Guillain-Barré Syndrome in a 67-year-old Male Post COVID-19 Vaccination (Astra Zeneca)

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Abstract
Since the COVID-19 pandemic has started in December 2019, millions of people have been infected all over the world and few vaccines have been invented recently. Extremely rare, Guillain-Barre Syndrome (GBS) was reported as a neurological complication after H1N1 flu vaccination. Currently, Pfizer and AstraZeneca vaccines are available to prevent infection with COVID-19. The first case of post-COVID-19 vaccine GBS has been detected in a secondary care hospital after vaccination with AstraZeneca. A 67-year-old man presented with an acute progressive ascending flaccid symmetrical motor neuropathy, and bilateral facial weakness which developed two weeks after receiving the first dose of AstraZeneca COVID-19 vaccine. His cerebrospinal fluid findings, nerve conduction result, and MRI brain result were all in favour of GBS diagnosis. The patient’s workup for all known infections associated with immune-mediated GBS was negative.

Keywords: COVID-19 infection, COVID-19 vaccine, Guillain-Barre Syndrome (GBS), Miller Fisher Syndrome (MFS)

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1. Introduction
Guillain-Barre Syndrome GBS is the most common and severe acute immune-mediated paralytic neuropathy with few variants which are usually preceded by an infection (the commonest is Campylobacter jejuni and less common are HIV, influenza virus, EBV, and CMV). [1,2,3,4]

Guillain-Barre Syndrome has been reported associated with, and post COVID-19 infection. [5,6]

Extremely rare, Guillain-Barre Syndrome was reported post flu vaccination. [7]

We report a 67-year-old male who presented to our hospital (15 days after receiving his first dose of COVID-19 AstraZeneca) with clinical features, cerebrospinal fluid findings, neurophysiological study, and MRI findings in favour of Guillain-Barre Syndrome. Other potential known infectious immune-mediated causes for GBS were excluded by our workup.

2. Case Presentation
A 67-year-old man presented to the Emergency department ED on 21st of February with the complaint of weakness of left side of the face was diagnosed as a lower motor facial palsy/Bell’s palsy and discharged with oral prednisolone. Four days later, he presented to ED with progressive worsening of the gait, bilateral leg weakness for two days, bilateral facial weakness, and difficulty in chewing food. There was no involvement of his upper limbs, and he had good control of the bowel and bladder. He is generally fully independent before his illness and lives with his family. He received the first dose of the AstraZeneca COVID-19 vaccine on 6th February 2021. There was no history of respiratory or gastrointestinal symptoms in the last 6 weeks before the onset of his weakness.

On examination, he had bilateral lower motor facial paralysis. No swallowing difficulty or double vision was noted. He had no ophthalmoplegia, or ataxia and his Glasgow Coma Scale was 15/15. The patient’s lower limb power was 3/5 on both sides with more proximal weakness, and areflexia. His sensation was intact, and plantar reflex was bilaterally flexor. Upper limbs power was 5/5 with areflexia. No respiratory involvement was noticed. He was known to have Hypertension and was on regular antihypertensive medications. The CT scan of the brain was normal. The laboratory investigations revealed hyponatremia, hyposmolality with normal thyroid, adrenal and renal functions. (Table 1)

The patient had a lumbar puncture and his cerebrospinal fluid CSF study revealed albumino-cytological dissociation with negative infection screen. (Table 1)

He was admitted to a monitored bed, developed watery diarrhea with no fever for three days, and the workup for infectious causes was negative. (Table 1)
Table 1. Significant blood tests and CSF results of the patient

| Test                        | Normal Level                     |
|-----------------------------|----------------------------------|
| Serum sodium                | 123 mmol/L (135-145 mmol/L)      |
| Serum osmolality            | 265 mOsmol/kg (280-290 mOsmol/kg)|
| Urine osmolality            | 275 mOsmol/kg (100-1200 mOsmol/kg)|
| Serum creatinine            | 50 umol/L (60-110 umol/L)        |
| Serum potassium             | 4.1 mmol/L (3.3-5.0 mmol/L)      |
| TSH thyroid stimulation hormone | 2.3 mIU/L (0.27-4.0 mIU/L)    |
| Free T4                     | 14 pmol/L (12-22 pmol/L)         |
| Cortisol                    | 430 nmol/L (120-600 nmol/L)      |

CSF cerebrospinal fluid

- Leucocytes count: 0^6/L (0-2^6/L)
- Neutrophil count: 0^6/L
- Protein: 3.9 g/L (0.25-0.45 g/L)
- Glucose: 4.8 mmol/L (blood glucose was 7 mmol/L)
- Lactate: 1.8 mmol/L
- Gram stain negative
- India ink stain negative
- CMV DNA PCR: Negative
- EBV DNA PCR: Negative
- Adenovirus DNA: Negative
- Varicella Zoster Virus DNA: Negative
- Herpes Simplex Virus DNA: Negative
- CSF culture: Negative > 72 hours
- COVID-19 RNA PCR swab: Negative (repeated x 3 after admission)
- Influenza A & B PCR: Negative
- RSV PCR respiratory syncytial virus: Negative

Serum viral Serology

- HIV 1 & 2 Antibody/Antigen: Negative
- EBV IgG: Positive
- EBV IgM: Negative
- CMV IgG: Positive
- CMV IgM: Negative
- Campylobacter IgA: Negative

Autoantibodies

- Antigangliosides antibodies GQB1: Negative

Blood culture: negative > 72 hours

Stool

- Culture: No growth of campylobacter, shigella or salmonella.
- Clostridium difficile PCR not detected
- Norovirus RNA: Negative

During his admission, there was no respiratory involvement, and 6 hourly spirometry was difficult due to his facial weakness. After being reviewed by the neurology team, IV immunoglobulin IVIG was prescribed 2gm/Kg IVIG daily for 5 days. Unfortunately, he developed weakness of the upper limbs after two days of IVIG therapy.

He was shifted to a high dependency unit under the care of the Neurophysiology team. His nerve conduction study NCS revealed features of an early GBS with an absence of f waves, and a slow conduction velocity was noted in the lower limbs (particularly the right peroneal nerve).

(Table 2)

His electromyography EMG was normal.

The patient’s COVID-19 PCR swab was negative on admission and on repeating three times. Due to the worsening of hyponatremia, he developed fluctuating level of consciousness. He was reviewed by endocrinology team, diagnosed as the syndrome of inappropriate antidiuretic hormone as part of autonomic manifestations of GBS, received IV hypertonic saline, and improved. He did not have involvement of his respiratory muscles, he received intensive physiotherapy with mild power improvement.

His MRI of the head showed enhancement of the facial nerve bilaterally at the fundus of the internal auditory meatus extending into the labyrinthine segment representing bilateral inflammatory facial nerve changes. (Figure 1)

MRI of the cervical spine showed moderate spondylotic changes at the C5-C6 level 1 without any significant cord compression.

All serological worksup for known immune-mediated infectious causes associated with GBS were negative. (Table 1)

Table 2: Nerve conduction study of both upper and lower limbs revealing findings of an early Guillain Barre Syndrome with absent f waves, slow conduction velocities in the lower limbs (particularly right peroneal nerve with sparing of superficial peroneal sensory potential.
### Table 2. Nerve Conduction of upper limbs and lower limbs

| Site                      | Latency (ms) | Neg. Amp (mV) | Neg. Dur (ms) | Neg. Area (ms*mV) | Distance (mm) | CV (m/s) | Min F-Lat (ms) |
|---------------------------|--------------|---------------|---------------|-------------------|---------------|----------|----------------|
| **Left Median (APB)**    |              |               |               |                   |               |          |                |
| Wrist                     | absent       | absent        | absent        | absent            |               |          |                |
| **Left Ulnar (ADM)**      |              |               |               |                   |               |          |                |
| Wrist                     | 3.4          | 2.5           | 7.8           | 12.6              |               |          | absent         |
| Bel elbow                 | 8.1          | 2.9           | -             | -                 | 250           | 53       |                |
| Ab elbow                  | 10.3         | 3.8           | 7.9           | 16.3              | 100           | 45       |                |
| **Left Peroneal (EDB)**   |              |               |               |                   |               |          |                |
| Ankle                     | 5.1          | 1.00          | 7.2           | 4.0               |               |          | absent         |
| Bel fib head              | 16.2         | 0.81          | 7.4           | 3.7               | 350           | 32       |                |
| Pop fossa                 | 18.7         | 0.64          | 7.7           | 2.9               | 110           | 45       |                |
| **Right Peroneal (EDB)**  |              |               |               |                   |               |          |                |
| Ankle                     | 5.3          | 1.60          | 8.6           | 7.6               |               |          |                |
| Bel fib head              | 18.7         | 0.92          | 7.5           | 4.3               | 365           | 27       |                |
| Pop fossa                 | 20.8         | 0.88          | 8.0           | 4.1               | 95            | 45       |                |
| **Left Tibial (AH)**      |              |               |               |                   |               |          |                |
| Ankle                     | 4.8          | 4.6           | 7.4           | 15.7              |               |          | absent         |
| Knee                      | 17.2         | 0.55          | 7.5           | 2.1               | 435           | 35       |                |
| **Start Lat**             | Start Lat (ms) | Latency (Peak) (ms) | Amplitude (P-P) (µV) | Distance (mm) | Start CV (m/s) |
| **Left Radial**           |              |               |               |                   |               |          |                |
| Forearm-Wrist             | 1.43         | 2.1           | 43            | 85                | 59            |          |                |
| **Left Sural**            |              |               |               |                   |               |          |                |
| Calf-Lat mall             | absent       | absent        | absent        | 75                | absent        |          |                |
| **Right Sural**           |              |               |               |                   |               |          |                |
| Calf-Lat mall             | 5.9          | 9.1           | 4             | -                 | -             |          |                |
| **Left Superficial peroneal** |              |               |               |                   |               |          |                |
| 14 cm-Ankle               | 1.35         | 1.93          | 20            | 75                | 56            |          |                |
| **Right Superficial peroneal** |              |               |               |                   |               |          |                |
| 14 cm-Ankle               | absent       | absent        | absent        | -                 | absent        |          |                |
| **Left Median & Ulnar Sensory** |              |               |               |                   |               |          |                |
| Index finger-Wrist        | 3.9          | 4.6           | 1             | 140               | 36            |          |                |
| Little finger-Wrist       | 2.9          | 3.7           | 2             | 130               | 45            |          |                |

**Figure 1.** MRI Head axial view with contrast gadolinium revealed enhancement of the facial nerve bilaterally at fundus of the internal auditory meatus (2 yellow arrows) extending into the labyrinthine segment representing bilateral inflammatory facial nerve changes
3. Discussion

The annual incidence of Guillain-Barre Syndrome in South East England was reported to be 1.2 cases per 100,000 population. [8]

Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) is the most common form of GBS in the United States and Europe in 85-90% of cases, while Miller Fisher Syndrome (characterized by ophthalmoplegia and ataxia associated with antigangliosides antibodies) is 10%. [9]

In a study involving 2,587 identified GBS patients, the most common associated manifestations of autonomic dysfunction in the hospitalized patients with GBS were diarrhea/constipation 15.5%, and hypernatremia 14.9%. [10]

Our patient’s serum sodium was 123 mmol/l on admission with a normal renal function, thyroid functions test, adrenal function, and no incriminated drug in his list of previous medications.

He developed loose motions after admission and his stool analysis, cultures, clostridium difficile PCR, norovirus RNA, and campylobacter jejuni culture and serology were negative. (Table 1)

The Cerebrospinal fluid CSF findings of GBS are normal white blood cells count with a high protein (cytoalbuminologic dissociation as in our patient) which occur within 66% of patients with GBS during the first week of symptoms. [11]

The infections with a known immune-mediated associated risk for GBS (Campylobacter jejuni, HIV, Influenza, Respiratory syncytial virus, and COVID-19) were all tested negative in our patient. [2,3,12]

Both Epstein Bar Virus EBV and Cytomegalovirus EBV serum serology revealed positive IgG and a negative IgM which reflect an old past infection, and both CSF PCR virology of EBV and CMV were negative. (Table 1)

In a review article regarding reported GBS cases related to COVID-19 infection (31 patients), the commonest presentation was paraesthesia of both lower and upper limbs accompanied with both lower limb weakness (3 out the 31 patients had bilateral facial weakness). Acute inflammatory demyelinating polyneuropathy (AIDP) was the commonest type, five patients required ICU admission, and all received IV immunoglobulins. [13]

Nerve conduction studies of our patient revealed findings of acute demyelinating polyneuropathy AIDP early stage of GBS. (Table 2)

Few cases of GBS have been reported after the H1N1 monovalent influenza vaccine in the USA and the UK. [14,15]

In our electronic search, we could not find any case report of GBS post-COVID-19 vaccination, but only one case report of Miller Fisher Syndrome has been reported post-COVID-19 vaccine of Pfizer Biontec). [16]

At the time of writing this case report, more than 3 million people in the European Union countries have been vaccinated by AstraZeneca COVID-19, and more than 30 million people in the United Kingdom have been vaccinated by COVID-19 vaccine (either AstraZeneca or Pfizer Biontec). [17]

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