

## Increased plasma amyloid- $\beta_{42}$ protein in sporadic inclusion body myositis

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Received: 14 January 2009 / Revised: 28 May 2009 / Accepted: 28 May 2009 / Published online: 6 June 2009  
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Sporadic inclusion body myositis (s-IBM) is the most frequently acquired myopathy above the age of 50 years. Although the pathogenesis of s-IBM is largely unknown, an underlying myodegenerative process involving amyloid  $\beta$  protein ( $A\beta$ ) accumulation has been proposed as a pathophysiological mechanism [1]. Here, we examined whether there are changes in the plasma levels of  $A\beta_{42}$  and  $A\beta_{40}$  in patients with s-IBM, patients with other inflammatory myopathies, and age-matched controls.

All patients diagnosed with an inflammatory myopathy before January 2006 were retrieved from the Dutch neuromuscular database (CRAMP = Computer Registry of All Myopathies and Polyneuropathies) [4]. Of the 152 registered patients, 49 patients were excluded because they could not be traced ( $n = 11$ ), were deceased ( $n = 26$ ) or declined to participate ( $n = 12$ ). We included 31 patients with s-IBM, 49 with polymyositis (PM) and 23 with dermatomyositis (DM). Thirty-four neurologically healthy spouses were selected as age-matched controls. Diagnosis of s-IBM, DM and PM was made according to established international criteria [3, 5]. Patients were visited at home.

Functional status was scored using the modified Rankin-scores, and the Barthel index. Furthermore, total body weight, use of steroids or other immunosuppressive medication and statins (HMG-CoA reductase inhibitors) were noted. Local ethical committee approval, and written informed consent from all participants, was obtained.

Plasma samples were aliquoted and frozen at  $-80^{\circ}\text{C}$  until the time of analysis. Plasma concentrations of  $A\beta_{42}$  were measured by a commercial ELISA (Innotest  $\beta$ -amyloid $_{(1-42)}$  High Sensitivity Test; Innogenetics, Gent, Belgium).  $A\beta_{40}$  concentrations were measured by a commercially available assay based on the xMAP technology (Biosource, Camarillo, CA, USA) on a LiquiChip 100S analyzer (Qiagen, Venlo, The Netherlands).

Comparisons of the plasma values between the groups were made using one-way ANOVA with Tukey post hoc test on logarithmically transformed data with covariate analysis of the baseline characteristics. Correlations between variables were calculated using Pearson's correlation coefficient. SPSS version 14.0 was used to analyze the data.

Baseline characteristics and plasma  $A\beta$  are shown in Tables 1 and 2. The median plasma  $A\beta_{42}$  levels were significantly increased in the s-IBM group versus controls and PM group. When we divided the s-IBM patients into two groups, with concentrations either above or below the median levels of  $A\beta_{42}$ , we neither found any differences in demographic data nor in disease severity. Also, age or Rankin-scores or Barthel index, medication use, time interval from blood draw to spinning and freezing or other baseline characteristics did not correlate with  $A\beta_{42}$  or  $A\beta_{40}$  levels in the individual groups.

This is the first study examining plasma levels of  $A\beta_{42}$  in patients with s-IBM compared to patients with other inflammatory myopathies and age-matched controls. Data

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**Table 1** Patient characteristics

	s-IBM ( <i>N</i> = 31)	PM ( <i>N</i> = 49)	DM ( <i>N</i> = 23)	Controls	<i>P</i> value
Mean (95% confidence interval I)					
Age	69 (65–73)	59 (55–63)	49 (43–55)	59 (53–64)	<0.001 <sup>a</sup>
Disease duration (years)	5.6 (3.8–7.3)	10.2 (8.0–12.3)	7.8 (5.1–10.6)	NA	0.02 <sup>a</sup>
Median (25–75%)					
Rankin score	2 (2–4)	2 (1–3)	1.5 (0–2)	NA	0.02 <sup>b</sup>
Barthel index	16 (14–19)	20 (18–20)	20 (20–20)	NA	0.002 <sup>b</sup>

NA not applicable

<sup>a</sup> One-way ANOVA

<sup>b</sup> Kruskal–Wallis test for multiple comparisons

**Table 2** Mean plasma concentration of A $\beta$ <sub>42</sub> and A $\beta$ <sub>40</sub>

	s-IBM ( <i>N</i> = 31)	PM ( <i>N</i> = 47)	DM ( <i>N</i> = 24)	Controls ( <i>N</i> = 34)	<i>P</i> value
Median (25–75%)					
A $\beta$ <sub>42</sub> pg/ml	37 (27–82)	28 (22–37)	36 (28–51)	28 (23–41)	IBM versus PM: <i>P</i> = 0.01 IBM versus Controls: <i>P</i> = 0.01
A $\beta$ <sub>40</sub> pg/ml	270 (230–312)	258 (212–308)	260 (231–305)	228 (200–250)	NS

NS not significant

of other studies hint to a degenerative contribution to the cause of s-IBM, where it was shown that intracellular amyloid deposits and A $\beta$  immunoreactivity were found in affected muscle fibers of patients with s-IBM [1]. In addition, recent transgenic mice studies have shown that the deposition of A $\beta$  may be a primary pathogenic mechanism in s-IBM [2].

This cross-sectional cohort study was designed for the sole purpose to test the hypothesis that the underlying neurodegenerative process in s-IBM could be reflected in altered A $\beta$  plasma levels. Because of this design, plasma A $\beta$  levels could not be correlated to the results of the muscle biopsies, because in many patients the diagnosis was made several years before we collected the plasma. Lack of matching in baseline characteristics (due to the intrinsic clinical characteristics of the included disorders) did not explain the differences in A $\beta$  levels. Surprisingly, plasma A $\beta$  levels were also increased in DM. A possible confounding factor could be that some of the DM patients could have developed IBM at time of this study, since there were older patients included in this group and the diagnosis was made previously, i.e., we did not perform new biopsies in patients that were diagnosed previously. Furthermore, kidney function can influence amyloid levels. Only one DM patient had a previous kidney problem in his medical history. The A $\beta$  plasma concentrations of this patient were within the range of his group. However, specific laboratory data of kidney functions at time of the study were not available. The

potential diagnostic value of plasma A $\beta$  testing seems limited in our cross-sectional cohort because of the considerable overlap in concentrations. Further prospective investigations are required, to fully elucidate this and, in addition, to evaluate if plasma A $\beta$  concentrations could be correlated to the severity or long-term outcome of this enigmatic disease.

**Acknowledgments** M.M. Verbeek was supported by a research grant from ZonMW Innovational Research (number 917.46.331, “Vidi Program”).

**Conflict of interest statement** The authors report no conflict of interest.

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