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NfL elevation may precede clinical exacerbation

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INTRODUCTION

Neurofilament light chains (NfL) have been shown to be highly correlated with disease activity in multiple sclerosis (MS). A MS patient participating in a study had CSF and serum biomarkers, including NfL, on a scheduled protocol, happened to have a significant exacerbation 4 weeks after biomarker sampling. There was a 3-fold increase in NfL while MRI showed no changes.

OBJECTIVE

To demonstrate to utility of NfL in measuring MS activity

METHODS

This is a single case from a series of 16 SPMS (secondary progressive MS) patients who had per protocol, clinical evaluation, EDSS, cranial MRI, CSF, blood sampling scheduled at baseline, 6 weeks and 28 weeks after dimethyl fumarate (DMF) was begun. There were 4 normal controls that underwent baseline evaluations only. Patients all were ages 25 to 65. EDSS scores at baseline were 3 to 6.5.

Table 1. Patient demographics

SPMS Patients	Percentage	Mean (SD)	Range
Female (n=16)	87.5 %	n/a	n/a
Race (n=16) - Caucasian	100 %	n/a	n/a
Age (n=16)	n/a	55.4 (8.93)	37-65
EDSS	n/a	4.44 (1.56)	3-6.5
Disease duration (in years)	n/a	22.5 (11.69)	3-39
MS Relapses (past 12 months)	n/a	0.19 (0.40)	0-1
Gad+ lesions	n/a	0 (0)	n/a

Data are mean (SD), n(%), unless otherwise stated. MS = multiple sclerosis. EDSS= expanded disability status scale.

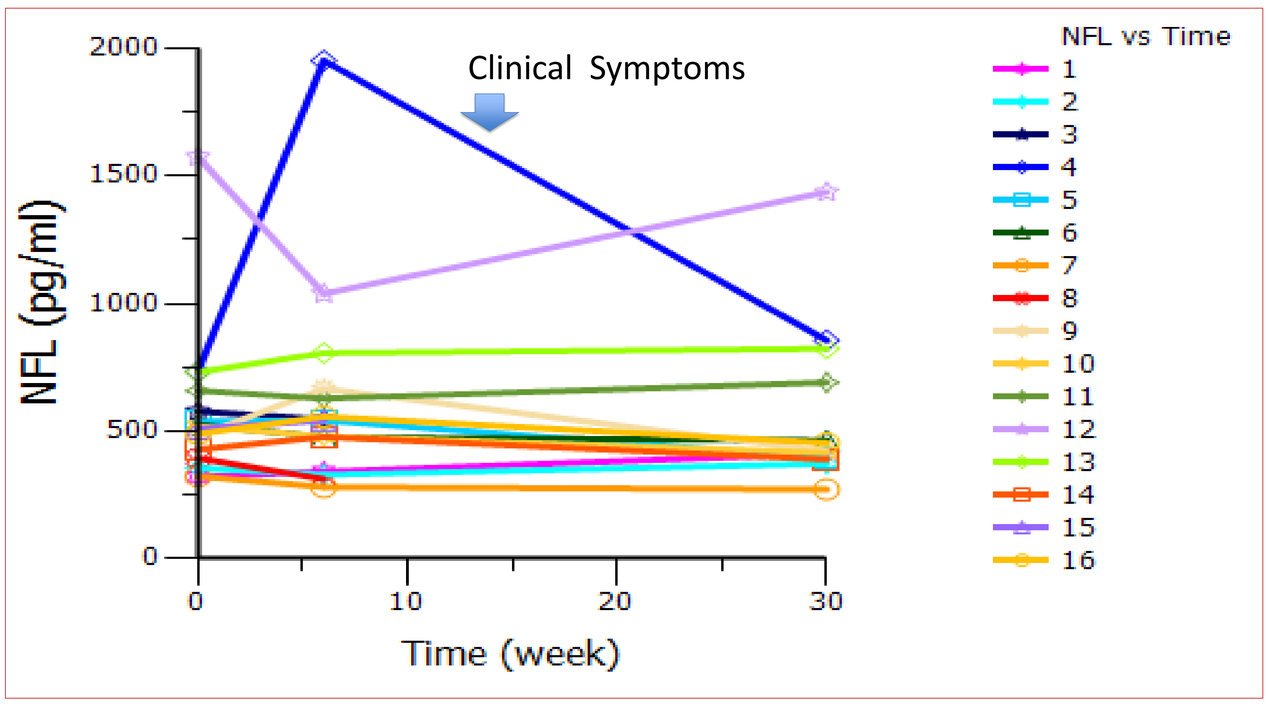
Table 2. Values of CSF NfL for patient no: 4

NfL values	CSF (pg/ml)
Baseline	733.1
6 weeks	1950
28 weeks	854

RESULTS

One patient experienced a clinical exacerbation 9 weeks after the 6 week evaluations with ataxia causing her EDSS to increase from 3.5 to 6.5. She had been clinically stable when seen for the 6 weeks evaluations. Cranial MRI with contrast was unchanged at the 6-week evaluation. MRIs at 28 weeks and 52 weeks were unchanged. Clinically she gradually improved so that at week 28 EDSS was 5.0. Her CSF NfL levels were: 733 pg./ml at baseline, 1950 pg./ml at 6 weeks and 854 pg./ml at 28 weeks. Serum NfL levels were approximately 30 fold lower than the CSF NfL levels. Analysis was by the single molecule array assay method (SIMOA).

Figure 1: NfL levels of CSF at baseline, 6-weeks, 28-weeks in the 16 patients with case report showing spike of NfL at 6-weeks.



DISCUSSION

This case provides data to suggest that NfL may increase prior to clinical symptoms and without MRI changes. Since there is only one NfL measurement between baseline and 28 weeks, the rate of increase of NfL levels immediately prior to clinical symptoms and how long NfL was elevated is unknown. These questions need to be explored.

CONCLUSION

The case demonstrated an increase in NfL levels preceding a significant clinical exacerbation in a PMS patient with no detected MRI change. This case supports the use of NfL as a relevant, sensitive and early biomarker for disease activity in MS. The data warrant investigation of NfL as a biomarker to monitor MS activity in MS patients using larger well characterized cohorts.

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