Coincidental onset of ocular myasthenia gravis following ChAdOx1 n-CoV-19 vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

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TO THE EDITOR:

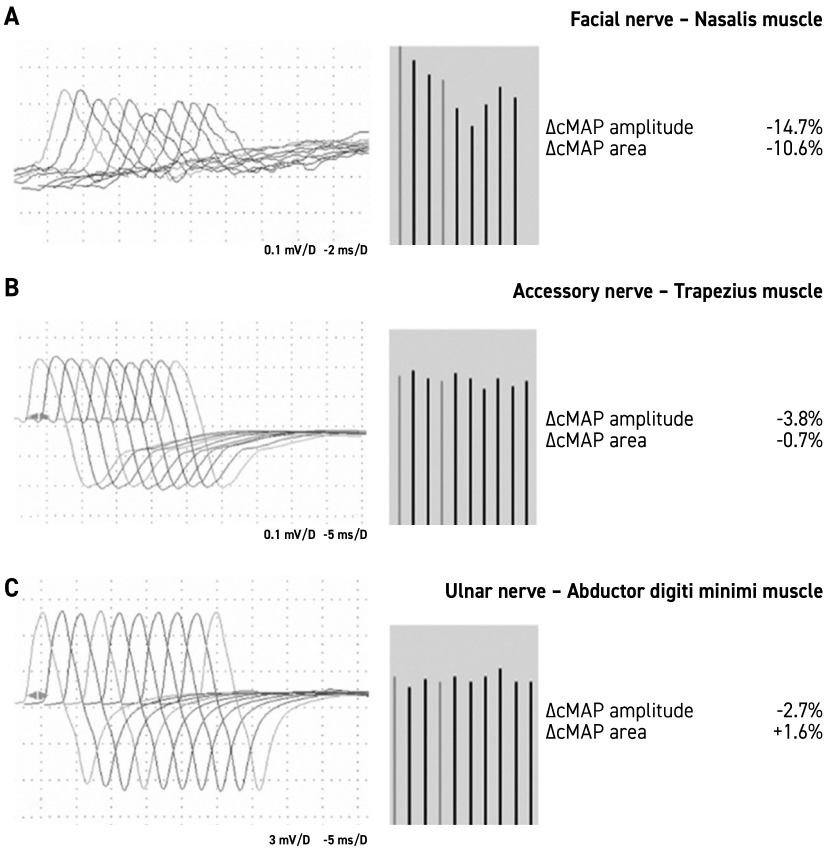
The Oxford-AstraZeneca vaccine ChAdOx1 (AZD1222, Vaxzevria) is playing a crucial role in counteracting the coronavirus disease-2019 (COVID-19) pandemic [1]. Since March 2021, reports of unexpected thrombotic events associated with thrombocytopenia and vaccination have been published [2]. To the best of our knowledge there is only one report about vaccination-associated myasthenia gravis (MG) occurring after a second dose of BNT162b2 (Pfizer-BioNTech) [3].

MG is an autoimmune disease in which antibodies bind to acetylcholine receptors (AChRs) or to functionally related molecules in the post-synaptic membrane at the neuromuscular junction [4,5]. MG can be triggered and worsened by infections, but no virus or other pathogens have been proven to have a specific link to MG [4,5].

We describe what we believe is the first reported case of ocular myasthenia gravis after AZD1222, Vaxzevria with onset a few days after the first dose. A 73-year-old male smoker had history of mild hypertension and myocardial infarction 10 years previously. He reported recent episodes of psoriasis in both elbows. The same night of the vaccination, the man developed myalgias and a fever up to 39°C, which was treated with paracetamol. The fever relapsed the following day. Eight days later, the patient exhibited painless left-sided ptosis without diplopia. The eye lid weakness worsened during the day, without other complaints of cranial or extremity weakness. Brain imaging excluded abnormalities. Exhaustive laboratory examinations ruled out common and uncommon causes of polyneuropathy; whereas, he had a positive rheumatoid factor (240 IU/ml, normal < 20 IU/ml) without signs of joints or arthritic involvement. Nasopharyngeal swab and real-time reverse transcriptase polymerase chain reaction testing for COVID-19 were negative. Low-frequency repetitive nerve stimulation showed 14.7% decrement in amplitude of nasalis muscle of the compound muscle action potential [Figure 1]. Thorax computed tomography excluded a thymoma. The serum titer of anti- AChR antibodies on day 20 after vaccine injection was 1.9 nmol/l (normal < 0.25 nmol/L). We administered pyridostigmine bromide (240 mg /daily) and the patient showed typical improvement unequivocally confirming the diagnosis of ocular MG.

Several considerations need to be contemplated. First, we were aware that the neurological onset beginning within days after exposure to the first of vaccine together with the presences of AChR antibodies in serum may imply a pre-existing memory cell population [4]. Therefore, even if the patient had no previous symptoms of fatigability, we could not rule out a pre-existing subclinical MG unmasked by a viral-like illness induced by the vaccination [4]. Second, it is well-known that infections are a major external causal factor for nearly all autoimmune disorders through an augmentation of T-cell signal-

Figure1. Low frequency (5Hz) repetitive nerve stimulation (RNS). Facial nerve stimulation shows a significant decrement of 14.7% in the amplitude of compound muscle action potential of the nasalis muscle [A], while the response in the accessory [B], and in the ulnar [C] nerves are normal



ing, which cause a pro-inflammatory environment due to a hyper-reactive antiviral immune response and a polyclonal activation of immunoactive cells, including autoreactive B- and T-lymphocytes [4,5].

Due to the urgent need to counteract COVID-19, diverse severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine types including inactivated nucleic acid, adenovirus-based vector, and recombinant subunits vaccines have been developed [1]. Primate adenovirus has been engineered to carry a relevant gene from the virus, usually the S gene for coronaviruses [1].The key advantage of vector vaccines is that the immunogen is expressed in the context of a heterologous viral infection, which induces the innate immune responses required for the adaptive immune responses [4]. Nevertheless, this strategy may induce prior immunity to the vectors; therefore, the included viral components in some subjects may cause unbalanced humoral and T-cell mediated autoimmunity [4]. Several mechanisms have been proposed for pathogen-triggered autoimmunity, including molecular mimicry, epitope spreading, bystander activation, and polyclonal activation [3,4]. In MG without thymoma, as in this case, an autoimmune process is presumed to initiate in the thymus following an unknown trigger and the resulting AChR-antibody-producing B cells become self-perpetuating in peripheral lymphatic tissue on the background of functionally defective regulatory T cells [4,5]. Defective generation of regulatory T cells, both in thymus and peripheral lymphatic tissues contribute to the maintenance of multiple tissue-specific autoimmune responses [5]. Both of these pathogenic processes may need some time to develop.

In our patient, the recent history of psoriasis might represent an immunological trait deserving consideration. Traditionally, psoriasis is considered as a T cell-controlled systemic inflammatory disease modulated by genetic susceptibility along with environmental factors. We think that clinicians should be aware of such rarely occurring neurological condition. In addition, we fully support the safety of SARS-CoV-2 vaccination in the general population because the induced immune response represents a potent protection against the infection [1].

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Capsule

Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a double-blind, randomized, phase 1 trial

To mitigate the effects of COVID-19, a vaccine is urgently needed. BBV152 is a whole-virion inactivated SARS-CoV-2 vaccine formulated with a toll-like receptor 7/8 agonist molecule adsorbed to alum (Algel-IMDG) or alum (Algel). **Ella** and colleagues performed a double-blind, multicenter, randomized, controlled phase 1 trial to assess the safety and immunogenicity of BBV152 at 11 hospitals across India. Between 13 and 30 July 2020, 827 participants were screened, of whom 375 were enrolled. Among the enrolled participants, 100 each were randomly assigned to the three vaccine groups, and 75 were randomly assigned to the control group (Algel only). After both doses, solicited local and systemic adverse reactions were reported by 17 (17%, 95% confidence interval [95%CI] 10.5–26.1) participants in the 3 µg with Algel-IMDG group, 21 (21%, 95%CI 13.8–30.5) in the 6 µg with Algel-IMDG group, 14 (14%, 95%CI 8.1–22.7) in the 6 µg with Algel group, and 10 (10%, 6.9–23.6) in the Algel-only group. The most common solicited adverse events were injection site pain (17 [5%] of 375 participants), headache (13 [3%]), fatigue (11 [3%]), fever (9 [2%]), and nausea or vomiting (7 [2%]). All solicited adverse events were mild (43 [69%] of 62) or moderate (19 [31%]) and were more frequent after the first dose. One serious adverse event of viral pneumonitis was reported in the 6 µg with Algel group, unrelated to the vaccine. Seroconversion rates (%) were 87.9, 91.9, and 82.8 in the 3 µg with Algel-IMDG, 6 µg with Algel-IMDG, and 6 µg with Algel groups, respectively. CD4+ and CD8+ T-cell responses were detected in a subset of 16 participants from both Algel-IMDG groups.

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