Neurofilament light chain, an early biomarker for polyneuropathy in hereditary transthyretin-related (ATTRv) amyloidosis

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INTRODUCTION

Serum neurofilament light chain (sNfL) is a sensitive marker for polyneuropathy (PNP) in hereditary transthyretin-related (ATTRv) amyloidosis patients and correlates with the severity of polyneuropathy (1-4). We hypothesized that sNfL may diagnose neuronal damage in patients with ATTRv amyloidosis before the onset of symptoms and before PNP can be detected by electromyography (EMG) examination.

OBJECTIVE

Is it possible to diagnose neuronal damage with the biomarker sNfL in patients with ATTRv amyloidosis before polyneuropathy can be detected by nerve conduction studies or clinical assessments?

METHODS

sNfL levels were assessed longitudinally in asymptomatic variant carriers (with and without detectable amyloid), ATTRv amyloidosis patients with PNP on treatment (either a transthyretin (TTR) stabilizer or patisiran, an RNA interference therapeutic), and variant carriers who developed PNP. PNP was established by EMG examination. The single-molecule array (SIMOA) assay was used to assess sNfL levels.

RESULTS

sNfL levels significantly increased over 1 year in 20 persistently asymptomatic carriers ($p<0.001$), with the strongest increase in variant carriers (N=8) with detectable amyloid in the subcutaneous abdominal fat tissue. In 23 symptomatic ATTRv amyloidosis patients with PNP on treatment with a TTR stabilizer, sNfL levels remained stable over 1 year. In 20 patients treated with an RNA interference therapeutic, sNfL levels significantly decreased after 1 year of treatment ($p=0.01$). In 8 out of 9 variant carriers who developed PNP a rise in the sNfL level could be observed before the onset of symptoms and establishment of PNP by EMG examination (Figure 1).

RESULTS

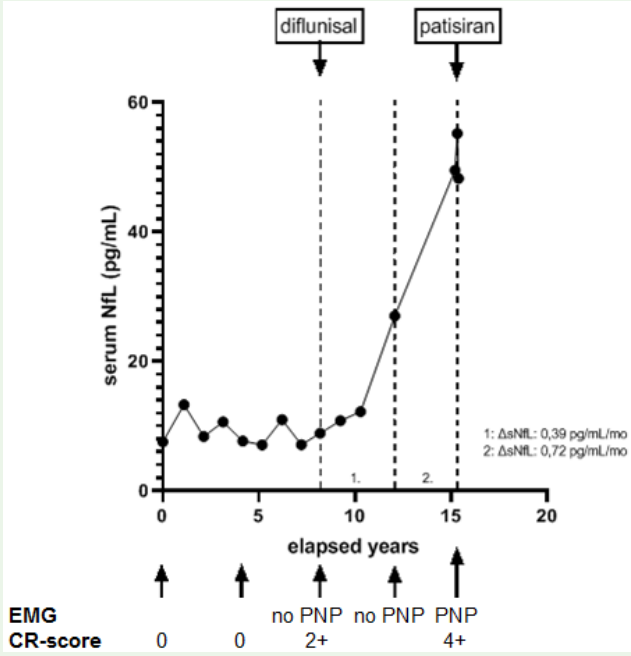

Figure 1. Changes in sNfL during time in a TTR variant carrier who developed PNP wherefore treatment was started. Congo red (CR) score of subcutaneous abdominal fat tissue is also shown.

CONCLUSIONS

- **sNfL is a marker for early neuronal damage since a rise in sNfL level occurs before abnormalities can be detected by EMG examination.**
- **Our data support the use of sNfL in monitoring disease progression, screening asymptomatic variant carriers and monitoring of treatment effect.**

Table 1. Patient characteristics.

	Persistently asymptomatic variant carriers (N = 20)		ATTRv amyloidosis patients with PNP on a TTR-stabilizer (N = 23)		ATTRv amyloidosis patients with PNP on an RNA interference therapeutic (N = 20)		Variant carriers who developed PNP (N = 9)	
	t = 0	t = 1	t = 0	t = 1	t=0	t = 1	t = 0	t = EMG positive
Male/Female	9/11		17/6		15/5		1/8	
Age (years)	45 ± 14	47 ± 14	58 ± 15	60 ± 16	60 ± 16	62 ± 15	43 ± 10	51±10
Follow-up (months)	0	26 ± 15	0	23 ± 12	0	14 ± 3.3	0	95 ± 65
NT-pro-BNP (ng/L)	58 ± 55	72 ± 85	1405 ± 2001	1900 ± 2527	989 ± 1445	1134 ± 1670	61	114 ± 52
Troponine T ng/L)	5 ± 2	6 ± 3	23 ± 19	25 ± 20	27 ± 19	26 ± 19	6	6 ± 1
Creatinine (umol/L)	74 ± 10	80 ± 13	83 ± 24	81 ± 28	79 ± 22	84 ± 31	75 ± 16	69 ± 14
sNfL (pg/mL)	9 ± 4	11 ± 5	59 ± 57	55 ± 47	82 ± 66	56 ± 51	11 ± 7	61 ± 39

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