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.

Eleven days prior to symptom onset, he received his first dose of Vaxzevria.

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 2**
A 43-year-old man presented with a 10-day history of myalgia, then pins and needles in his hands and feet, severe pain in his neck, urinary retention, severe bilateral facial weakness, dysphagia, altered taste and paraesthesia in his tongue.

A recent UK-based study found no causal association between GBS and COVID-19 infection.2 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 Vaxzevria1 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.2

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.


Table 1

<table>
<thead>
<tr>
<th>Case</th>
<th>1</th>
<th>2</th>
<th>3</th>
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<tr>
<td>Gender</td>
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<tr>
<td>Age</td>
<td>66</td>
<td>43</td>
<td>51</td>
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<tr>
<td>Days from vaccine to symptom onset</td>
<td>7</td>
<td>11</td>
<td>7</td>
<td>12</td>
<td>8</td>
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<tr>
<td>Days from vaccine to facial weakness</td>
<td>17</td>
<td>17</td>
<td>14</td>
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<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>
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<tr>
<td>CSF white cells (0–5/μL)</td>
<td>2</td>
<td>23</td>
<td>1</td>
<td>1</td>
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<td>CSF viral PCR*</td>
<td>Negative</td>
<td>Negative</td>
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<tr>
<td>Lyme serology (IgM and IgG)</td>
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<tr>
<td>Anti-ganglioside antibodies†</td>
<td>Negative</td>
<td>Negative</td>
<td>GM3 positive</td>
<td>Not tested</td>
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<tr>
<td>CMV serology (IgM and IgG)</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Not tested</td>
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<tr>
<td>Brain imaging</td>
<td>MRI pre and post GAD contrast: normal except for bilateral smooth contrast enhancement along whole facial nerve</td>
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<tr>
<td>Sensory NCS</td>
<td>UL and LL: reduced SNAP amplitude</td>
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<tr>
<td>Motor NCS</td>
<td>UL and LL: Prolonged DMLs, and F-wave latencies</td>
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<tr>
<td>Facial NCS</td>
<td>Prolonged DMLs</td>
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<td>Facial EMG</td>
<td>Not tested</td>
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<tr>
<td>Chest X-ray</td>
<td>Normal</td>
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<tr>
<td>Treatment</td>
<td>IVIg</td>
<td></td>
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<tr>
<td>Outcome</td>
<td>10 weeks from symptom onset</td>
<td></td>
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</tbody>
</table>

Abnormal laboratory results are highlighted in bold.

*CSF viral PCR: Enterovirus PCR, Herpes simplex virus type 1 PCR, Herpes simplex virus type 2 PCR, Parechovirus PCR, Varicella zoster PCR.
†Anti-ganglioside antibody subtypes (GD1a, GD1b, GD2, GD3, GM2, GM3, GM4, G1a, G1b, G1m, G0b).
CB, conduction block; CMAP, compound muscle action potential; 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.

More often than not, ongoing clinical improvement occurred as a consequence of GBS. In the biphasic and narrative paradigm, the early window was characterized by motor weakness, while the latter was characterized by sensory and autonomic abnormalities. Some patients had recovery of sensation and autonomic nerve function during the biphasic window. The global health status of these patients improved gradually over time, with most patients achieving full recovery within 12 weeks of symptom onset. Favourable prognosis in most cases with good response to intravenous immunoglobulin or spontaneous improvement.

Although a mild phenotype, early recognition and diagnosis may help prevent complications like falls and provide opportunity for early specialist rehabilitation. 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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Acknowledgements We would like to thank Dr Charles Hillier, neurology consultant in Poole Hospital, for consenting and sharing his case.

Contributors GBB and DP were responsible for the planning, drafting, execution and final amendments to this letter as first coauthors. SC and EP were involved in the drafting and execution stages. MC, JD, SR, AA, OT, SS, JF, DA and HAK are contributing authors in the critical revision and provision of supplementary information. UK has contributed to planning, execution, critical revision and final amendments and is the overall guarantor to this letter.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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Received 5 May 2021
Accepted 28 June 2021

Published Online First 14 July 2021

J Neurol Neurosurg Psychiatry 2022;93:341–342.
doi:10.1136/jnnp-2021-327027

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