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Serum neurofilament light chain and autonomic neuropathy in hereditary transthyretin-related amyloidosis

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INTRODUCTION

Serum neurofilament light chain (sNfL), a cytoskeletal protein released in blood during axonal damage, is a biomarker for polyneuropathy in hereditary transthyretin-related (ATTRv) amyloidosis. Whether sNfL reflects autonomic neuropathy is not known.

OBJECTIVE

The purpose of this study is to establish the relationship between sNfL and autonomic neuropathy among patients with myocardial sympathetic neuronal damage due to ATTRv amyloidosis.

METHODS

Levels of sNfL were retrospectively measured in transthyretin-gene variant carriers and ATTRv amyloidosis patients who received autonomic function tests, technetium-99m hydroxy diphosphonate scintigraphy ([^{99m}Tc]Tc-HDP scintigraphy), iodine-123 metaiodobenzylguanidine ([^{123}I]mIBG) scintigraphy, and nerve conduction studies (N=38).

RESULTS

15 patients had an abnormal [^{123}I]mIBG scintigraphy. sNfL levels were increased in patients with an abnormal [^{123}I]mIBG scintigraphy compared to patients with a normal [^{123}I]mIBG scintigraphy. sNfL levels were also increased in patients with autonomic dysfunction as measured by the Ewing battery tests. Univariate analysis indicated a relation between sNfL and presence of cardiomyopathy (based on [^{99m}Tc]Tc-HDP scintigraphy), cardiac autonomic neuropathy and polyneuropathy. In multivariate regression analysis only polyneuropathy was an independent predictor of sNfL levels.

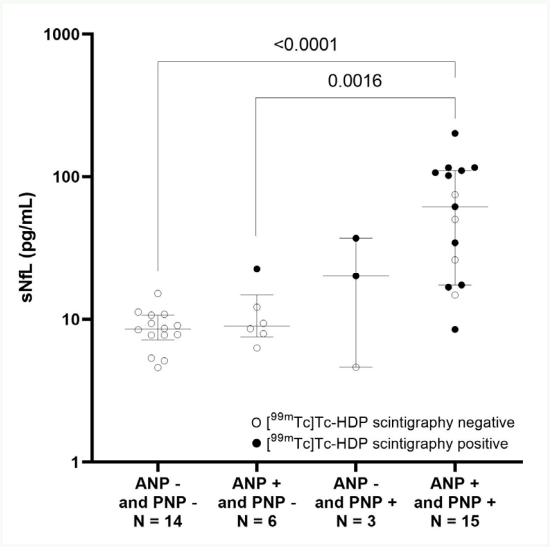
Table 1. *Univariable and multivariable linear regression analysis for ^{10}log sNfL.*

	Univariable Analysis			Multivariable Analysis (R^2=0.78)		
	Beta	*CI*	*p-value*	*Beta*	*CI*	*p-value*
General						
Age (years)	0.25	-0.08 - 0.53	0.13			
Cardiomyopathy						
^{10}Log heart-to-contralateral ratio	0.70	0.49 - 0.83	< .01	0.22	-0.02 - 0.45	0.07
Abnormal [^{99m}Tc]Tc-HDP scintigraphy (yes/ no)	0.69	0.47 - 0.83	< .01			
Cardiac autonomic neuropathy						
Late heart-to-mediastinum ratio	-0.63	-0.79 - -0.38	< .01			
Wash-out rate (%)	0.66	0.44 - 0.81	< .01			
Abnormal [^{123}I]mIBG-scintigraphy (yes/ no)	0.61	0.36 - 0.78	< .01	0.18	-0.01 - 0.42	0.06
Peripheral neuropathy						
Polyneuropathy disability score	0.83	0.69 - 0.91	< .01	0.58	0.35 - 0.78	< .01
^{10}Log Sural nerve action potential amplitude (uV)	-0.64	-0.80 - -0.38	< .01			
Polyneuropathy (yes/no)	0.71	0.51 - 0.84	< .01			
Autonomic neuropathy						
Autonomic neuropathy (yes/ no)	0.45	0.16 - 0.68	.04	0.06	-0.12 - 0.26	0.44
Other biomarkers						
NT-proBNP (ng/L)	0.66	0.43 - 0.81	< .01			
Troponin T (ng/L)	0.73	0.54 - 0.85	< .01			
Troponin I (pg/mL)	0.04	-0.30 - 0.37	0.82			
Creatinine (µmol/L)	0.28	-0.05 - 0.55	0.09			
CK (U/L)	0.12	-0.22 - 0.44	0.49			
CKMB (µg/L)	0.60	0.32 - 0.78	< .01			

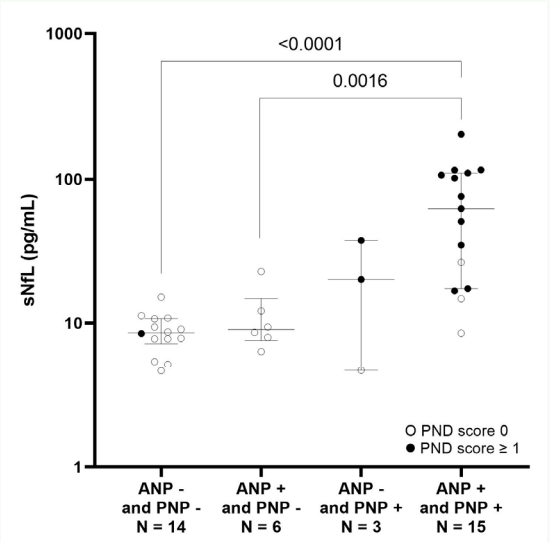
Beta refers to influence on ^{10}log sNfL. [^{99m}Tc]Tc-HDP scintigraphy: technetium-99m hydroxy diphosphonate scintigraphy; [^{123}I]mIBG-scintigraphy: Iodine-123 metaiodobenzylguanidine scintigraphy; NT-proBNP: N-terminal pro-B-type peptide; CK: creatinine kinase; CKMB: creatine kinase myocardial band; sNfL: serum neurofilament light chain.

RESULTS

A.



B.



A. Serum neurofilament light chain (sNfL) in patients with or without autonomic neuropathy (ANP) and with or without cardiomyopathy (negative or positive [99mTc]Tc-HDP scintigraphy). PNP: polyneuropathy.
B. Serum neurofilament light chain (sNfL) in patients with or without autonomic neuropathy (ANP) and with or without polyneuropathy (PNP) represented by the polyneuropathy disability score (PND score). ANP is defined as either abnormal [^{123}I]mIBG scintigraphy and/ or abnormal autonomic function tests.

CONCLUSIONS

Increased sNfL levels in ATTRv amyloidosis with autonomic neuropathy are caused by the concurrent presence of polyneuropathy and do not reflect autonomic neuropathy.

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