Guillain-Barré Syndrome following ChAdOx1-S/nCoV-19 Vaccine

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As of April 22, 2021, around 1.5 million individuals in three districts of Kerala, India had been vaccinated with COVID-19 vaccines. Over 80% of these individuals (1.2 million) received the ChAdOx1-S/nCoV-19 vaccine. In this population, during this period of 4 weeks (mid-March to mid-April 2021), we observed seven cases of Guillain-Barre syndrome (GBS) that occurred within 2 weeks of the first dose of vaccination. All seven patients developed severe GBS. The frequency of GBS was 1.4- to 10-fold higher than that expected in this period for a population of this magnitude. In addition, the frequency of bilateral facial weakness, which typically occurs in <20% of GBS cases, suggests a pattern associated with the vaccination. While the benefits of vaccination substantially outweigh the risk of this relatively rare outcome (5.8 per million), clinicians should be alert to this possible adverse event, as six out of seven patients progressed to areflexic quadriplegia and required mechanical ventilatory support.

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As of April 22, 2021, more than 727 million doses of SARS/nCoV2 vaccines have been administered worldwide. ChAdOx1-S vaccine (Covishield™/Vaxzevria, Astra-Zeneca) has been administered in 116 countries, BNT-162b1 (Pfizer-BioNTech) in 83, mRNA-1273 (Moderna) in 36 and Ad26.COV2.S (Janssen) in two countries. In India, over 104 million doses of the SARS-CoV-2 vaccine have been administered and 13.5 million people have been fully vaccinated (1% of the population). The ChAdOx1-S vaccine (Astra Zeneca) has been used in >80% of the recipients.[1] In three districts of Kerala state (Ernakulam, Kottayam & Kannur) in India, approximately 1.2 million individuals had received the ChAdOx1-S vaccine as of April 22, 2021.[2]

Neurological complications such as cerebral venous sinus thrombosis (CSVT) due to vaccine-induced immune thrombotic thrombocytopenia (now termed thrombosis with thrombocytopenia syndrome [TTS]) following adenovector-based COVID-19 vaccines have recently been reported.[3] To date, one case of Guillain Barre Syndrome (GBS) has also been reported after Pfizer BNT-162b1 vaccination in the US.[4] Here, we report seven patients who developed GBS in very proximate temporal relationship to the first dose of ChAdOx1-S vaccination in a 4-week period (mid-March to mid-April, 2021).

Cases

The details of the initial four cases are presented here, while the clinical presentations of cases 5–7 are presented in the Table S1.

Case 1: A 43-year-old woman presented 10 days after the first dose of ChAdOx1-S vaccination with upper back pain. She progressed over the next 10 days to areflexic quadriparesis with facial diplegia and respiratory failure and required mechanical ventilation. Nerve conduction study showed a demyelinating neuropathy and cerebrospinal fluid (CSF) had albuminocytological dissociation (protein 72.2g/L, cell count 5/μL). She was treated with intravenous immunoglobulin (IVIg) but required mechanical ventilation on day 11 for respiratory distress (Table S1).

Case 2: A 67-year-old woman presented 14 days after the first dose of vaccination with distal paraesthesia in all four limbs. Over the next 2 days, she developed facial diplegia, dysphagia, and increasing limb weakness (motor strength 1/5). Subsequently, she developed a right abducens palsy and respiratory failure requiring mechanical

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ventilation, while being treated with IVIg. Plasmapheresis was initiated and she was extubated on day 15.

Case 3: A 53-year-old woman presented 12 days after her first dose of vaccine with bilateral lower limb numbness and weakness, right-sided facial and tongue numbness, and back pain. At the initial examination, her motor strength was grade 3/5 in all four limbs. Over the next 4 days, she developed right trigeminal sensory impairment, bilateral lower motor neuron facial palsy, and areflexic flaccid quadriplegia (MRC sum score 5), requiring mechanical ventilation.

Case 4: A 68-year-old woman presented 14 days after the first dose of vaccination with bilateral upper and lower limb numbness and weakness with dysphagia. Her initial motor strength was grade 4/5 in all four limbs. Over the next 4 days, she developed profound bilateral facial numbness along with bilateral lower motor neuron facial weakness and areflexic flaccid quadriplegia (MRC sum score 7).

In Patients 3 and 4, MRI brain and spine were normal (performed for evaluation of trigeminal sensory loss) and serum ganglioside antibodies were negative.

As of this report, six patients are still bedbound and undergoing rehabilitation (Hughes stage IV), whereas Case 1 has completely recovered.

Discussion

In this report, we describe seven patients who developed GBS within 2 weeks of the first dose of the ChAdOx1-S vaccine during a 4-week period (mid-March to mid-April, 2021.)

A calculated Naranjo adverse reaction scale score of 3 suggested a possible association between vaccination and GBS.[5]

Our patients were in their 5th to 7th decades of life and predominantly female (Female: Male ratio - 6:1). All patients progressed to areflexic quadriplegia, and six of the seven cases required mechanical ventilation for respiratory failure. All seven cases had bilateral facial paresis, which usually occurs in fewer than 20% of unselected GBS cases.[6] Four patients (57%) also developed other cranial neuropathies such as abducens palsy and trigeminal sensory nerve involvement, which are rare (<5%) in reports of GBS from India.[7]

The incidence of GBS in the community worldwide is approximately 17 cases per million per year. An analysis of previous post-vaccination periods (1976/1977 Swine flu and 2008/2009 H1N1 vaccination programs) has not revealed an increased incidence of post-vaccination GBS.[8] An association has also not been established between COVID-19 infection and GBS.[9] Therefore, an increase in the incidence of post-COVID vaccination GBS is thought unlikely.[10] Nevertheless, it is worth noting that as of March 24, 2021, the Food and Drug Administration (FDA) has updated warnings about GBS with another vaccine [GlaxoSmithKline's SHINGRIX™ (Zoster Vaccine Recombinant, Adjuvanted)] after noting three excess cases of GBS per million within 42 days of administration of the vaccine.[11]

The incidence of GBS in India is approximately 6–40 cases per million per year, with a seasonal variation, peaking in the rainy season (June–September).[12,13] With a denominator of 1.2 million people, the expected cases of GBS per year are approximately seven to 48 annually or between 0.58 to four cases of GBS every 4 weeks. Thus, with seven cases of GBS in1.2 million people (5.8 per million), a 1.4-to-10-fold rise in the incidence of GBS was observed.

Overall, our experience should prompt all physicians to be vigilant in recognizing GBS in patients who have received the ChAdOx1-S vaccine. While the risk per patient (5.8 per million) may be relatively low, our observations suggest that this clinically distinct GBS variant is more severe than usual and may require mechanical ventilation.

As in the case of the 'thrombosis with thrombocytopenia syndrome' (TTS), GBS seems to be associated with the first dose of ChAdOx1-S vaccine and the incidence seems to be higher within 14 days of administration However, the pathogenic mechanisms in post-vaccination GBS remain unclear.

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None.

Author Contributions

B.V.M., P.K., A.A.S. and H.S.M. contributed to the study concept and design.

B.V.M., P.K., R.P., S.P., and S.C. participated in the data acquisition and analysis.

B.V.M., P.K., A.A.S. and H.S.M. contributed to the drafting of the manuscript.

Potential Conflicts of Interest

Nothing to report.

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