Bilateral facial weakness with paraesthesia variant of Guillain-Barré syndrome following Vaxzevria COVID-19 vaccine

Guillain-Barré syndrome (GBS) is a heterogeneous disorder causing muscle weakness, sensory change, dysautonomia and often involving cranial neuropathies. An immune response to recent infection or to triggers such as vaccines, is thought to be responsible. Immunological cross-reaction with the peripheral nerve causes subsequent demyelinating or axonal damage.

GBS is a continuous spectrum of disease rather than discrete phenotypes. Recognised GBS variants in order of frequency are: (1) classical; (2) Miller Fisher syndrome; (3) pharyngeal-cervical-brachial; (4) bifacial weakness with paraesthesia of limbs (BFP); and (5) paraparetic.1

At the time of publication, no reports of BFP variant GBS post COVID-19 vaccination have been described. We report five remarkably similar cases of BFP post-Vaxzevria. All of them presented to Wessex hospitals: Queen Alexandra Hospital, Portsmouth; Southampton General Hospital; Poole Hospital; and St Mary’s Hospital, Isle of Wight, within a 3-month period.

CASE 1
A 66-year-old man developed interscapular back and leg pain, particularly severe at night, 1 week after his first dose of Vaxzevria. He had paraesthesia of both hands and feet and was unsteady. Ten days later, he developed bilateral facial weakness with numbness of the tongue and mouth. Examination revealed marked bilateral lower motor neuron (LMN) facial weakness. Tone, power and reflexes were normal in the limbs except absent right ankle jerk. Light touch and pinprick sensation was reduced symmetrically in both lower limbs to the knee and vibration to the ankles. His gait was ataxic.

Examination revealed severe bilateral LMN facial weakness. Limb tone was normal, with full power except mild weakness in right hip flexion. Reflexes were initially present but then subsequently lost. Plantar responses were flexor. He had a patchy, asymmetrical glove and stocking reduction in pinprick sensation and a sensory ataxia.

CASE 3
A 51-year-old man presented with a 3-week history of severe cramping pain in his legs starting a week after receiving Vaxzevria. Three days later he developed numbness in his feet and hands, spreading proximally to the ankles. One week prior to admission, he developed progressive right facial weakness before it then became severe and bilateral after 5 days.

On examination there was complete bilateral LMN facial weakness. Tone, power and reflexes in limbs were normal. Sensation was impaired in all modalities in all limbs with a sensory ataxia.

CASE 4
A 71-year-old woman had COVID-19 infection 5 weeks prior to Vaxzevria vaccination. Twelve days after vaccination, she had lower back and abdominal pain. Three days later, she developed altered taste and sequential facial weakness within 24 hours. After 4 days, she developed mild proximal leg weakness.

Examination on admission revealed severe bilateral LMN facial weakness and slight weakness in hip flexion bilaterally. She had absent knee and left ankle reflexes with normal sensory examination.

CASE 5
A 53-year-old man experienced lower back discomfort and radicular pain, 8 days following vaccination with Vaxzevria. Six days later, he developed facial, perioral and lower limb paraesthesia progressing to severe simultaneous bilateral facial weakness.

On examination he had severe LMN bilateral facial weakness but normal power elsewhere. Upper limb reflexes were depressed; however, lower limb reflexes were normal. There was mild distal lower limb sensory loss to vibration and pinprick.

Test results, treatments and outcomes are shown in table 1.

A recent UK-based study found no causal association between GBS and COVID-19 infection.5 The incidence of GBS in 2020 decreased compared with previous years, because of national lockdowns and social safety measures against COVID-19 resulting in reduced transmission of other viral illnesses and also those with mild disease not seeking medical review.2

One reported case of GBS has been attributed to the Pfizer COVID-19 vaccine,1 and one to Vaxzevria4 though neither patients presented with facial weakness. In the Johnson & Johnson COVID-19 vaccine trial, one case of GBS was reported in the vaccine arm and one in the placebo.3

The incidence of post-vaccination GBS in its rarity is unknown and still debated. Our case series of patients presented prior to easing of the third English national lockdown restrictions, strengthening the case for a vaccine-mediated aetiology. The incidence of five cases of the very uncommon BFP variant of GBS occurring within 2 weeks of Vaxzevria is further suggestive of an aetiological link.

Furthermore, we compared the GBS cases in one hospital, Southampton General Hospital, during March–April 2020 and 2021, when there were similar lockdown conditions in England. In 2020 there were two cases of classic GBS (age 59–68) and one case of Miller Fisher variant (age 12). In 2021, in addition to two of the BFP cases from this letter (2 and 3), there were three cases of classical GBS (age range 64–79), making five cases, with the excess compared with the previous year being accounted for by the BFP-GBS cases. Of the three classical GBS cases, one received the first dose of Vaxzevria 1 week prior to symptom onset, the other two, who received Pfizer, had the first dose of vaccine 4–6 weeks prior to symptom onset, and so of uncertain significance.

Our cases were remarkably clinically homogeneous:

- 7–12 days interval between vaccination to symptom onset; supporting temporal causality between immunisation and illness.
- Phenotypic features of severe facial diplegia and paraesthesia.
- Lack of respiratory muscle involvement avoiding intensive care admission.
- Consistently high cerebrospinal fluid protein levels.
- Bilateral facial nerve enhancement on MRI imaging.
- Electrodiagnostics showing demyelination.
- Favourable prognosis in most cases with good response to intravenous immunoglobulin or spontaneous improvement.

Our case series of patients presented prior to easing of the third English national lockdown restrictions, strengthening the case for a vaccine-mediated aetiology.
Table 1 Demographics, results, and clinical outcomes

<table>
<thead>
<tr>
<th>Case</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Age</td>
<td>66</td>
<td>43</td>
<td>51</td>
<td>71</td>
<td>53</td>
</tr>
<tr>
<td>Days from vaccine to symptom onset</td>
<td>7</td>
<td>11</td>
<td>7</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Days from vaccine to facial weakness</td>
<td>17</td>
<td>17</td>
<td>14</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>CSF protein (0–0.5 g/L)</td>
<td>1.99</td>
<td>2.81</td>
<td>5.14</td>
<td>0.96</td>
<td>1.22</td>
</tr>
<tr>
<td>CSF white cells (0–5/μL)</td>
<td>2</td>
<td>23</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>CSF viral PCR*</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Lyme serology (IgM and IgG)</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-ganglioside antibodies†</td>
<td>Negative</td>
<td>Negative</td>
<td>GM3 positive</td>
<td>GM4 borderline</td>
<td>Negative</td>
</tr>
<tr>
<td>CMV serology (IgM and IgG)</td>
<td>Negative</td>
<td>Not tested</td>
<td>Negative</td>
<td>Negative</td>
<td>Not tested</td>
</tr>
<tr>
<td>Brain imaging</td>
<td>MRI pre and post GAD contrast: normal except for bilateral smooth contrast enhancement along whole facial nerve</td>
<td>Normal MRI, No post contrast study performed</td>
<td>Normal CT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensory NCS</td>
<td>UL and LL: reduced SNAP amplitude</td>
<td>UL: absent SNAPs</td>
<td>LL: reduced SNAP amplitudes</td>
<td>LL: normal</td>
<td>Not tested</td>
</tr>
<tr>
<td>Motor NCS</td>
<td>UL and LL: Prolonged DMLs, and F-wave latencies Slow CV Dispersed CMAPs and CB</td>
<td>UL and LL: Prolonged DMLs, and F-wave latencies Slow CV Dispersed CMAPs and CB</td>
<td>UL and LL: Dispersed CMAPs</td>
<td>Tibial F wave latencies prolonged</td>
<td>UL and LL: Prolonged DMLs Dispersed CMAPs</td>
</tr>
<tr>
<td>Facial NCS</td>
<td>Prolonged DMLs</td>
<td>Absent</td>
<td>Normal except blink reflexes absent</td>
<td>Not tested</td>
<td>Not tested</td>
</tr>
<tr>
<td>Facial EMG</td>
<td>Not tested</td>
<td>Few fibrillations, no voluntary motor units</td>
<td>Very reduced voluntary motor units</td>
<td>Not tested</td>
<td>Not tested</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Treatment</td>
<td>IVig</td>
<td>IVig</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Outcome</td>
<td>10 weeks from symptom onset</td>
<td>9 weeks from symptom onset</td>
<td>10 weeks from symptom onset</td>
<td>12 weeks from symptom onset</td>
<td>7 weeks from symptom onset</td>
</tr>
<tr>
<td>Facial weakness resolved. Pain and paraesthesia improving. Intact reflexes including right ankle jerk.</td>
<td>20% improvement in facial weakness. Ataxic gait and pain static. Areflexia persists. No longer in urinary retention.</td>
<td>95% improvement in facial weakness. Ataxic gait 80% better. 25% improvement in pain and paraesthesia.</td>
<td>Residual mild facial weakness, proximal leg weakness and mild paraesthesia. Reflexes regained.</td>
<td>95% resolution of facial weakness, pain and paraesthesia.</td>
<td></td>
</tr>
</tbody>
</table>

Abnormal laboratory results are highlighted in bold.

*CSF viral PCR: Enterovirus PCR, Enterovirus type 1 PCR, Herpes simplex virus type 2 PCR, Parechovirus PCR, Varicella zoster PCR.
†Anti-ganglioside antibody subtypes (GD1a, GD1b, GD2, GD3, GM2, GM3, GT1a, GT1b, GM1, GQ1b).
CB, conduction block; CMAP, compound muscle action potential; CMV, Cytomegalovirus; CSF, cerebrospinal fluid; CV, conduction velocities; DML, distal motor latency; GAD, Gadolinium; IVIg, Intravenous immunoglobulin; LL, lower limb; NCS, nerve conduction studies; SNAP, sensory nerve action potential; UL, upper limb.

Although a mild phenotype, early recognition and diagnosis may help prevent complications like falls and provide opportunity for early specialist referral. Post-vaccination GBS remains rare and with COVID-19 claiming approximately 4 million deaths worldwide to date, vaccination against COVID-19 remains a global health priority. International surveillance for this potential complication is important.

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