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Myasthenia gravis with ocular symptoms following a ChAdOx1 nCoV-19 vaccination: A case report

Min Chae Kang [a], Kyung-Ah Park [a,*], Ju-Hong Min [b,**], Sei Yeul Oh [a]

[a] Department of Ophthalmology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea
[b] Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea

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ABSTRACT

Purpose: We report on the case of a 35-year-old man who developed myasthenia gravis with ocular symptoms following a ChAdOx1 nCoV-19 vaccine injection.

Observations: A 35-year-old man complained of binocular diplopia one month following ChAdOx1 nCoV-19 vaccination. He had weak infraduction of the left eye. Upper and lower extremity strength was normal on presentation. A serum antiacetylcholine receptor antibody titer was elevated at 1.60 nmol/L. His diplopia improved temporarily following the application of an ice pack for 2 min.

Conclusions and importance: This case report describes a rare occurrence of myasthenia gravis with ocular symptoms as a potential complication of ChAdOx1 nCoV-19 vaccination.

1. Introduction

In December 2019, the World Health Organization announced that a novel coronavirus, SARS-CoV-2, was responsible for a pandemic outbreak of coronavirus disease-19 (COVID-19). More than four million people worldwide have died because of this ongoing outbreak. Currently available vaccines have shown excellent and promising results in preventing symptomatic COVID-19.[1–4] However, vaccine side effects may occur, although this risk is low.[5–12] There may be undocumented complications following commercial release because only a limited number of people participated in the clinical trials.[13]

Available SARS-CoV-2 vaccines include the ChAdOx1 nCoV-19 vaccine (AZD1222) that was developed at Oxford University. This consists of a replication-deficient chimpanzee adenoviral vector ChAdOx1. This vaccine contains the SARS-CoV-2 spike protein (nCoV-19) gene,[1] and has shown excellent efficacy and safety profiles.[1]

The "*COVID-19 vaccine AstraZeneca analysis print*" lists all United Kingdom spontaneous reports of suspected adverse drug reactions to the ChAdOx1 nCoV-19 vaccine that had been received between April 01, 2021, and June 30, 2021. Various ophthalmic reactions involving the eyelid, anterior segment, retina, optic nerve, and extraocular muscles were reported in this document, including two cases of ocular myasthenia, as well as 12 cases of myasthenia gravis and three cases of myasthenia gravis crises. However, the list does not imply a causal link between the vaccine and these listed diseases. Until now, only a few cases of myasthenia gravis following nCoV-19 vaccination have been published.[14–18]

In our case report, we describe in detail the clinical presentation of a 35-year-old man who developed myasthenia gravis with ocular symptoms following a ChAdOx1 nCoV-19 vaccine injection.

2. Case report

This 35-year-old, healthy man was referred to our clinic because of binocular double vision that had started about three weeks earlier. There was no significant past medical history, such as diabetes mellitus, hypertension, hyperlipidemia, cardiovascular disorder, or autoimmune disease. There was no significant surgical history or social history. He denied any trauma history. The only medication he had received recently was the first dose of the AstraZeneca adenovirus vectored vaccine ChAdOx1 nCoV-19 (AZD1222) one month earlier. On the evening of vaccination, he developed headache, dizziness, numbness in

* Corresponding author. Department of Ophthalmology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul, 06351, South Korea.
** Corresponding author. Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul, 06351, South Korea.
E-mail addresses: kparkoph@skku.edu (K.-A. Park), juhongm@skku.edu (J.-H. Min).

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both upper and lower extremities, and diarrhea. He developed nausea four days following the vaccination, and all these symptoms then spontaneously resolved. One week after the vaccination, the patient developed an acute-onset of vertical binocular diplopia. On review of the case, there were no other symptoms.

On ocular examination, his visual acuity was 20/20 and intraocular pressure was normal in both eyes. We measured an 8 prism diopters (PDs) left hypertropia. The extraocular motility test showed full ductions of his right eye. But we observed a 75% infraduction in the left eye. His diplopia temporarily improved following ice packing for 2 min. Both pupils reacted normally to direct light, and we observed no disability in afferent pupillary reactions. The anterior segment examination showed normal findings, and the fundus examination revealed a healthy-appearing optic nerve. Retinas in both eyes were without significant torsion.

His upper and lower extremity strength on both sides was normal, as were his deep tendon reflexes.

Our review of a pre- and post-contrast high-resolution cranial nerve magnetic resonance 3-D imaging using a 3-T system (Magnetom Skyra; Siemens Healthineers, Erlangen, Germany) revealed no abnormality in the cranial nerve III, IV, or VI pathways, and we found no abnormality on magnetic resonance angiography.

Laboratory tests, including white blood cell count, hemoglobin level, erythrocyte sedimentation, C-reactive protein, and electrolytes were all normal. Serological investigations revealed a positive antinuclear antibody result, whereas the patient's antineutrophil cytoplasmic antibody showed a negative result. The anticardiolipin antibody, ganglioside antibody, and thyroid antibody were all noted to have been within normal range. Acetylcholine receptor antibodies were noted as 1.60 nmol/L, which was above the normal limit (normal range 0–0.500 nmol/L). Based on the above results, the patient was diagnosed with myasthenia gravis with ocular symptoms. No thymus abnormality was observed on chest computed tomography.

3. Discussion

Myasthenia gravis is an autoimmune disease caused by autoantibodies to the acetylcholine receptors at the neuromuscular junction. The availability of acetylcholine receptors at the postsynaptic neuromuscular junction decreases because of antibody destruction and the inflammatory response in myasthenia gravis patients. Most patients with myasthenia gravis commonly have an initial presentation of ocular manifestations, such as pupil-sparing ptosis and/or diplopia.[19] A myasthenia gravis diagnosis can be confirmed by seropositivity of acetylcholine receptor antibodies or of antibodies to other neuromuscular junction proteins, including antimuscle specific tyrosine kinase. Finding elevated acetylcholine receptor antibody levels is highly specific for myasthenia gravis, although only 85%–90% of patients with generalized myasthenia gravis and 50% of ocular myasthenia gravis patients have detectable antibodies.[20]

The key pathogenic mechanism of autoimmune disease such as myasthenia gravis is thought to be molecular mimicry by which viral or bacterial agents trigger an immune response against autoantigens.[21–23] In the development of myasthenia gravis, antibodies produced by an inflammatory reaction to an external agent can cross react with the acetylcholine receptors because of molecular resemblance. This leads to damage.[24,25] The production of autoantibodies for myasthenia gravis is a B cell-dependent process and plays an important role in the loss of self-tolerance and dysregulation.[25]

Reports on autoimmune reactions following vaccination would probably constitute less than 0.01% of all vaccinations performed worldwide, although underreporting may bias these calculations.[21] As infectious agents may induce autoimmunity, we can assume that vaccinations may also trigger autoimmunity in a similar way. Thus, vaccination should be considered as part of the mosaic of autoimmunity, in which abrogation of one autoimmune disease may concomitantly induce another autoimmune disease.[21] But we should also consider the possibility that the onset of myasthenia gravis symptoms with vaccination could be coincidental. We cannot rule out that a pre-existing subclinical myasthenia gravis might by unmasked by a viral-like illness following vaccination even if the patient had had no symptoms.[26]

Myasthenia gravis following vaccination is rare, and only a few reports of myasthenia gravis following human papillomavirus or hepatitis B vaccinations have been previously published.[27,28] Also, a few cases of myasthenia gravis following nCoV-19 vaccination have recently been published.[14–18] One case developed myasthenia gravis after the ChAdOx1 nCoV-19 vaccine administration,[15] as in this case, and some cases developed myasthenia gravis after administration of other types of vaccines.[14,16–18] Among them, there were four case reports of generalized myasthenia gravis, occurring after the second dose of BNT162b2 (Pfizer-BioNTech)[14,16,18] and after the second dose of Moderna nCoV-19 vaccination, and one case report of myasthenia gravis with ocular symptoms only.[15] In one case report, a patient who had only ocular symptoms exhibited left-sided ptosis eight days after receiving his first dose of ChAdOx1 nCoV-19 vaccination.[15] His low-frequency repetitive nerve stimulation showed a decreased amplitude, and a serum anti-AChR antibody titer was 1.9 nmol/L at 20 days post-vaccination.

4. Conclusion

This case report implies that COVID-19 vaccination may cause myasthenia gravis with ocular symptoms. The underlying mechanism of the disease following vaccination requires further investigation.

Patient consent

Informed consent was obtained from this patient at the Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The following authors have no financial disclosures: MCK, KAP, JHM, SYO.

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