

Acute Hemichorea-Hemiballismus Following COVID-19 (AZD1222) Vaccination

Achieving immunity to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) through vaccination is a key worldwide public health strategy for controlling the coronavirus disease 2019 (COVID-19) pandemic. The ChAdOx1 nCoV-19 (AZD1222; AstraZeneca) vaccine, consisting of an adenoviral vector containing the SARS-CoV-2 spike protein gene, has been shown to be efficacious against COVID-19 with an acceptable safety profile.¹ To date, AZD1222 has been licensed in more than 150 countries worldwide, and monitoring for potential adverse effects of COVID-19 vaccines is ongoing. Although *de novo* movement disorders have been reported in response to COVID-19 infection,² such complications after vaccination have yet to be formally reported (excluding videos on social media platforms³). AZD1222 was licensed in Australia in early 2021 wherein rates of vaccination increased against a background of minimal community transmission of SARS-CoV-2, providing an opportunity to observe clusters of adverse reactions. We report two consecutive, strikingly similar presentations of acute hemichorea/hemiballismus after AZD1222.

Case 1 (Supporting Information Video S1) is an 88-year-old man who presented 16 days after the first dose of AZD1222 having been awoken by involuntary movements of the left arm, leg, and face that worsened throughout the day. He had a medical history of treated dyslipidemia, hypertension, and gout.

Case 2 (Supporting Information Video S2) is an 84-year-old man who presented 40 days after the first dose of AZD1222 with acute onset of involuntary hyperkinetic movements of the left upper and lower limbs noted initially while watching television, worsening through the evening, and interfering with sleep. He had a history of asthma, allergic aspergillosis, and primary

orthostatic hypertension and treated colorectal, esophageal, and prostate carcinomas in remission.

In both cases, there were no other neurological or systemic symptoms. There was no personal or family history of movement disorders. The neurological examination in both cases demonstrated continuous, nonpatterned, small-amplitude movements of the affected arm and leg, with superimposed proximal irregular large-amplitude movements consistent with hemichorea-hemiballismus. Mild parkinsonism affecting the contralateral side was noted in case 1. The remainder of the neurological and systemic examination was unremarkable.


An extensive panel of investigations (Table 1) including magnetic resonance imaging (see Supporting Information) did not reveal an alternative cause. An autoimmune postvaccination reaction was hypothesized, and both patients were given a short course of steroids (three daily doses of 1 g intravenous methylprednisolone), with case 1 demonstrating a prompt and significant resolution within 24 hours of the first dose. Case 2 had partial spontaneous improvement after the first day but had persistent symptoms that resolved after 3 days of corticosteroids.

We describe two cases of acute and reversible hemichorea-hemiballismus after AZD1222 vaccination. Based on the steroid-responsiveness of our cases, an inflammatory mechanism was proposed. This is in line with a recent report of a patient with worsening levodopa-induced dyskinesias after receiving the BNT162b2 (Pfizer/BioNTech) mRNA vaccine,⁴ and preclinical studies supporting a role of neuroinflammation in levodopa-induced dyskinesia generally.⁵ The unilateral symptomatology in our cases is interesting; however, similarly focal presentations in the setting of systemic autoimmune disorders, such as Sydenham's chorea, have been reported.⁶ Alternatively, subclinical Parkinsonism affecting the contralateral side (case 1) could also have masked a bilateral process. Extrapolating from the neuropathology of COVID-19-associated neurological dysfunction,⁷ we speculate a focal immune-mediated endotheliopathy induced by the spike protein as a mechanism explaining the presentations reported in this letter.

Overall, COVID-19 vaccines have been demonstrated to be safe and effective, and idiosyncratic neurological reactions after vaccination are rare and tend to be monophasic. These cases highlight the need for careful clinical observation to aid pharmacovigilance efforts and the importance of large epidemiological studies to confirm potential neurological postvaccination reactions. ■

Data Availability Statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

Elie Matar, MBBS, BSc (Adv),^{1,2*} 

David Manser, MBBS, BSc (Adv),¹

Judith M. Spies, MBBS, PhD,¹

John M. Worthington, MBBS, BSc (Med),¹ and

Kaitlyn L. Parratt, MBBS^{1*}

¹Department of Neurology, Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia, and ²Central Clinical School, University of Sydney, Sydney, New South Wales, Australia

© 2021 International Parkinson and Movement Disorder Society

Key Words: ChAdOx1 nCoV-19; COVID-19; vaccine; AZD1222; hemichorea; hemiballismus; movement disorder

***Correspondence to:** Dr. Kaitlyn Parratt, Department of Neurology, Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia; E-mail: kaitlyn@sharpneurology.com; or Dr. Elie Matar, Central Clinical School, University of Sydney, Sydney, New South Wales, Australia; E-mail: elie.matar@sydney.edu.au

Relevant conflicts of interest/financial disclosures: E.M., D.M., J.M.S., J.M.W., and K.L.P. are employed by New South Wales Health. E.M. was supported by a National Health and Medical Research Council postgraduate research fellowship and the Australian and New Zealand Association of Neurology Education and Research Foundation.

Full financial disclosures and author roles may be found in the online version of this article.

Received: 10 August 2021; **Revised:** 31 August 2021; **Accepted:** 2 September 2021

Published online 28 September 2021 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.28796

TABLE 1 Investigations performed to exclude secondary causes of hemichorea-ballism

Category	Investigations Performed	Case 1	Case 2
Routine	Full blood count, electrolytes, calcium, magnesium, phosphate, liver function tests, INR, serum glucose, HBA1c, CRP, ESR, TSH, T4	Normal range	Normal range
Autoimmune/vasculitis (serum)	ANAs, ENAs, ANCA, anti-RFs, anti-CCPs, dsDNAs, C3, C4, cryoglobulins, serum electrophoresis and immunofixation, anti-cardiolipin antibody (IgM and IgG), lupus anticoagulant, B2 glycoprotein antibody, thyroid microsomal and thyroglobulin antibodies	IgG Kappa paraprotein detected (11 g/L). Otherwise negative.	Negative
Autoimmune encephalitis/paraneoplastic (serum and CSF)	Anti-NMDAR, anti-CASPR2, anti-LGI-1, anti-GABA-B, anti-DPPX, anti-IgLON5, anti-VGCC, anti-Yo, ANNA-1, ANNA-2, amphiphysin antibodies, anti-Ma2, anti-AMPA, anti-GAD	Negative	Negative
Infectious	Anti-DNAse, syphilis EIA, hepatitis B core antibody, hepatitis B surface antigen, HIV 1 and HIV 2 antibodies, CMV PCR	Prior exposure to hepatitis B (immune). Otherwise negative.	Negative
Minerals	Ceruloplasmin, serum copper	Normal	Normal
CSF	Cell count, differential, MCS, cryptococcal antigens, viral PCR including HSV and VZV, oligoclonal bands, protein, glucose, lactate	0 leukocytes, 1 erythrocyte. Elevated protein (0.7 g/L). Otherwise negative.	1 leukocyte, 3 erythrocytes. Elevated protein (0.67 g/L). Otherwise negative.
Imaging	Chest X-ray, magnetic resonance imaging, magnetic resonance angiography, CT (aortic arch to circle of Willis), FDG PET (brain and whole body) [case 1], CT of neck, chest, abdomen and pelvis [case 2]	Chronic small vessel ischemic change. No acute stroke (mild). No basal ganglia signal. No vessel abnormalities. Normal otherwise.	Chronic small vessel ischemic change. No acute stroke (mild). No basal ganglia signal. No vessel abnormalities. Normal otherwise.
Other	Cardiac telemetry	Sinus rhythm	Sinus rhythm

Routine and specialized investigations performed for the exclusion of alternative causes of hemichorea-hemiballismus.

AMPA, AMPA receptor; ANA, antinuclear antibody; ANCA, anti-neutrophil cytoplasmic antibody; ANNA, antineuronal nuclear antibody; anti-CCP, cyclic-citrullinated peptide antibody; anti-RF, rheumatoid factor antibody; C3, C4, complement; CMV, cytomegalovirus; CRP, C-reactive protein; CSF, cerebrospinal fluid; CT, computed tomography; dsDNA, double-stranded DNA antibody; EIA, Enzyme immunoassay; ENA, extractable nuclear antigen antibody; ESR, erythrocyte sedimentation rate; FDG, fluorodeoxyglucose; GAD, glutamic acid decarboxylase; HBA1c, glycosylated hemoglobin; HSV, herpes simplex virus; INR, international normalized ratio; MCS, Microscopy, culture and sensitivities; NMDAR, N-methyl-D-aspartate receptor; PCR, polymerase chain reaction; PET, positron emission tomography; TSH, thyroid-stimulating hormone; VGCC, Voltage gated calcium channel antibody; VZV, varicella zoster virus.

References

- Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet* 2021;397(10269):99–111.
- Ghosh R, Biswas U, Roy D, et al. De novo movement disorders and COVID-19: exploring the Interface. *Mov Disord Clin Pract* 2021; 8(5):669–680.
- Kim DD, Kung CS, Perez DL. Helping the public understand adverse events associated with COVID-19 vaccinations: lessons learned from functional neurological disorder. *JAMA Neurol* 2021;78(7):789–790.
- Erro R, Buonomo AR, Barone P, Pellicchia MT. Severe dyskinesia after administration of SARS-CoV2 mRNA vaccine in Parkinson disease. *Mov Disord* 2021. <https://doi.org/10.1002/mds.28772>
- Bishop C. Neuroinflammation: fanning the fire of l-dopa-induced dyskinesia. *Mov Disord* 2019;34(12):1758–1760.
- Dilenge ME, Shevell MI, Dinh L. Restricted unilateral Sydenham's chorea: reversible contralateral striatal hypermetabolism demonstrated on single photon emission computed tomographic scanning. *J Child Neurol* 1999;14(8):509–513.
- Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. *Lancet* 2020;395(10234):1417–1418.

Supporting Data

Additional Supporting Information may be found in the online version of this article at the publisher's web-site.