Neurofilament light as a biomarker in MS: What is the current perception among UK MS specialists?

Background

Multiple sclerosis (MS) displays a highly variable clinical course that ranges from reversible episodes of impairment to severe disability with neuronal damage present from an early stage.1 Due to the unpredictable and heterogeneous nature of both the disease course and treatment response, biomarkers reflecting these processes are in high demand.2 Neurofilaments are neuron-specific cytoskeletal proteins that can be released following axonal damage.1 As such, elevated levels of neurofilament light chains (NfL) in cerebrospinal fluid (CSF) or peripheral blood are thought to reflect axonal damage and neuronal death in MS. They are emerging as a promising biomarker for the evaluation of disease activity and treatment response.1 However, the potential benefit of NfL testing for the clinical management of MS remains uncertain.

Aim and methods

In order to assess the potential impact of NfL testing, a survey was conducted on the clinical management of MS. 22 MS consultants and 1 MS specialist nurse based in the UK completed a 14-question survey between 1 August and 31 August 2018. The objectives of this survey were to gain insights into:

1. The current understanding of NfL as a biomarker in MS
2. How NfL relates to distinct disease processes
3. The potential role for NfL in MS disease monitoring
4. MS specialists current level of experience in measuring NfL
5. The interest in measuring NfL in patients if a test was readily available

The survey questions were structured to be answered either on a rating scale of 1 to 10 (with 1 being the lowest rating and 10 being the highest), or through a multiple choice format.

Summary and conclusions

The survey results provide an indication of how UK MS specialists view the potential impact of NfL testing in MS.

The majority of participants were aware of the value of NfL as a biomarker of neuronal damage in MS, and would use a test if available.

However, further clarity on how NfL levels relate to underlying disease processes is still required.

Clinical scenarios where participants felt NfL assessment could add value included:

- The confirmation of aggressive disease at diagnosis
- To evaluate patient prognosis, to monitor disease progression and response to therapy, and for the confirmation of relapse
- To build a more complete picture of the disease

Barriers to the use of NfL in clinical practice

- Lack of clarity on the correlation between NfL levels and the underlying pathological processes it reflects
- Cost of serum assay and access to serum via lumbar puncture
- Clinicians lack confidence in NfL due to lack of knowledge when compared with magnetic resonance imaging (MRI)

Results

General opinion on NfL

Among the 23 MS specialists surveyed, the mean rating for understanding NfL as a biomarker of MS was 6.6 (range 3–10).

While the vast majority (91.3%) of participants thought that NfL levels were reflective of neuronal damage in MS, there was less consensus around:

- the association with clinical and radiological activity (Figure 1)
- the relation to acute inflammatory processes (Figure 2)
- the predictive value for disease progression (Figure 2)

Nine of the 23 MS specialists surveyed (39.1%) indicated that they already had experience with or currently measured NfL levels in their clinical practice.

NfL in clinical trials

The vast majority (91.3%) of participants thought that NfL levels should be monitored in clinical trials, with the potential of NfL as a target to establish no evidence of disease activity (NEDA) status highlighted (Figure 3).

NfL in clinical practice

The participants thought that NfL level measurement would add value to clinical and MRI monitoring in MS, and could be a useful measure of subclinical activity (Figure 4).

If a test was available, 95.6% of participants would be interested in measuring CSF or blood NfL levels in their patients.

Specific patient groups and clinical situations where the participants would measure NfL levels are highlighted in Figures 5 and 6, respectively.

References


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Abbreviations

CSF=cerebrospinal fluid; DMT=disease-modifying therapy; MRI=magnetic resonance imaging; MS=multiple sclerosis; NEDA=No Evidence of Disease Activity; NfL=neurofilament light.