ABSTRACT

The aims of the thesis were to assess diagnostic markers for monitoring of the disease progression in patients with clinically isolated syndrome (CIS) and laboratory markers of efficacy of the interferon beta (IFNß) therapy. This thesis includes 4 studies.

The first study was focused on evaluation of cognitive impairment and its structural correlates in patients with CIS. Using comprehensive neuropsychological testing and brain magnetic resonance imaging (MRI) with volumetric analyses we found cognitive impairment in 18–37 % of CIS patients in almost all cognitive domains. Brain volume was reduced predominantly in fronto-temporal regions and the thalamus. Next, visuo-spatial impairment was associated with lower white matter volume in patients with CIS.

The two other studies evaluated neuropsychiatric symptoms, life satisfaction, health-related quality of life and their mutual relationships. In addition, one of these two studies evaluated structural correlates of neuropsychiatric symptoms on brain MRI. Using a battery of specific questionnaires, we demonstrated depressive symptoms and anxiety in patients with CIS, lower life satisfaction, lower health-related quality of life and close mutual relationships. The quality of life was associated more with cognitive functioning than with disability in patients with CIS. Neuropsychiatric symptoms were related to white matter atrophy and increased lesion load volume in temporal, occipital and insular area.

The fourth study was focused on evaluation of laboratory markers of efficacy of the IFNβ therapy by using levels of Myxovirus resistance protein (MxA) and neutralizing antibodies (NAbs). We did not find association between baseline MxA mRNA levels and responsiveness to IFN β therapy. Next, there was no association between clinical activity and levels of mRNA MxA. In NAbs negative patients, mean levels of MxA mRNA did not significantly differ between the groups classified based on the relapse status. However, we found that NAbs negative patients form a heterogeneous group and it is desirable to evaluate levels of MxA mRNA in addition to NAbs assessment.

The results of our studies suggest that cognitive impairment is present in up to one third of CIS patients and includes almost all cognitive domains. Depressive and anxiety symptoms are 13

present in patients with CIS and are related to lower life satisfaction and lower health-related quality of life. CIS patients have cortical and subcortical atrophy and there is relationship between white matter atrophy, visual-spatial impairment, and neuropsychiatric symptoms, which are also related to increased lesion load volume in certain brain areas. We did not confirm the relationship between the baseline levels of MxA mRNA, responsiveness to IFNβ therapy and clinical activity in NAbs negative patients. However, we found that in NAbs negative patients the effect of IFNβ therapy may not always be preserved. The results of our studies may help in identifying the specific markers for monitoring of disease progression and responsiveness to therapy in patients in the early stages of multiple sclerosis, which allows us to initiate a specific treatment leading to improvement of their health-related quality of life and to delay the progression of their disability.

Key words: clinically isolated syndrome, cognitive impairment, neuropsychiatric symptoms, quality of life, magnetic resonance, interferon ß, Myxovirus resistance protein A, neutralizing antibodies