LETTER TO THE EDITOR

Reply: Biomarkers of ‘acute-onset’ chronic inflammatory demyelinating polyneuropathy

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Sir,

‘In my end is my beginning’

~ T.S. Eliot, East Coker

In keeping with the quotation by T.S. Eliot, the clear delineation of CIDP phenotypic variants remains a difficult and often circular process. The search for antigenic targets in CIDP has continued for almost 30 years, but to date there is still no well-defined link between molecular targets and particular phenotypes. Although Devaux and colleagues (2012) identified 30% of CIDP patients with antibodies to nodal antigens, the precise molecular antigenic target was not identifiable in most patients. In line with the comments from Miura and colleagues, we agree that identification of pathogenic antigens will improve treatment and management for CIDP patients. Similar to the approaches as outlined by Miura and colleagues, our group and many others have been investigating potential antigenic targets in CIDP (Yan et al., 2001; Devaux et al., 2012; Querol et al., 2013). While it is clear that there are a number of antigenic targets, further studies will be required to investigate nodal, paranodal and myelin-related targets to achieve the aim of characterizing this diverse group of pathologies.

At present, acute-onset CIDP can only be diagnosed in retrospect (Lunn and Willison, 2009). Although serological assessment can provide useful information towards understanding pathogenesis in inflammatory neuropathies, it requires specialized techniques not routinely available at local health services. In addition, the time interval required for such services may lead to substantial delays in treatment and management and may therefore not be well suited for use in the prompt differentiation of conditions such as AIDP and acute onset CIDP. Accordingly, immunological features are not currently included in diagnostic guidelines for CIDP (Rajabally et al., 2009).

There is currently no immunological parameter available to differentiate between acute onset CIDP and AIDP patients. Miura and colleagues present data concerning the nodal adhesion protein contactin 1, detecting anti-contactin 1 antibodies in 4% of CIDP and AIDP patients, respectively. However, contactin 1 antibodies were not identified in any patients with acute-onset CIDP. In contrast to these complex immunological approaches, neurophysiological techniques offer an instantaneous snapshot of axonal function. The pattern of nerve excitability change identified in patients with acute-onset CIDP in our study was strikingly different to that observed in patients with AIDP. Specifically, patients with acute-onset CIDP demonstrated increased threshold change in threshold electrotonus and superexcitability, whereas patients with AIDP demonstrated reduced superexcitability (Sung et al., 2014). Consequently, nerve excitability studies may provide a neurophysiological ‘signature’ to differentiate these cohorts, and as a consequence to better target individualized treatment strategies.

The assessment of nerve excitability from compound potentials has a long history, from measurements of chronaxie by Georges Weiss in 1901, to galvanic-faradic testing in the 1950s (Kiernan et al., 2005). Over the past 30 years the assessment of nerve excitability has again risen to the fore and now represents a clinically useful and accessible technique. Nerve excitability testing equipment is now commercially available with semi-automated...
protocols (Kiernan et al., 2000) and wide network of use in the clinical setting. Further, such approaches enable immediate feedback and results, necessary for the early identification and differentiation of acute onset CIDP.

While both neurophysiological and immunological techniques provide important insights into the pathophysiology and clinical phenotype in inflammatory neuropathies (Bae et al., 2014), it seems that the best way forward will be through a combination of approaches to better define clinical phenotype, neurophysiological and serological profiles. Whereas CIDP has become a ‘catch-all’ diagnosis, it is becoming increasingly clear that not all CIDP is equal, and that there is a spectrum of conditions under the CIDP umbrella. Measures to improve patient classification and profiling will inevitably improve our understanding of the underlying pathological processes and assist in the prompt identification of patients with CIDP variants such as acute onset CIDP. In contrast to the earlier quote, perhaps we may return to a further comment by T.S. Eliot:

‘In my beginning is my end.’

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