Third Nerve Palsy: Rare Adverse Event following Covid-19 Vaccination

Indira B Deshmukh*, Sheyas R Burute , Shraddha Pore, Atmik Singh

Department of Pharmacology, Govt Medical College Miraj, Maharashtra, India.

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Abstract

Drugs Controller General of India (DCGI) in April 2022 approved the emergency use authorisation of Corbevax and Covaxin COVID 19 vaccines in children. Corbevax is a protein subunit COVID 19 vaccine developed by Texas Children's Hospital. Third nerve palsy is rarely reported following protein sub- unit COVID vaccines. We report a case of a 13-year-old male who presented to a tertiary care hospital with complaints of giddiness, headache, diplopia and drooping of left eye within one hour of receiving Corbevax vaccine in school. He was subsequently diagnosed with third nerve palsy and treated with corticosteroids and lubricant eye drops. He recovered fully and was discharged after four days. Causality assessment as per World Health Organization (WHO) guidelines for the causality assessment of Adverse Events Following Immunization (AEFI) was consistent. Protein sub unit vaccines can rarely cause third nerve palsy.
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Keywords: Covid- 19; Third Nerve Palsy; Vaccine

Introduction

The COVID-19 outbreak brought unforeseen challenges to a human existence. In response, extensive efforts were undertaken to create an efficient vaccine against this novel virus, leading to a race for vaccine development. To effectively counter the spread of COVID-19, it was imperative for all nations to prioritize universal vaccination with a reliable and secure vaccine (1). The development and distribution of COVID-19 vaccines had been a significant achievement in the global response to the pandemic.

Drugs Controller General of India (DCGI) in April 2022 approved the emergency use authorisation of Corbevax and Covaxin COVID 19 vaccines in children. Corbevax is a protein subunit COVID 19 vaccine developed by Texas Children's Hospital (2).

Vaccines have been shown to be highly effective in preventing COVID-19 infections, hospitalizations, and deaths. However, as with any vaccine, there have been reports of rare side effects and adverse reactions following COVID vaccination. The majority of these adverse effects correspond to mild and limited symptoms, such as fever, chills, fatigue, headache, joint and muscle pain, malaise, and nausea (3). Neurological side effects to SARS-CoV-2 vaccinations are usually mild, of short duration, self-limiting. However, in some cases, these side effects are severe and require hospitalization or even admission to an intensive care unit (ICU) (4).

Oculomotor nerve palsy is a condition that affects the third cranial nerve, which is responsible for controlling the movement of certain eye muscles. This condition can cause symptoms such as drooping eyelids, double vision, and difficulty moving the eye in certain directions (5). While oculomotor nerve palsy can occur for a variety of reasons, including trauma or infection, it has been reported to the Vaccine Adverse Event Reporting System (VAERS) as a potential side effect of routine vaccination (6). The association between vaccine administration and the onset of oculomotor nerve palsy has been previously reported with the inactivated Influenza Vaccine, and the Measles Mumps Rubella vaccine (7). Reports have shown that COVID-19 infections can lead to various neuro-ophthalmic conditions, such as cranial nerve palsies affecting the third (III), sixth (VI), and seventh (VII) nerves, ocular myasthenia gravis, and ptosis as part of Guillain-Barré syndrome (GBS) (8).

VAERS is a system for reporting potential adverse events

Corresponding Author: Dr Indira B Deshmukh
Address: Department of Pharmacology, Govt Medical College Miraj, Maharashtra, India.
Email: indiradeshmukh87@gmail.com

following vaccination, and it is possible that some reported events may be coincidental or due to other factors. It is important to note that just because a side effect is reported to VAERS does not necessarily mean that the vaccine caused the side effect. However, the reporting of adverse events to VAERS is an important tool for monitoring vaccine safety and identifying potential issues.

We came across only three studies reporting third nerve palsy following SARS-CoV-2 vaccination. The mechanism behind the occurrence of nerve palsies following SARS-CoV-2 vaccination has not been fully understood at this time. Furthermore, there is currently no established protocol or guidance regarding the completion of the vaccination schedule and immunization status in individuals who experience such events. Due to the relatively limited data available on these specific adverse events, further research and investigation are needed to better understand the relationship, potential causes, and appropriate management strategies in such cases. We report a case of third nerve palsy in 13 old following SARS-CoV-2 vaccination.

Case report

On June 30, 2022, a 13-year-old male received his second dose of the COVID-19 vaccine, specifically Corbevax, around 1:45 pm. Up until that time, the patient appeared to be in good health. However, shortly after the vaccination, at approximately 2:30 pm, he began experiencing symptoms including giddiness, headache, diplopia (double vision), and drooping of the left eyelid and deviation of the left eyeball towards the lateral side. These symptoms had a sudden onset, were progressive in nature, and did not involve any pain. The patient was referred to our hospital by paediatrician.

He had no history of obesity, systemic vasculitis, headache, neurological or thyroid disease. He 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 such as headache, jaw or tongue claudication, polymyalgia rheumatica, visual loss. On a general physical examination, his blood pressure was 110/60 mm hg, pulse 110 /minute. Systemic examination was done and no any significant finding was there. On ophthalmological examination, the patient presented mydriasis with severe ptosis in his left eye, compromising the visual axis. Pupillary light reflex showed an unreactive left pupil to the illumination. 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. His visual acuity was 6/9 in her right eye, and 6/6 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, 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. Fundoscopy in both eyes was normal with no signs of diabetic retinopathy, venous or arterial occlusions, and no optic nerve pallor or thinning. No indications of myasthenia gravis disease were observed during the examination. The sustained upward gaze did not result in an increase in ptosis.

During the neurological examination, the patient was alert oriented, and cooperative. His speech was clear and fluent. A thorough assessment of the cranial nerves did not reveal any significant findings. Facial sensation and corneal responses were intact. His face exhibited symmetry, and he had normal hearing abilities. The elevation of the palate was symmetrical. Phonation, head-turning, and shoulder shrug were all normal. Additionally, his tongue appeared midline with normal movements and no signs of atrophy. During the motor examination, the patient did not exhibit any pronator drift of outstretched arms. Muscle bulk, tone, and symmetry were within normal limits. Bilateral strength was graded as 5/5, indicating full strength. Reflexes at the biceps, triceps, knees, and ankles were symmetric and graded as 4/4. Plantar responses showed a flexor response. Sensitivity in the fingers and toes to light touch, pinprick, position sense, and vibration sense was normal. Coordination was intact, as evidenced by the absence of dysmetria during finger-to-nose and heel-knee-shin tests. Rapid alternating and fine finger movements were also intact. The Romberg test was negative, indicating no loss of balance with eyes closed. The patient maintained a normal posture. Gait was steady, and the patient demonstrated normal walking on toes and heels. In addition, the patient performed a normal tandem gait with one eye closed.

On blood work, his complete blood count (CBC), CSF cytology, CSF culture and Gram staining were unremarkable. COVID-19 testing by polymerase chain reaction was done to rule out COVID-19 infection and was negative. Imaging of the brain that, the magnetic resonance imaging (MRI) of the brain showed mild prominence of CSF sleeve surrounding left optic nerve indicative of early subtle changes in the neurology that suggest an inflammatory or demyelinating process.

Thus, with the help of history and clinical examination and investigation we rule out tumour, vascular ischemia, trauma, haemorrhage, aneurysm, myasthenia gravis n came to conclusion that third nerve palsy is adverse event of Corbevax vaccination.

He was treated injection Methyl prednisolone 500 mg

iv in 500 ml Normal saline and injection Pantoprazole 40 mg iv, Carboxymethylcellulose eye drops 0.5 %. Ophthalmic examination showed steady improvement and 4 days after his symptoms had completely resolved.

Discussion

The global pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had an extraordinary impact on public health. The infection can manifest in a wide range of ways, from asymptomatic cases and mild respiratory symptoms to severe respiratory distress that can be life -threating. Furthermore, it is important to note that SARS-CoV-2 can affect multiple organs throughout the body, making it systemic illness rather than solely a respiratory condition (9). Most adverse reactions to vaccines result from excessive immune responses and inflammatory damage. Clinical trials undergo rigorous safety monitoring before vaccine authorization, but some serious adverse events may go undetected due to limited follow-up duration, small sample size, restrictive eligibility criteria, and participant selection that may not represent the general population. COVID-19 vaccines, underwent an accelerated development process due to the urgent need to address the pandemic and its devastating impact on lives. Due to the urgent need posed by high mortality rates and the wide-reaching impact of the virus, the development stages of these vaccines were accelerated without compromising safety (10).

The complexity of determining adverse reaction causal relationship following vaccination is challenging. The WHO has developed a four-step algorithm for assessing causality in Adverse Events Following Immunization (AEFI). These guidelines provide a systematic approach to determine the relationship between a vaccine and reported adverse events.

The first step of the algorithm involves considering whether there is compelling evidence for alternative causes of the adverse event. In our case compressive, vascular cause ruled out with the help of history, physical examination, blood test and imaging study.

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. In our case oculomotor dysfunction occurred on same day following first dose of vaccination which is suggestive of temporal association. Up to our knowledge only four cases of oculomotor nerve palsy following Covid vaccination were published. Numerous reports have provided evidence that cranial nerve palsies, including oculomotor nerve involvement, can be observed as part of the neurological manifestations associated with COVID-19 infection (11,12).

In published case report by Kerberg Anthony Kerbage,Sara F. Haddad , oculomotor nerve palsy after Pfizer-BioNTech COVID-19 vaccine , shows similar symptoms as like in our case also suggest temporal association between Covid vaccination and occurrence of oculomotor nerve palsy.

The WHO guidelines recommend considering any robust evidence contradicting a causal link between oculomotor nerve palsy and the COVID-19 vaccine. However, a comprehensive examination of all available literature published since the start of the pandemic revealed no data that would disprove the possibility of an association between the COVID-19 vaccine and this condition. Maria Mirabela Manea Dorin Dragoș Iulia Enache et al., observed various cranial neuropathy following Covid vaccination highlighting need for prolonged surveillance of Covid-19 vaccine.

Maria Pia Cicalese,Francesca Ferrua , Federica Barzaghi, et al., noticed isolated incomplete third nerve palsy after 3days after the first administration of Moderna mRNA-1273 SARS-CoV-2 vaccine They came with conclusion causality consistent casual association with vaccine after doing various laboratory teste to demonstrated titre of antibodies with luciferase immunoprecipitation . In our case confirmation by checking antibody levels were not done due to unavailability of these test at hospital.

A recent review found that cranial nerve palsies after COVID-19 infection typically resolved on their own within 2-6 weeks. In our case, although the oculomotor palsy resolved within 4 days of occurrence; a rapid antigen test had been done to rule out COVID 19 and hence the likely hood of the oculomotor palsy occurring after COVID-19 vaccination rather than the infection itself increases.

WHO guideline also asks for finding strong evidence against casual association between oculomotor nerve palsy and vaccine. We have not come across any such evidence in available literature.

Considering the available arguments, while we cannot definitively confirm a causal association between oculomotor nerve palsy and the COVID-19 vaccine, it is considered plausible, and we can categorize it as "consistent" according to the WHO algorithm's final step.

Pathogenesis of this rare side effect is uncertain. An analogy can be drawn with facial nerve palsy, which has been associated with adverse events from other vaccines. The mechanism is thought to involve an immunomodulatory response that damages myelin sheaths and surrounding axons within cells. In theory, after COVID-19 vaccination, a similar immune response could lead to damage through antigenic mimicry or bystander activation of autoreactive T cells.10However further studies are required to understand pathogenesis.

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Conflict of interest
The author declares no conflict of interest, financial or otherwise.

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