Guillain–Barré syndrome following coronavirus disease vaccine: First report from Nepal

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Abstract
ChAdOx1 nCoV-19 is an effective and well-tolerated coronavirus disease 2019 vaccine. However, rare cases of serious adverse events have been reported with it. We report a patient who did not have active or prior coronavirus disease 2019 infection, who developed Guillain–Barré syndrome 7 days following the first dose of ChAdOx1 nCoV-19 vaccination. He was treated with intravenous immunoglobulin, with stabilization of the disease. Proper monitoring and prompt reporting of such cases are required to ensure the safety of the vaccine.

Keywords
ChAdOx1 nCoV-19, coronavirus disease 2019, Guillain–Barré syndrome, vaccination

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Introduction
Coronavirus disease 2019 (COVID-19) pandemic originating from Wuhan-China at the end of 2019 is the biggest global challenge we have faced since World War II. Vaccine development, trials, licensing are going at a rapid pace which is a must to fight against this global pandemic. Among them, COVISHIELD (ChAdOx1 nCoV-19) vaccine is a recombinant, replication-deficient chimpanzee adenovirus vector encoding the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Spike (S) glycoprotein produced in genetically modified human embryonic kidney (HEK) 293 cells with reported efficacy of 70.4% after two standard doses.

Nepal commenced a mass public immunization program against SARS-CoV-2 in 27 January 2021, and till 27 January 2022, 51% of the Nepalese population have received at least one dose. In addition, 38% of Nepalese population have received full doses among five approved vaccines. Neurological complications such as cerebral venous sinus thrombosis, Guillain–Barré syndrome (GBS), transverse myelitis following adenovector-based COVID-19 vaccines have recently been reported. To our knowledge, we report a first case of GBS in a 48-year-old male from Nepal after the first dose of ChAdOx1 nCoV-19 vaccination.

Case presentation
A 48-year-old gentleman presented to the emergency department with weakness of bilateral upper and lower limbs for 7 days, and slurring of speech for 6 days. On 15 February 2021, he had received his first dose of COVISHIELD (ChAdOx1 nCoV-19 coronavirus) vaccine. On the seventh post-vaccination day, patient noticed weakness of all four limbs on waking up in the morning. The weakness was more pronounced in lower limbs than upper limbs which restricted him to attain sitting position from supine, requiring support for waking up and ambulation, but he could freely move his toes. In addition, he complained of burning and tingling sensation in all four limbs, weakness in closing both eyes resulting their slight opening while sleeping. On the eighth post-vaccination day, he complained of slurring of speech, difficulty in swallowing both liquids and solids. The

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Table 1. Nerve conduction study: motor.

| Nerve  | Latency (ms) | Amplitude (µV) | NCV (m/s) |
|--------|--------------|----------------|-----------|
|        | D | P | D | P |          |
| Rt. CPN | 8.1 | 14 | 1.3 | 1.0 | 76.9 |
| Rt. PTN | 7.9 | 17.0 | 3.9 | 1.9 | 43.1 |
| Rt. Median | 3.3 | 8.2 | 1.2 | 1.0 | 63 |
| Rt. Ulnar | 1.2 | NS | 0.37 | NS |          |

D: distal; P: proximal; Rt.: right; NCV: nerve conduction velocity; NS: not stimulated; CPN: common peroneal nerve; PTN: posterior tibial nerve.

Table 2. Nerve conduction study: sensory.

| Nerve      | Latency (ms) | Amplitude (µV) | NCV (m/s) |
|------------|--------------|----------------|-----------|
| Rt. median | 2.5 | 24.9 | 47.6 |
| Rt. ulnar  | 1.7 | 26.0 | 66.3 |

Rt.: right; NCV: nerve conduction velocity.

weakness was gradually progressive involving upper limbs as well. On the twelfth post-vaccination day, he had fever and generalized body ache. However, there was no history of aspiration, nasal regurgitation or nasal intonation, headache, photophobia, double vision, abnormal body movements, loss of consciousness, and bowel or bladder incontinence. He had no history suggestive of gastrointestinal or respiratory illness prior to the onset of his symptoms, similar illnesses in the past, no significant familial, medical, surgical, traumatic, and vaccination (except ChAdOx1 nCoV-19 coronavirus vaccine) history.

On examination, his vitals were stable (heart rate 76/min, respiratory rate 20/min, blood pressure 140/80 mm Hg), afebrile, higher mental function was intact, cranial nerves were normal except cranial nerve VII palsy which resulted in weakness of eye closure more pronounced on left, absence of wrinkling on forehead, deviation of face to right, cranial nerve XI weakness resulting in the absence of shoulder shrug. Muscle bulk was normal, with reduced tone across joints. Power of shoulder abduction was 2/5, adduction 2/5, elbow flexion 4/5, extension 3/5, wrist flexion and extension 5/5, handgrip strength 50%, hip abduction and adduction 2/5, hip flexion and extension 2/5, knee flexion and extension 4/5, and toe flexion and extension 4/5. There was hyporeflexia of biceps, triceps, and absent reflexes in knee and ankle. Plantar reflex was mute on both sides. Sensation to touch, pain, and vibration was intact.

Hemoglobin was 14.5 gm/dL, Na⁺ 134 mEq/L, K⁺ 4 mEq/L, Ca²⁺ 8.3 mg/dL, alanine aminotransferase 270 U/L, aspartate aminotransferase 115 U/L, gamma glutamyl transferase 70 U/L (11–50), albumin 36 gm/L (38–49), urea 8 mmol/L, creatinine 87 µmol/L. Nerve conduction study was suggestive median and ulnar motor axonal neuropathy, tibial, and peroneal demyelinating motor neuropathy (Table 1). Sensory nerve conduction was normal (Table 2). Premature ventricular contractions were observed in electrocardiogram. Cerebrospinal fluid (CSF) reported sugar 3.8 mmol/L, protein 18 mg/dL, and 5 white blood cells with 100% lymphocytes. Magnetic resonance imaging brain and screening of whole spine were normal.

Based on clinical and laboratory findings, a diagnosis of GBS was made. After being admitted to Intensive Care Unit (ICU), he was commenced on intravenous immunoglobulin (IVIg) at the dose of 0.4 gm per day for 5 days. His condition started improving the second day following infusion. There was no complication during or after treatment. He was discharged after 2 weeks of hospital stay. On follow-up after 3 months, patient completely recovered with no sensory or motor sequela.

Discussion

The onset of neurological illness 7 days after vaccination and a lack of history of any recent infections including COVID-19 or other vaccinations make ChAdOx1 nCoV-19 vaccine a possible trigger for GBS in our patient. However, one must be cautious to ascribe the COVID-19 vaccination as a cause of it. This warrants robust post-vaccination surveillance, which requires both accurate clinical diagnosis and robust national reporting mechanisms.

The development of a post-vaccination neurological syndrome could result from the generation of host antibodies that cross-react with proteins present in peripheral myelin. There are reports of GBS after COVID-19 infection. Patients with GBS who had COVID-19 have a higher rate of Acute Inflammatory Demyelinating Polyneuropathy (AIDP), severe weakness requiring ICU hospitalization, and hypotension than those without COVID-19.

The ChAdOx1 nCoV-19 vaccine, which induces antibodies against SARS-CoV-2 spike glycoprotein, can mimic an actual infection and theoretically produce GBS. GBS can be caused by human adenoviral infections, and these adenoviruses are utilized in the ChAdOx1 nCoV-19 vaccination, which might possibly be a GBS trigger. Furthermore, in SARS-CoV-2-associated GBS, the human leukocyte antigen haplotype profile, which is determined by the host’s genetic composition, may play a role.

Vaccine adverse event report system (VAERS) defines vaccine-associated GBS as the onset of GBS symptoms within a 6-week period of receiving the vaccine. Vaccines that have been associated with GBS till date are: 1976 swine flu influenza vaccine, 2009 H1N1 influenza A vaccine, Measles–Mumps Rubella vaccine, human papilloma virus vaccine, quadrivalent meningococcal conjugate vaccine MC4 (Menactra), oral polio vaccine, Semple rabies vaccine, and tetanus toxoid containing vaccines. A case series from India reported seven patients who developed GBS within 2 weeks of the first dose of the ChAdOx1S vaccine. Similarly, our patient had onset of symptom 7 days after the vaccination. Quadripareisis,
sensory impairment in all four limbs as the main complaints and bilateral facial nerve palsy as sign was in line with previous studies.\textsuperscript{5,18} In a series of Maramattom et al.,\textsuperscript{5} six out of seven patients had respiratory failure. However, our patient did not progress to much severe illness, likely due to good response to the early IVIg treatment.

In our case, CSF count of 5 cells/µL with 100% lymphocytes was seen, which is a supportive feature for the diagnosis of GBS. Criteria for albumino-cytologic dissociation were not met because CSF protein was normal as measured on the eighth day of onset which can be the case in 17% of cases.\textsuperscript{19} Nerve conduction test revealed the pattern of motor axonal neuropathy (attached in Table 1). This observation was different from a case series where the majority had demyelinating neuropathy.\textsuperscript{5} However, both axonal and demyelinating subtypes were identified in a larger retrospective review, suggesting that pathogenesis can be diverse despite exposure to the same causal triggering event.\textsuperscript{18} The duration between onset of symptoms and nadir was 2 days in our case, which is in line with findings of Park et al. who reported median duration between the onset of symptoms to nadir 3 (interquartile range (IQR), 2–7 days).\textsuperscript{18} Our patient fell under Level 2 of the Brighton criteria.\textsuperscript{19} Despite the fact that complete recovery has only been reported in a small percentage of post-vaccination GBS cases, this was the experience with our patient.\textsuperscript{18}

### Conclusion

In the context of recent COVID-19 immunization, the specific presentation of sudden onset weakness of all four limbs as the primary symptom may represent a distinctive hallmark of GBS. As the number of vaccinations increases, it is critical to stay vigilant so that any potential elevated risk can be adequately addressed since early recognition and treatment can result in better recovery.

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### Author contributions

R.O. contributed to conceptualization, drafting, revising, and final approval of manuscript. P.L., S.P., B.P., D.U., and N.T contributed to data collection, data analysis, drafting, and final approval of manuscript. R.O., R.K., B.P.G., R.R., N.G., and A.S. contributed to case management and final approval of manuscript.

### Data availability

All data are provided within this review and data within original published papers noted in this review.

### Declaration of conflicting interests

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### Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

### Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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