

## Guillain–Barré syndrome in general practice:

clinical features suggestive of early diagnosis

### INTRODUCTION

The year 2016 marks 100 years since the first description of Guillain–Barré syndrome (GBS), which is now recognised as the commonest cause of acute post-infectious flaccid paralysis worldwide.<sup>1</sup> Although rare (with an incidence of 1–2 cases per 100 000), GBS remains an important neurological emergency. The majority of patients with GBS develop ascending paralysis, which starts in the legs and typically spreads to the arms. Cranial nerve involvement is also common and 25% of patients develop respiratory depression and require mechanical ventilation. In Miller Fisher syndrome, which is a rare variant of GBS, cranial nerve involvement and ataxia predominate. Awareness of early symptoms and signs can lead to earlier referral to secondary care, and therefore earlier treatment. In this mini-review we highlight the core clinical features of GBS and discuss important differential diagnoses.

### PATHOGENESIS

GBS is a post-infectious neuropathy and known to be triggered by certain infections,<sup>2</sup> including *Campylobacter jejuni*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, Epstein–Barr virus, cytomegalovirus, hepatitis E, and influenza virus.<sup>2,3</sup> One question patients may ask their GP is: can the flu vaccine trigger GBS? Although this was thought to be a problem in the 1976 swine flu epidemic, recent studies have shown that the flu vaccine does not trigger GBS, and in fact patients who contract influenza virus are at greater risk of developing GBS.<sup>3</sup>

### CLINICAL PRESENTATION

A diagnosis of GBS is usually made based on history and examination alone (Box 1).<sup>4</sup> Most patients (>60%) describe antecedent infectious symptoms.<sup>3</sup> Infectious diarrhoea caused by *C. jejuni* and upper respiratory tract infections are the most important triggers. Only a very small proportion (0.1%)

### Box 1. Clinical features of Guillain–Barré syndrome and Miller Fisher syndrome<sup>a</sup>

#### Clinical features

- Antecedent infectious symptoms
- Presence of distal paraesthesias at or before the onset of weakness
- Symmetrical weakness
- Monophasic disease course with interval between onset and nadir of weakness of 12 hours to 28 days, followed by clinical plateau

#### Guillain–Barré syndrome

- Weakness and areflexia in all four limbs.
- +/- cranial nerve involvement and respiratory depression.

#### Miller Fisher syndrome

- Ophthalmoplegia, ataxia, areflexia.

<sup>a</sup>Adapted from Wakerley et al 2014.<sup>4</sup>

of patients with *C. jejuni* gastroenteritis develops GBS. Typically, neurological symptoms start between 3 days and 6 weeks after exposure. Sensory symptoms frequently appear before or at the onset of weakness and many patients complain of a tingling or pricking sensation (paraesthesias) in their hands and feet. Characteristically this is very symmetrical and generally progressive. Distal numbness and limb or back pain are also common. Some patients may also complain of progressive limb weakness or altered gait. Weakness is also characteristically symmetrical and usually involves the lower limbs first. Deep-tendon reflexes are absent in 90% of patients with GBS, although this may not be evident at first. Respiratory depression and cranial neuropathy often occur later. Although the nadir of neurological symptoms may be reached in as little as 12 hours, progression beyond 28 days is atypical. Rarely patients present with cranial nerve involvement, for example, diplopia, slurred speech, or swallowing difficulties. Progressive bilateral ophthalmoplegia and ataxia is suggestive of Miller Fisher syndrome. Very rarely patients may present with localised weakness that

Virginia A Head, MRCP, Gloucester Royal Hospital, Gloucester. Benjamin R Wakerley, PhD, MRCP, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford.

#### Address for correspondence

Benjamin R Wakerley, Department of Neurology, Gloucestershire Royal Hospital, Gloucester, Gloucestershire, GL1 3NN, UK.

E-mail: benwakerley@fastmail.fm

Submitted: 2 November 2015; Editor's response: 11 November 2015; final acceptance: 3 December 2015.

©British Journal of General Practice 2016;

66: 218–219.

DOI: 10.3399/bjgp16X684733

## Box 2. Differential diagnoses of Guillain-Barré syndrome and Miller Fisher syndrome

### Guillain-Barré syndrome

- Transverse myelitis
- Ischaemic or mechanical spinal cord injury
- Peripheral neuropathies (for example, Lyme disease)
- Myasthenia gravis

### Miller Fisher syndrome

- Myasthenia gravis
- Brainstem stroke or inflammation

is restricted to either the face or to the oropharyngeal muscles, neck, and upper limbs.

### DIFFERENTIAL DIAGNOSIS

Diagnosis of GBS, Miller Fisher syndrome, and their subtypes can be challenging in early disease, but many differentials can be excluded based on history and examination alone (Box 2).<sup>5</sup> Other than GBS, very few conditions cause rapidly progressive quadriplegia and cranial neuropathy. Acute cervical spinal cord injury is the most important differential when symptoms and signs are restricted to the limbs. Spinal stenosis should always be considered if there is a recent history of falls, especially in older people, whereas transverse myelitis is more common in younger patients. Spinal injury is characterised by brisk deep-tendon reflexes, a sensory level, and often new-onset bladder disturbance. Peripheral neuropathies may develop acutely but this is rare. Miller Fisher syndrome is frequently mistaken as myasthenia gravis or brainstem stroke, but these can be excluded if there is fatigability or very acute onset respectively.

### DIAGNOSTIC TESTS

Once in hospital, patients typically have brain and spinal cord imaging to exclude a structural cause, followed by lumbar puncture, which characteristically demonstrates raised cerebrospinal fluid protein in the absence of inflammatory cells. Nerve conduction studies help to confirm the diagnosis, but, like cerebrospinal fluid, are non-diagnostic in up to 50% of patients in the first week of disease. The presence of anti-ganglioside (IgG) antibodies supports diagnosis, but should not be relied on.

### TREATMENT

Unlike many inflammatory conditions, corticosteroids are of no benefit in GBS. Not all patients require treatment, but in most centres intravenous immunoglobulin or plasma exchange are initiated if weakness is rapidly progressive or if there is significant bulbar or respiratory muscle compromise.<sup>1</sup> Although immunotherapy can halt progression, 25% of patients still require admission to the intensive care unit for mechanical ventilation. Hospitalisation can therefore be protracted. Most patients require neurorehabilitation, which may need to be continued in the community.

### PROGNOSIS

Despite modern treatment 3% of patients with GBS still die and 20% are left severely disabled.<sup>6</sup> Late complications of

GBS, including neuropathic pain, postural hypotension, and fatigue may persist for many months beyond sensorimotor recovery, and primary care practitioners may well be involved in managing these chronic symptoms. One-third of patients report ongoing pain 1 year after recovery, and opioids, gabapentin, and carbamazepine can be effective in managing this.

### HOW URGENTLY SHOULD I REFER AND TO WHOM?

Patients with suspected GBS should be discussed urgently with the local neurology or acute medical team, with the view of admission to hospital for further investigations the same day. Unless immobile or in respiratory distress an ambulance is rarely necessary. Many patients who present with non-specific sensory disturbance will not have GBS, but may still require less urgent neurology referral. Patients should be advised that if their symptoms progress rapidly, or if they develop any weakness (limb or cranial nerve) or bladder disturbance, they should present to their local emergency room immediately.

### CASE EXAMPLE

A previously healthy young male presented with a 3-day history of progressive limb weakness associated with pins and needles in his hands and feet. Two weeks beforehand he had complained of an upper respiratory tract infection. There was no history of recent head or neck injury. On examination he appeared systemically well. His cranial nerves were normal and there were no cerebellar signs. Limb tone was normal. There was mild weakness in all four limbs and grip strength was reduced. He had difficulty standing from the sitting position. Although he reported distal paraesthesias, sensory examination was grossly normal. His deep-tendon reflexes were globally absent. Based on history and examination a diagnosis of acute post-infectious neuropathy secondary to GBS could be made.

### Provenance

Freely submitted; externally peer reviewed.

### Acknowledgement

The authors are grateful to Steve Collyer, a GP with a specialist interest in neurology, for his suggestions and critical reading of the manuscript.

### Discuss this article

Contribute and read comments about this article: [bjgp.org/letters](https://bjgp.org/letters)

### REFERENCES

1. Yuki N, Hartung HP. Guillain-Barré syndrome. *N Engl J Med* 2012; **366**(24): 2294–2304.
2. Wakerley BR, Yuki N. Infectious and noninfectious triggers in Guillain-Barré syndrome. *Expert Rev Clin Immunol* 2013; **9**(7): 627–639.
3. van den Berg B, van der Eijk AA, Pas SD, *et al.* Guillain-Barré syndrome associated with preceding hepatitis E virus infection. *Neurology* 2014; **82**(6): 491–497.
4. Wakerley BR, Uncini A, Yuki N. Guillain-Barré and Miller Fisher syndromes: new diagnostic classification. *Nat Rev Neurol* 2014; **10**(9): 537–544.
5. Wakerley BR, Yuki N. Mimics and chameleons in Guillain-Barré and Miller Fisher syndromes. *Pract Neurol* 2015; **15**(2): 90–99.
6. Fokke C, van den Berg B, Drenthen J, *et al.* Diagnosis of Guillain-Barré syndrome and validation of Brighton criteria. *Brain* 2014; **137**(Pt 1): 33–43.