Neurofilament light chain measurement in hereditary transthyretin-related amyloidosis patients with myocardial sympathetic neuronal damage: substitution for ^{123}I-meta-iodobenzylguanidine scintigraphy?

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INTRODUCTION

The use of iodine-123 labelled meta-iodobenzylguanidine (^{123}I-MIBG), a chemical modified analogue of norepinephrine, plays an important role in the evaluation of sympathetic innervation in cardiac amyloidosis. MIBG normally accumulates in vesicles in sympathetic nerve endings close to myocardial cells. Reduced uptake and increased loss of MIBG probably reflects damage of the cardiac sympathetic nerves. Serum neurofilament light chain (sNfL) is a biomarker for neuronal damage and levels of sNfL reflect polyneuropathy severity in hereditary transthyretin-related (ATTRv) amyloidosis. Unexpectedly, sNfL levels also correlated with troponin T, a biomarker for cardiac damage. This observation has not yet been explained. It can be hypothesized that cardiac neuronal damage explains the correlation between sNfL and troponin T .

OBJECTIVE

To establish the possible relation between sNfL and myocardial sympathetic neuronal damage in patients with ATTRv amyloidosis.

METHODS

Levels of sNfL were measured in ATTRv patients who had undergone an ^{123}I-MIBG scintigraphy, autonomic function testing and nerve conduction studies (N=36). The single-molecule array (SIMOA) assay was used to assess sNfL levels. Myocardial sympathetic neuronal damage was detected using ^{123}I-MIBG scintigraphy: either late heart-to-mediastinum ratio (HMR) <2.0 or wash-out rate >20% was considered as abnormal ^{123}I-MIBG scintigraphy parameters.

RESULTS

	Univariate analysis		Multivariate analyses	
	B (% CI)	*p-*	*B (% CI)*	*p-*
Age (years)	0,007 (-0,005 -	0,230		
Polyneuropathy	0,599 (0,346 -	0,000	0,252 (0,026 -	0,030
Autonomic neuropathy (yes/no)	0,529 (0,219 - 0,839)	0,001	0,207 (-0,004 - 0,417)	0,054
Small fiber neuropathy (yes/no)	0,425 (0,018 - 0,833)	0,041		
Troponin T	0,019 (0,014 -	0,000	0,014 (0,008 -	0,000
Abnormal baseline MIBG scintigraphy (yes/no)	0,565 (0,303 - 0,827)	0,000	0,031 (-0,218 - 0,280)	0,800

Table 1. Univariate and multivariate linear regression analysis for log10 sNfL in carriers of a TTR mutation (N=13) and ATTRv patients (N=23).

RESULTS

2 of the 13 TTR mutation carriers and 13 of the 23 ATTRv amyloidosis patients had an abnormal ^{123}I-MIBG-scintigraphy at baseline. sNfL levels were significantly increased in patients with an abnormal ^{123}I-MIBG scintigraphy compared to patients with a normal ^{123}I-MIBG scintigraphy (p=0.0006). Late HMR negatively correlated with sNfL (r= -0.60 p=<0.0001) and wash-out rate correlated positively with sNfL (r= 0.65, p=<0.0001). Univariate analysis indicates a relation between sNfL and polyneuropathy, autonomic neuropathy, troponin T, late HMR, wash-out rate and abnormal ^{123}I-MIBG-scintigraphy at baseline. In multivariate regression analysis polyneuropathy and troponin T were independent predictors of sNfL levels ($F(4,29)= 21.180$, p=< 0.000, $R^2 = 0.745$).

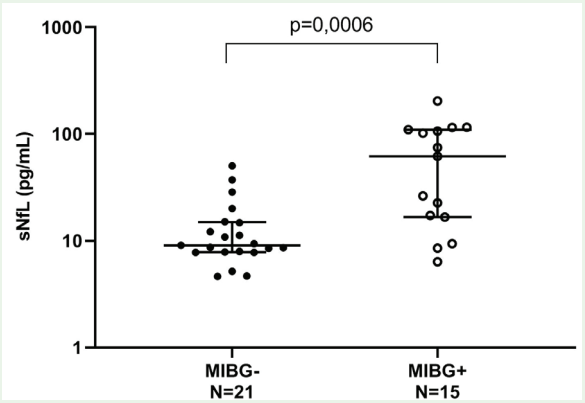

Figure 1. sNfL in patients with a normal/ negative ^{123}I-MIBG scintigraphy (MIBG -) and an abnormal/ positive ^{123}I-MIBG scintigraphy(MIBG +).

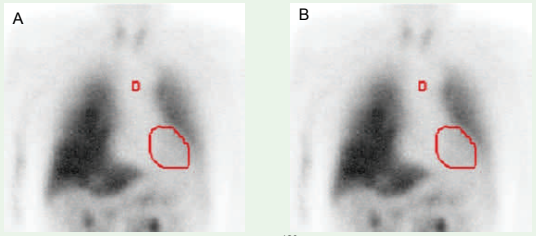

Figure 2. ATTRv patient with an abnormal/ positive ^{123}I-MIBG scintigraphy. ***A.*** Early HMR ratio 1,84. ***B.*** Late HMR ratio 1,34. Wash-out rate 27% (normal value <20%).

CONCLUSIONS

- **Myocardial sympathetic neuronal damage based on ^{123}I-MIBG scintigraphy correlates with sNfL, but it is not an independent predictor of sNfL.**
- **Increased sNfL levels in ATTRv patients with an abnormal ^{123}I-MIBG scintigraphy are probably caused by the presence of polyneuropathy in these patients.**

REFERENCES

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