Nature Reviews Neurology published online 15 September 2015; doi:10.1038/nrneurol.2015.115

Polyneuritis cranialis—subtype of Guillain–Barré syndrome?

Benjamin R. Wakerley and Nobuhiro Yuki

Recently we, along with the rest of the GBS Classification Group, outlined a new diagnostic classification system for Guillain–Barré syndrome (GBS) and Miller Fisher syndrome (MFS). This classification was based on the clinical features of each disease (Guillain–Barré and Miller Fisher syndromes—new diagnostic classification. *Nat. Rev. Neurol.* **10**, 537–544; 2014).[1] We argued that the majority of cases could be classified into discrete subtypes of GBS or MFS—or, in some instances, overlap between subtypes—on the basis of their phenotypic appearances. There remains, however, some ambiguity as to how best classify a small subset of patients, who develop multiple, often asymmetric, cranial neuropathies in the absence of ataxia or limb weakness.

Guillain and his contemporaries[2,3] recognized that some patients developed a postinfectious syndrome that was associated with albuminocytological dissociation and affected the cranial nerves without clinical involvement of the limbs. Historically, patients with these symptoms have been referred to as having 'polyneuritis cranialis', a descriptive term that has been used in other cases of multiple cranial neuropathy regardless of aetiology. A case of polyneuritis cranialis (or isolated multiple cranial neuropathy) that was attributable to GBS was reported alongside diagnostic criteria for GBS and MFS established in 1990,[4] but this term has not appeared in more-recent definitions[5,6] and has thus avoided nosological consideration.[1]

In a recent review, we examined the clinical features of 15 historical cases of polyneuritis cranialis attributed to GBS.[7] In the majority of cases, patients displayed a combination of ocular signs (ophthalmoplegia, ptosis or pupillary changes) and bulbar signs (dysarthria or dysphagia), which were often associated with facial weakness. Unlike other GBS subtypes, weakness was frequently asymmetric. In the absence of ataxia or cervical–brachial weakness, these patients lacked the cardinal features required to make a diagnosis of MFS or pharyngeal–cervical–brachial weakness. Furthermore, cranial neuropathy was too extensive to be attributed to any single subtype of MFS or pharyngeal–cervical–brachial weakness, and therefore a diagnosis of acute ophthalmoparesis[8] or acute oropharyngeal palsy[9] could not be made.

One interpretation of these cases is that polyneuritis cranialis might represent an overlap between less extensive subtypes of MFS (acute ophthalmoparesis) and pharyngeal–cervical–brachial weakness (acute pharyngeal weakness). In some patients, this notion was supported serologically by the presence of antibodies against gangliosides GQ1b and GT1a, which have also been isolated from patients with acute ophthalmoparesis[8] and acute oropharyngeal palsy.[9]

Phenotypically, however, the majority of patients diagnosed with polyneuritis cranialis also displayed facial weakness, which has only rarely been reported in association with acute ophthalmoparesis, and not reported with acute pharyngeal weakness. Therefore, the pattern of weakness in polyneuritis cranialis extends beyond what would be predicted from the overlap between these two rare subtypes. Furthermore, facial weakness in these patients cannot be attributed to bifacial weakness with paraesthesias,[10] which is caused by demyelinating neuropathy and not associated with antiganglioside antibodies. A substantial proportion of patients with polyneuritis cranialis also displayed asymmetrical neuropathy, which, although

Table 1 | Clinical features of GBS spectrum disorders

Category	Clinical features		
	Pattern of weakness	Ataxia	Hypersomnolence
GBS			
Classic GBS	Four limbs	No or minimal	No
Pharyngeal–cervical–brachial weakness*	Bulbar, cervical and upper limbs	No	No
Acute pharyngeal weakness‡	Bulbar	No	No
Paraparetic GBS*	Lower limbs	No	No
Bilateral facial weakness with paraesthesias*	Facial	No	No
GBS–MFS interface			
Polyneuritis cranialis	Bulbar with ophthalmoparesis	No	No
MFS			
Classic MFS	Ophthalmoparesis	Yes	No
Acute ophthalmoparesis§	Ophthalmoparesis	No	No
Acute ataxic neuropathy§	No weakness	Yes	No
Acute ptosis§	Ptosis	No	No
Acute mydriasis§	Paralytic mydriasis	No	No
Bickerstaff brainstem encephalitis‖	Ophthalmoparesis	Yes	Yes
Acute ataxic hypersomnolence¶	No weakness	Yes	Yes

*Localized subtype of GBS. ‡Incomplete form of pharyngeal–cervical–brachial weakness. §Incomplete forms of MFS; ‖CNS subtype of MFS; ¶Incomplete form of BBE. Abbreviations: GBS, Guillain–Barré syndrome; MFS, Miller Fisher syndrome.

reported, occurs only rarely in patients with MFS or GBS. Given the improbability of an asymmetric overlap between two rare subtypes that are not commonly associated with facial weakness, we propose that a more plausible explanation is that polyneuritis cranialis is a separate subtype altogether, which lies at the interface between MFS and GBS (Table 1).

*Department of Neurology, Gloucestershire Royal Hospital, Great Western Road, Gloucester GL1 3NN, UK (**B.R.W.**). Brain and Mind Centre, University of Sydney, 94 Mallett Street, Camperdown NSW 2050, Australia (**N.Y.**). Correspondence to: B.R.W.*
benwakerley@fastmail.fm

Competing interests
The authors declare no competing interests.

1. Wakerley, B. R. *et al.* Guillain-Barré and Miller Fisher syndromes: new diagnostic classification. *Nat. Rev. Neurol.* **10**, 537–544 (2014).
2. Guillain, G. & Kreis, B. Sur deux cas de polyradiculo-neurité avec hyperalbuminose du liquid céphalo-rachidiens sans réaction cellulaire [French]. *Paris Med.* **2**, 224–247 (1937).
3. Van Bogaert, M. & Maere, M. Les polyradiculonévrites crâniennes bilatérales avec dissociation albumino cytologique: forms crâniennes des polyradiculonévrites du type Guillain et Barré [French]. *J. Belge. Neurol. Psychiat*. **38**, 275–281 (1938).
4. Asbury, A. K. & Cornblath, D. R. Assessment of current diagnostic criteria for Guillain–Barré syndrome. *Ann. Neurol.* **27** (Suppl.), S21–S24 (1990).
5. van der Meché, F. G. *et al.* Diagnostic and classification criteria for the Guillain–Barré syndrome. *Eur. Neurol.* **45**, 133–139 (2001).
6. Sejvar, J. J. *et al.* Guillain–Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. *Vaccine* **29**, 599–612 (2011).
7. Wakerley, B. R., Yuki, N. Polyneuritis cranialis: oculopharyngeal subtype of Guillain–Barré syndrome. *J. Neurol.* http://dx.doi.org/10.1007/s00415-015-7678-7.
8. Yuki, N., Odaka, M. & Hirata, K. Acute ophthalmoparesis (without ataxia) associated with anti-GQ1b IgG antibody: clinical features. *Ophthalmology* **108**, 196–200 (2001).
9. O'Leary, C. P. *et al.* Acute oropharyngeal palsy is associated with antibodies to GQ1b and GT1a gangliosides. *J. Neurol. Neurosurg. Psychiatry* **61**, 649–651 (1996).
10. Susuki, K., Koga, M., Hirata, K., Isogai, E. & Yuki, N. A Guillain–Barré syndrome variant with prominent facial diplegia. *J. Neurol*. **256**, 1899–1905 (2009).