no evidence of active Covid-19 infection. He was afebrile, without headache, anosmia, ageusia, respiratory and gastrointestinal symptoms. However, he mentioned that he have received Bharat BioTech Covid-19 vaccine two weeks before and had felt chills and fever for 48 hours following vaccination. Best corrected visual acuity was 20/20 (OU) and intraocular pressure was within normal range in both eyes. Pupils were round, reactive to light with symmetric normal size. Relative afferent pupillary defect was negative. Ocular motility revealed esotropia and limition of abduction in the right eye (−2 to −3) (Fig. 1). There was no pathological finding in slit lamp examination, fundoscopy (Fig. 2), and OCT imaging. Complete blood count and other lab data were within normal range. Chest X-ray was normal and Covid-19 PCR test was negative Brain and orbital magnetic resonance imaging (MRI) were normal. Given the temporal relationship, the patient was diagnosed with an abducens nerve palsy with a likely association to the Covid-19 vaccine.

Abducens nerve palsy has been demonstrated as the most common neuro-ophthalmic manifestation of Covid-19 with different suggested mechanisms such as inflammation, micro vascular ischemic as well as viral and bacterial infection [2]. However, no exact pathophysiology has been defined yet. Researchers have suggested that Covid-19 is a

Figure 1. Horizontal gaze examination showed limitation in abduction of right eye.

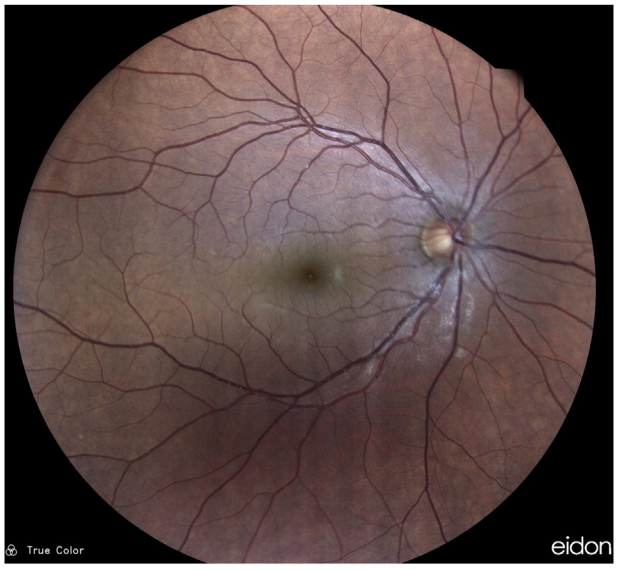

Figure 2. Fundus imaging showed normal findings.

neurotropic virus, however, the pathophysiology of Covid-19 neurotropism has not been clarified completely. Covid-19 virus attacks host cells angiotensin converting enzyme 2 (ACE-2) via spike protein S1 [8]. The ACE2 has been detected in various tissues e.g. neural, glial, gastrointestinal and pulmonary cells which make them susceptible to Covid-19 invasion. Covid-19 virus could involve central nervous system by different pathways:

- direct invasion of virus to peripheral nervous system such as olfactory bulb and retrograde invasion toward medulla;
- hematogenous distribution via endothelial cells invasion leading to blood brain barrier breakdown;
- migration of virus infected leukocyte cells to CNS by diapedesis secondary to pro-inflammatory cytokines [1,8].

Another mechanism for neurological involvement of Covid-19 is aberrant immune response due to pro-inflammatory cytokines [2]. Previously, Falcone et al. reported a case of left six nerve palsy three days after respiratory symptoms of Covid-19 without recovery after two months. Authors proposed that direct or indirect invasion of virus to abducens nerve is the main mechanism for nerve palsy [3]. Francis reported a 69-years-old female patient with horizontal diplopia eight days after a positive PCR test of Covid-19. The case was diagnosed as abducens nerve palsy. Diplopia were completely resolved spontaneously, 5 weeks later [2]. Greer et al. reported two case of isolated six nerve palsy in early course of Covid-19 disease [1]. Another case of Covid-19 developed horizontal diplopia due to six nerve palsy in the initial days of Covid-19 disease. Brain MRI showed normal finding and after 7 days of treatments, the patient recovered gradually, however intermittent diplopia persisted after discharge [6].

Our patient was not suffering from Covid-19 infection but had history of receiving Bharat BioTech Covid-19 vaccine two weeks ago. Given the temporal relationship, we presumed that six nerve palsy in the present patient could be attributed to immune mediated microvascular ischemia or vasculitis in the microvascular branches of abducens nerve or brain stem secondary to Covid-19 vaccination. Such delay of occurrence could be explained by the time needed for immune system complex formation and deposition in the setting of third type hypersensitivity. Other explanations for occurrence of 6 nerve paresis in this patient might be inflammatory cascade subsequent to Covid-19 vaccination or thromboembolic events. Recently, Reyes-Capo presented a case of acute abducens nerve palsy, two days after Covid-19 vaccination. Their patient had a relatively high level of ESR without any previous history of trauma, and ophthalmological disorders. As they found no risk factor, the authors proposed that Pfizer-BionTech mRNA Covid-19 vaccine could be the causative factor of six nerve palsy in the reported patient [7].

Abducens nerve palsies is the most frequent ocular motor palsy following routine immunization, followed by oculomotor and trochlear nerve palsies [9]. In previously published papers, six nerve palsy had been reported as soon as two days and as far as three weeks after hepatitis B, influenza and measles-mumps-rubella vaccination [10—12]. The main suggested mechanism of action in these cases have been immune-mediated reaction causing demyelination and localized arteritis or microvascular infarction in the microvessels of abducens nerve.

As our patient had no history of predisposing disorders such as HTN or diabetic mellitus or previous history of head trauma or microvascular events, and we did not find any pathological findings in lab data and imaging studies, we think that Covid-19 Vaccine is the most probable cause of abducens nerve palsy in our patient.

To conclude, the present report is the second report of six nerve paresis due to covis-19 vaccine and the first one following Bharat BioTech Covid-19 vaccine. As Covid-19 public vaccination has been started in many countries, ophthalmologists and neuro-ophthalmologists should be aware that similar to Covid-19 infection, neuro-ophthalmic complications including 6 nerve paresis could occur as a side effect of Covid-19 virus vaccine.

Statement of ethics

The protocol of study was approved by local ethical committee of Shiraz University of Medical Sciences (ID: 2345891). The patient signed written consent form to publishing his data.

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Author contributions

Dr. Khalili, Dr. Jamali, Dr. Sadati and Dr. Jahanbani-Ardakani had same contribution in conception and study design, data collection and manuscript drafting. Critical revision was performed by Dr. Jahanbani-Ardakani.

Data availability statement

The data that support the findings of this study are available from the corresponding author, [H. J.-A.], upon reasonable request.

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Disclosure of interest

The authors declare that they have no competing interest.

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