NEUROFILAMENT LIGHT CHAIN, A PROMISING BIOMARKER FOR POLYNEUROPATHY IN SYSTEMIC AL AND ATTR AMYLOIDOSIS

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INTRODUCTION

- Detection of polyneuropathy (PNP) in an early stage of AL and ATTRv amyloidosis is crucial for prognosis and choice of treatment.
- There is a clear clinical need for an easily applicable biomarker for both early detection and severity of PNP in systemic amyloidosis.
- Neurofilament light chain (NfL), a major cytoskeletal protein of neurons, is released into the blood after axonal damage.
- Serum NfL (sNfL) has been shown to be a promising biomarker for PNP in several diseases affecting the peripheral nerves system [1,2].
- Recently, NfL appeared to be also increased in serum of ATTRv amyloidosis patients with PNP [3].

OBJECTIVE

To study NfL in serum of AL amyloidosis patients with PNP and to confirm the observation that sNfL is increased in ATTRv amyloidosis patients with PNP

METHODS

In this pilot study NfL levels were assessed in serum of patients with well-defined AL and ATTRv amyloidosis and healthy controls (**Table 1**). The following patients were included:

- Patients with AL amyloidosis and evident symptoms of PNP (AL+PNP+)
- Patients with AL amyloidosis without any symptoms of PNP (AL+PNP-)
- Patients with ATTRv amyloidosis and symptoms of PNP confirmed by electromyography (EMG) (ATTR+PNP+)
- Asymptomatic individuals with a proven pathogenic mutation in the TTR gene, negative abdominal fat biopsy and a normal EMG (TTRv-carriers)
- Healthy controls were age- and sex-matched for both the AL+PNP- group (HC AL) and the TTRv-carriers (HC ATTR)

The Single-molecule array assay (Simoa) was used to quantify sNfL concentrations. All serum samples were collected before any treatment was started.

RESULTS

Table 1. *Patient characteristics.*

	AL+PNP-	AL+PNP+	TTRv-carriers	ATTR+PNP+
	n=10	n=10	n=15	n=15
Age in years, median (IQR)	66.6 (59.9-70.7)	69.6 (61.4-72.9)	41.0 (32.1-56.3)	60.9 (47.9-68.5)
Sex (M/F)	5/5	6/4	7/8	10/5
FLC difference in mg/L, median (IQR)	168.8 (60.7-355.7)	132.0 (62.3-569.9)	-	-
NT-proBNP in ng/L, median (IQR)	517.5 (333.8-652.3)	4462.0 (910.3-10963.8)	56.0 (21.5-85.3)	586.0 (79.0-1409.0)
Cardial involvement (%)	20	80	0	80
Creatinine in umol/L, median (IQR)	84.0 (76.5-118.3)	82.0 (68.8-169.0)	76.0 (64.0-84.0)	73.0 (66.0-91.0)

RESULTS

sNfL levels were increased both in AL+PNP+ patients (median 149, IQR 64.2-329 pg/ml, P<0.001) and in AL+PNP- patients (median 22.7, IQR 18.6-37.6 pg/ml, P<0.005) compared to the HC AL group (median 13.6, IQR 9.80-17.3 pg/ml). sNfL levels were higher in AL+PNP+ patients compared to AL+PNP- patients (P<0.005). sNfL levels were also increased in ATTR+PNP+ patients (median 66.4, IQR 18.2-138 pg/ml), compared to both the HC ATTR group (median 8.80, IQR 6.50-11.4 pg/ml, P<0.0001) and the TTR-carriers (median 6.90, IQR 4.80-11.8 pg/ml, P<0.0001). sNfL levels did not differ between the TTRv-carriers and the HC ATTR group (P=0.340) (**Figure 1**).

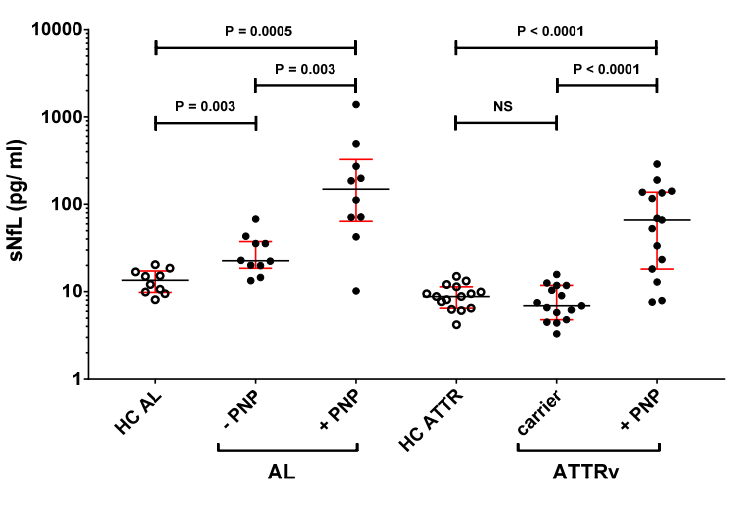

Figure 1. *Serum neurofilament light chain (sNfL) levels (pg/mL) in AL amyloidosis patients without (AL -PNP), with polyneuropathy (AL+PNP), asymptomatic TTRv-mutation carriers (ATTRv-carrier), ATTRv -amyloidosis patients with polyneuropathy (ATTRv+PNP) and age- and sex-matched healthy controls (HC AL and HC ATTR).*

In a group comprising all healthy controls (median 9.9 interquartile range (IQR) 7.9-15.0 pg/ml) sNfL levels correlated with age (r= 0.57, P=0.007). This correlation was also found found in TTRv-carriers (r= 0.76, p=0.001).

CONCLUSIONS

- **NfL is increased in serum of both AL and ATTRv amyloidosis patients with PNP.**
- **Our pilot study indicates NfL to be a promising biomarker for detection of PNP in systemic amyloidosis.**
- **Larger groups and longitudinal studies are needed to confirm these findings and further investigate the value of NfL as a biomarker for early detection, for disease severity, for follow-up and for response to treatment of PNP in systemic amyloidosis.**

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