Serum neurofilaments predict recovery after acute optic neuritis

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Introduction

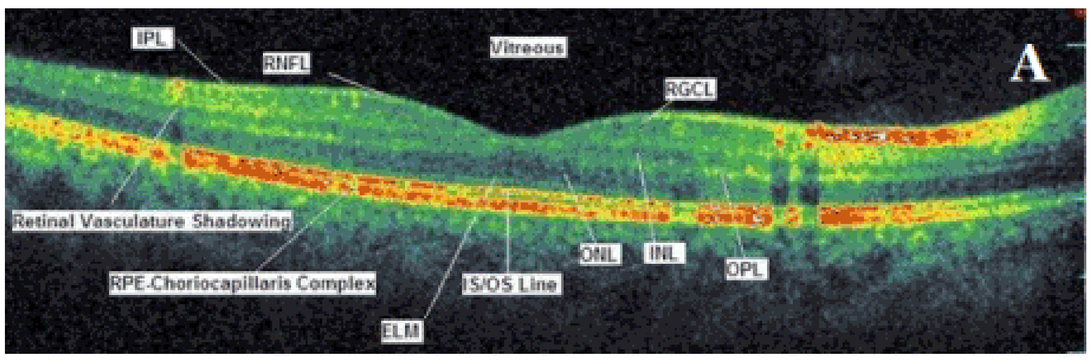
•Optic neuritis is an immune-mediated disease of the optic nerve, strongly associated with multiple sclerosis (MS);

•Although the visual prognosis of optic neuritis is generally favourable, the degree of remission varies considerably;

•The degree of clinical remission is associated with the degree of optic nerve axonal loss, that can be quantified accurately by Optic Coeherence Tomography (OCT);

•The neurofilament light chain (NfL) is part of the axonal cytoskeletal neurofilaments and is released upon immune-mediated axonal damage during optic neuritis and MS;

•We aimed to investigate if NfL levels sampled close after symptom onset would predict the outcome after optic neuritis.



Methods

•Patients. Patients have been prospectively recruited from June 2013. They all had optic neuritis as a first demyelinating episode and serum was sampled within 3 months (median 1.5, interquartile range (IQR) 0.8– 2.6) months after onset;

•Visual tests. At baseline and follow-up patients underwent a diagnostic programme including tests of visual acuity by standard as well as low contrast letter acuity (LCLA) Sloan charts at 2.5% and 1.25%;

•OCT analysis. Retinal layers (RNFL, GCL, IPL, INL, GCIP thickness have been measured using a high-resolutic spectral-domain OCT (SD-OCT) device using the Spectrali 3.5 mm standard circle scan protocol (Heidelberg Spectrali OCT: Spectralis; Heidelberg Engineering, Heidelber Germany). For the follow-up scans the AutoRescan™ featu has been used, allowing to automatically place follow-u scans in precisely the same location as the baseline sca minimizing subjective operator placement and alignme error;

•NfL analysis. Blood samples have been collected in acu phases by venipuncture and stored at -80° C in cryogenic vials since then. The Simoa platform (Quanterix Corp, Boston, MA, USA) has ben used for quantifying NfL levels;

•Statistical analysis. Multilevel mixed effect models have been used to assess the prognostic factor of baseline NfL levels on longitudinal changes in visual outcomes.

Results

A total of 31 patients (mean age 37.3 SD 8.7 years, 71% females) have been recruited and followed up (mean 27.6, SD 12.3) for an acute optic neuritis; eleven patients (35%) had enhancing lesiong at the optic nerve at baseline, 17 (55%), had oligoclonal bands, and the median baseline level of serum NfL was 11.5 pg/ml (IQR 4.3-17.4)

Table 1. Baseline characteristics of the cohorts

	All eyes (n = 62)	Optic neuritis eyes (n = 31)	Asymptomatic eyes (n= 31)
Mean Visual Acuity ± SD	8.91 ± 4.78	7.83 ± 5.21	9.82 ± 2.63
Mean LCLA 2.5% ± SD	1.97 ± 1.48	1.37 ± 1.42	2.59 ± 1.69
Mean LCLA 1.25% ± SD	1.68 ± 1.44	1.09 ± 1.34	2.36 ± 1.49
Mean RNFL thickness (µm) ± SD	94.75 ± 11.78	90.52 ± 14.72	95.88 ± 10.65
Mean GCL thickness (µm) ± SD	1.03 ± 0.14	0.93 ± 0.15	1.06 ± 0.13
Mean IPL thickness (µm) ± SD	0.86 ± 0.10	0.79 ± 0.11	0.88 ± 0.08
Mean INL thickness (µm) ± SD	0.95 ± 0.07	0.96 ± 0.09	0.95 ± 0.07
Mean GCIPL thickness (µm) ± SD	1.50 ± 0.50	1.52 ± 0.51	1.49 ± 0.50

Figure 1. Baseline neurofilaments levels and visual outcomes

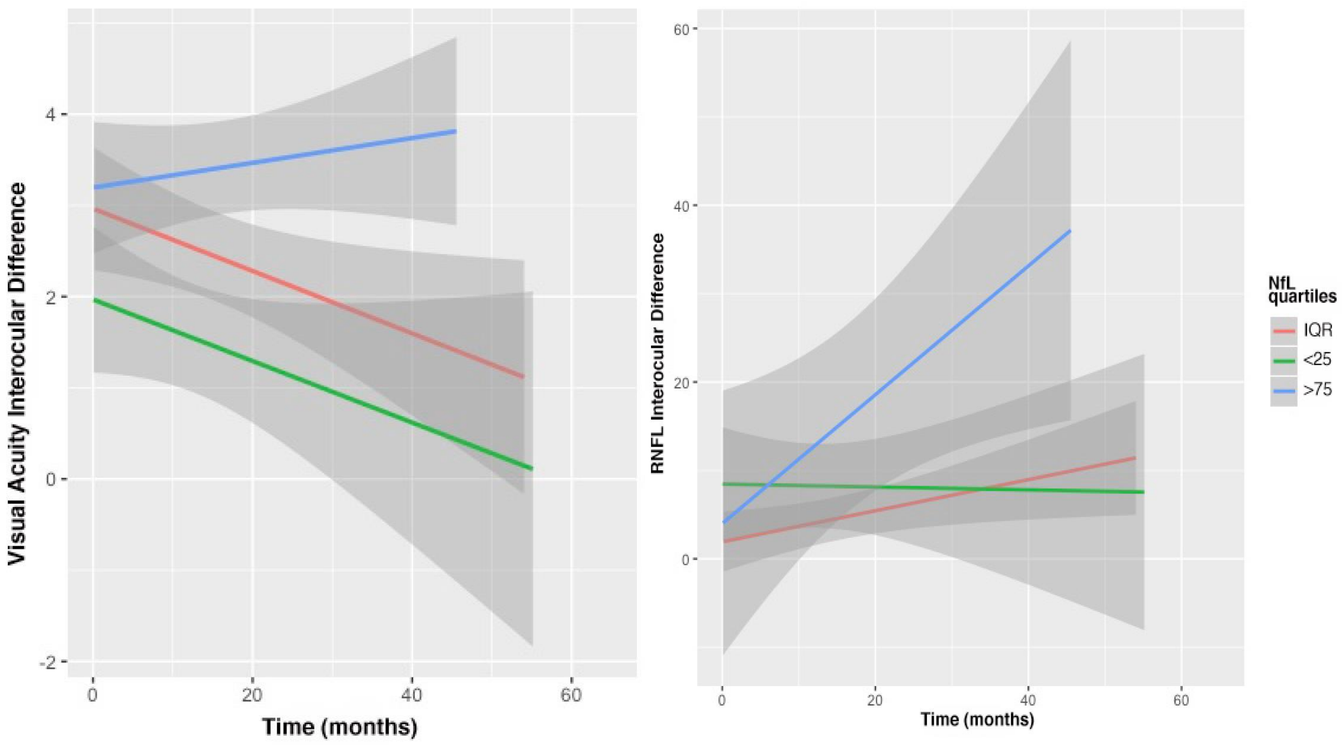


Table 2. Baseline neurofilaments levels and visual outcomes

	Baseline Neurofilament Levels		
	<25%ile	25-75%ile	> 75%ile
Inter-Ocular Visual Acuity Difference	0.13 (0.023)	reference	0.05 (0.02) §
Inter-Ocular LCLA 2.5% Difference	0.01 (0.02)	reference	-0.02 (0.02)
Inter-Ocular LCLA 1.25% Difference	-0.01 (0.02)	reference	-0.01 (0.02)
Inter-Ocular RNFL thickness (µm) Difference	-0.31 (0.20)	reference	0.64 (0.20) §§
Inter-Ocular GCL thickness (µm) Difference	-0.01 (0.01)	reference	(0.01) (0.01)
Inter-Ocular IPL thickness (µm) Difference	0.04 (0.07)	reference	(0.05 (0.06)
Inter-Ocular INL thickness (µm) Difference	0.00 (0.01)	reference	0.01 (0.01)
Inter-Ocular GCIPL thickness (µm) Difference	0.01 (0.01)	reference	0.02 (0.01)

Conclusions

•After an acute optic neuritis, patients improved substantially during the follow-up period in their visual acuity; however, a significant thinning in different OCT parameters was detectable from baseline to follow-up;

•Serum levels of NfL measured in the acute phase of optic neuritis predict both visual outcome and the degree of permanent neuronal and axonal loss as measured by OCT;

•NfL are promising biomarkers candidate for neuroprotective or regenerative clinical treatment trials aiming to prevent neuronal damage after relapse in MS and in optic neuritis;

•Further prospective studies enrolling a larger number of patients with acute optic neuritis are needed to validate our results.