


Acknowledgments

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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References

- Zech M, Jech R, Boesch S, et al. Monogenic variants in dystonia: an exome-wide sequencing study. *Lancet Neurol* 2020;19(11):908–918.
- Hao M, Pu W, Li Y, et al. The HuaBiao project: whole-exome sequencing of 5000 Han Chinese individuals. *J Genet Genomics* 2021;48(11):1032–1035.
- Lefebvre JL, Kostadinov D, Chen WV, Maniatis T, Sanes JR. Protocadherins mediate dendritic self-avoidance in the mammalian nervous system. *Nature* 2012;488(7412):517–521.
- Mancia Leon WR, Spatzza J, Rakela B, et al. Clustered gamma-protocadherins regulate cortical interneuron programmed cell death. *Elife* 2020;9:e55374
- Carriere CH, Wang WX, Sing AD, et al. The gamma-Protocadherins regulate the survival of GABAergic interneurons during developmental cell death. *J Neurosci* 2020;40(45):8652–8668.

Supporting Data

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Two Cousins with Acute Hemichorea after BBIBP-CorV (Sinopharm) COVID-19 Vaccine



The recent COVID-19 pandemic has affected the world in several ways and caused many challenges. COVID-19 vaccines have variable degrees of immunogenicity and safety.¹

Here we report on two adolescents who developed hemichorea after receiving BBIBP-CorV (Sinopharm), an inactivated virus COVID-19 vaccine.

Case 1: A 13-year-old boy presented to our Movement Disorders clinic 7 days after receiving his first dose of

BBIBP-CorV (Sinopharm) inactivated virus. He began to experience left-sided involuntary movements. His past medical history was unremarkable, and he was otherwise healthy. He did not experience fever, cough, sore throat, or other symptoms. He was born full-term by vaginal delivery to nonconsanguineous parents and did not have any pre- and postnatal complications. His family history was unremarkable.

On examination, the boy had large-amplitude choreic movements affecting the right side of his body that affected his gait (Video S1-A). He did not have chorea in the face, abnormal tongue movements, or speech impairment. The remainder of the examination was unremarkable.

Case 2: A paternal cousin of the first, who was an 18-years-old man, received BBIBP-CorV (Sinopharm) 1 week after case 1 and after 7 days developed left-sided hemichorea. His past medical history was negative, and he was also born to nonconsanguineous parents. On examination, he had choreic movements that mainly affected the left upper limb and shoulder (Video S2) but also involved the left lower limb. His face was not affected, and he did not have abnormal tongue movements or speech impairment. The remainder of the examination was normal.

Extensive laboratory investigations of the blood and cerebrospinal fluid were carried out in both patients and were unremarkable (Table 1).

Brain MRI (magnetic resonance imaging) of case 1 showed multiple white matter lesions, one of them enhanced with gadolinium (Fig. 1). Patient 2 had few nonspecific white matter lesions (not shown).

Both were treated with intravenous methylprednisolone (1 g/d) for 3 days followed by oral prednisolone (50 mg/d) and tetrabenazine (25 mg/d), which caused moderate improvement after a 2-week follow-up (Video S1-B). At 1-month follow-up, patient 1 improved, and patient 2 still had mild choreic movements.

This is a description of hemichorea in two adolescents after Sinopharm vaccination, which is one of the most widely used COVID-19 vaccines globally.

Three cases with hemichorea have been reported previously, 2 after AZD1222 vaccination and 1 after Pfizer-BioNTech COVID-19 vaccination, but all reported patients were in their 80s.^{2,3}

The pathophysiology of hemichorea in these cases is not clear, but several theories have been described for hemichorea after COVID-19 vaccination. These include focal immune-mediated endotheliopathy induced by the spike protein² and functional disturbance in contralateral thalamus, which was confirmed by single-photon emission computed tomography.³

On the contrary, Decio et al reported an 11-year-old girl who developed chorea after the human papillomavirus

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Key Words: Hemichorea, BBIBP-CorV (Sinopharm), COVID-19

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TABLE 1 Laboratory investing to exclude secondary causes

Laboratory results	Investigations	Case 1	Case 2
CSF	Cell count, differential, protein, glucose, oligoclonal bands, culture, Sars-Cov-2 PCR	0 RBC, 0 WBC, protein 51 (g/L), glucose 56 (mg/dL) Otherwise negative	3 RBC, 4 WBC, protein 34 (g/L), glucose 64 (mg/dL) Otherwise negative
Autoimmune encephalitis/paraneoplastic (serum and CSF)	Anti-NMDAR, anti-CASPR2, anti-LGI-1, anti-GABA-B, anti-DPPX, anti-VGCC, anti-Yo, ANNA-1, ANNA-2, amphiphysin antibodies, anti-Ma2, anti-AMPA, anti-GAD	Negative	Negative
Vasculitis/autoimmune (serum)	ANAs, ENAs, ANCAs, anti-RFs, anti-CCPs, dsDNAs, C3, C4, cryoglobulins, anticardiolipin antibody (IgM and IgG), lupus anticoagulant, B2 glycoprotein antibody, PLP	Negative	Negative
Routine lab tests	Full blood count, electrolytes, calcium, magnesium, sodium, potassium, phosphate, liver function tests, INR, serum glucose, HbA1c, CRP, ESR, TSH, T4, BUN, creatinine, copper, ceruloplasmin	All in normal ranges (BS: 101)	All in normal ranges (BS: 111)

Abbreviations: CSF, cerebrospinal fluid; PCR, polymerase chain reaction; VGCC, voltage-gated calcium channel receptor; ANA, antinuclear antibody; AMPAR, AMPA receptor; GAD, glutamic acid decarboxylase; ENA, extractable nuclear antigen antibody; ANCA, anti-neutrophil cytoplasmic antibody; anti-RF, rheumatoid factor antibody; anti-CCP, cyclic-citrullinated peptide antibody; dsDNA, double-stranded DNA antibody; C3, C4, complement; INR, international normalized ratio; HbA1c, glycosylated hemoglobin; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; TSH, thyroid-stimulating hormone; BUN, blood urea nitrogen.

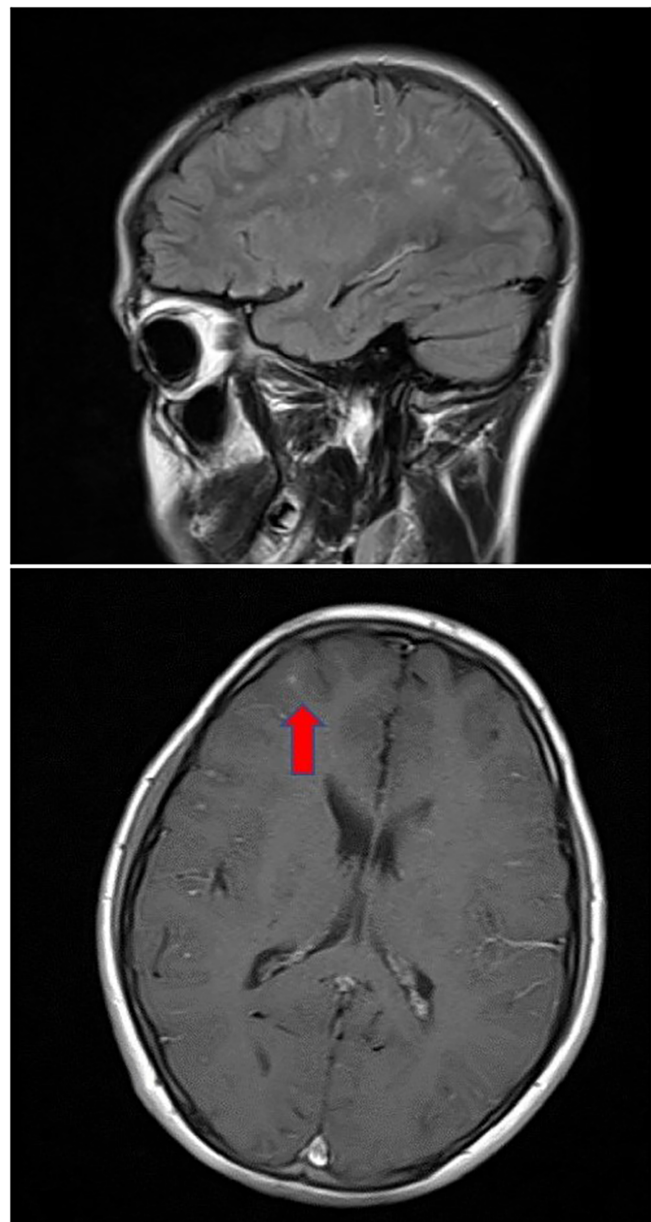


FIG. 1. Sagittal fluid-attenuated inversion recovery magnetic resonance imaging (FLAIR MRI) imaging (top image) shows multiple white matter lesions, and axial T1 with gadolinium (bottom image) demonstrates a juxtacortical gadolinium-enhancing lesion. [Color figure can be viewed at wileyonlinelibrary.com]

vaccine. She responded to steroids, which supported an autoimmune mechanism as the pathophysiology.⁴

In addition, a 62-year-old man has been reported with acute chorea after getting a Sars-Cov-2 infection, and the authors concluded that inflammation may have played a role in the development of chorea in this patient.⁵


Presentation of hemichorea in our patients suggests an inflammatory mechanism, as the first patient had inflammatory white matter changes on brain MRI, but the occurrence in the two cousins may indicate the possibility of a genetic predisposition as a factor for developing this phenomenon.

Although COVID-19 vaccines are generally safe, and neurological complications are rare and self-limited, these 2 cases

suggest that movement disorders can be a complication of vaccines. ■

Data Availability Statement

Data is available on request.

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References

1. Matarneh AS, Al-battah AH, Farooqui K, Ghamoody M, Alhatou M. COVID-19 vaccine causing Guillain-Barre syndrome, a rare potential side effect. *Clin Case Rep* 2021;9(9):1–5.
2. Matar E, Manser D, Spies JM, Worthington JM, Parratt KL. Acute Hemichorea-Hemiballismus following COVID-19 (AZD1222) vaccination. *Mov Disord* 2021;19:2–4.
3. Ryu DW, Lim EY, Cho AH. A case of hemichorea following administration of the Pfizer-BioNTech COVID-19 vaccine. *Neurol Sci* 2021; 43:771–773. <https://doi.org/10.1007/s10072-021-05763-5>
4. Decio A, Balottin U, De Giorgis V, Veggiotti P. Acute chorea in a child receiving second dose of human papilloma virus vaccine. *Pediatr Allergy Immunol* 2014;25(3):295–296.
5. Cotta Ramusino M, Perini G, Corrao G, Farina L, Berzero G, Ceroni M, et al. Sars-Cov-2 in a patient with acute chorea: innocent bystander or unexpected actor? *Mov Disord Clin Pract* 2021;8(6): 950–953.

Supporting Data

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

Effect of Public Interest in Magnetic Resonance Imaging–Guided Focused Ultrasound on Enrolment for Deep Brain Stimulation

Deep brain stimulation (DBS) of the ventromedial nucleus of the thalamus (VIM) is an established treatment for medication-refractory essential tremor (ET), approved more than two decades ago.¹ More recently, magnetic resonance

imaging–guided focused ultrasound (MRgFUS)-thalamotomy has been used to effectively treat ET.² In MRgFUS, more than a thousand transducers focus ultrasound into the deep brain, thus creating a thermoablation without craniotomy.³ MRgFUS adoption is rapidly expanding and so is the list of approved and experimental indications, including tremor-dominant Parkinson's disease.³

Not surprisingly, there has been significant public interest in MRgFUS given its less invasive approach, further fueled by increasing numbers of mainstream media articles recently.^{4,5}

Precisely since MRgFUS adoption in Toronto in 2013, we noted a significant increase in the number of patients referred to our movement disorders center for tremor management. Thus, we decided to focus on the referral pattern of tremor patients during the years 2014 to 2018 to have enough time to record the final decision. We gathered information on 176 patients referred for tremor management: 123 ET, 32 Parkinson's disease (including 4 with “antecedent ET”), 10 dystonic tremor, and 9 other tremor syndromes (6 multiple sclerosis, 2 orthostatic, and 1 neuropathic tremor); 2 patients were rediagnosed with functional tremor. We observed a significant increase in referrals compared with the years immediately before (Fig. 1A). Although only 3% of patients were referred by physicians for MRgFUS and 65% for surgical management in general (Fig. 1B), most patients referred for surgery were interested specifically in MRgFUS, perceived as a nonsurgical and safer option. Notably, no patients referred for FUS (and very few patients referred for general surgical approach) specifically knew about DBS, perceived as an experimental procedure by many. Although self-reported interest in FUS was high and brought patients to our center, most (53%) were optimally controlled with medication, 30% received VIM DBS, and only 9% eventually received MRgFUS (Fig. 1C). The decision between DBS or MRgFUS was individualized based on our internal decisional process, developed in the absence of head-to-head studies.⁶ In brief, DBS was preferred in younger patients, most likely needing long-term adjustments of the stimulation settings, whereas older patients were more often treated with MRgFUS given its minimally invasive nature. A limitation in our observation is the inherent bias derived by the fact that our center is one of the few in Canada to provide MRgFUS and is even more unique in providing it not only for ET.

In conclusion, the public interest on MRgFUS led to an increase of referrals for tremor management that eventually resulted in more patients receiving DBS. Interestingly, although the vast majority of patients were referred by neurologists and were all on some antitremor drug, medications changes achieved more successful clinical response for most patients, although they may still require surgery in the future. Most often this involved the adoption of one or more first-line anti-ET drugs.

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