APPLICATIONS OF NEW LABORATORY MARKER ASSAYS IN NEUROLOGICAL DIAGNOSES – A PILOT STUDY

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225 consecutive patients with different neurological diseases and 101 individuals as the control were examined between 2002–2004. Cystatin C, arginase-I, τ -protein and β -amyloid were measured. Individuals with CNS inflammation had significantly lower Cystatin-C index (CSF/serum) values. There was no diagnostic significance of the Arginase-I assay in CSF was verified. The CSF τ -protein/ β -amyloid index was shown to be a sufficient efficacy for neurodegenerative disease diagnosis.

INTRODUCTION

There is much current information on the use of new laboratory markers in the diagnosis of some neurological diseases primarily about degenerative and inflammatory origin.

Simple analysis of cerebrospinal fluid (CSF) laboratory markers has only limited significance but recently published information deals with diagnostic use of the entire CSF markers.

The first aim of our work was diagnostic evaluation of CSF cystatin C and arginase-I analysis in individuals with various neurological diagnoses.

The second aim of our work was evaluation of previously published diagnostic efficacy of CSF τ -protein/ β -amyloid index in patients with neurodegenerative diseases.

METHODS

225 consecutive patients and 101 individuals without neurological diseases from the clinical departments of the Šternberk Hospital and the Institute of Neurology Faculty Hospital Olomouc were examined between 2002–2004.

The groups were divided into 9 subgroups (1-ischemic stroke, $n=12$; 2-hemorrhagic stroke, $n=13$; 3-sclerosis multiplex-RS, $n=37$; 4-bacterial CNS inflammation, $n=11$; 5-serous CNS inflammation, $n=24$; 6-polyradiculoneuritis, $n=13$; 7-Alzheimer disease, $n=34$; 8-individuals without important neurological abnormalities, $n=101$; 9-neuropathy, $n=29$).

CSF samples were drawn from the patients for diagnostic reasons. The serum and CSF samples were separated in a cooled centrifuge at 4 °C with 3000g and subsequently frozen at –80 °C for ELISA analysis.

CSF total τ -protein (ELISA, Biosource, UK) CSF β -amyloid (ELISA, Innogenetics, Belgium), CSF Arginase-I (ELISA, Biovendor, Brno, the Czech Republic), serum and CSF Cystatin-C concentrations (ELISA, Biovendor, Brno, The Czech Republic) were performed on all individuals, too. Cystatin C was determined with satisfying analytical parameters (intrassay coefficient of variation (CV) = 4.9 %, interassay CV = 9.1 %). Concentrations of Arginase-I, Cystatin C, total τ -protein and β -amyloid were determined after defrosting during the course of one day.

The study was approved by the ethics commission of the Hospital Šternberk and the Medical Faculty UP Olomouc.

The data obtained were processed by means of the software Medcalc (Medcalc, Mariakerke, Belgium). The value $p < 0.05$ was considered as statistically significant.

RESULTS

Cystatin-C in serum: individuals with neurodegenerative diseases (NDD, $n=34$) had the lowest Cystatin-C values of all subgroups (median 0.69 mg/l) but values did not significantly differ between groups.

Cystatin-C in CSF: values did not significantly differ.

Cystatin C index: individuals with CNS inflammation had significantly lower values than individuals without neurological diseases (median 2.5 vs 4.9; $p=0.001$). Diagnostic sensitivity of the Cystatin-C index was 85 %, specificity 54 % (AUC 0.76; 95 % CI 0.64–0.83) for CNS inflammation (Fig 1).

Diagnostic efficacy for polyneuropathy diagnosis was not sufficient.

Arginase-I in CSF: no significant differences were detected in concentrations between groups. 57 % of

Fig. 1. Index Cystatin C ROC for CNS inflammation

Fig. 2. Index Csf τ -protein/ β -amyloid ROC for neurodegenerative CNS diseases

individuals with CNS inflammation had measurable Arginase-I concentrations, 33 % of individuals without CNS inflammation had measurable Arginase-I concentrations. No significant correlations between Arginase-I and other markers were demonstrated.

As a secondary finding we also show significant diagnostic efficacy of τ -protein/ β -amyloid indexes in patients with neurodegenerative CNS diseases; diagnostic sensitivity in index value > 0.5 was 69 % and specificity 74 % (AUC 0.76) (Fig. 2).

No significant differences were detected in ROC comparison of indexes τ -protein/ β -amyloid and Hulstaert calculation (ROCs AUC 0.88 vs 0.88).

CONCLUSIONS

Individuals with CNS inflammation have significantly lower Cystatin-C index values. Cystatin-C index assay is for inflammation CNS diagnosis sufficiently effective. No diagnostic significance of Arginase-I assay in CSF was verified in patients with inflammatory or autoimmune CNS diseases. τ -protein/ β -amyloid index in CSF was proven to be a sufficient efficacy for NDD diagnosis.

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