IS THE MEASUREMENT OF BRAIN ATROPHY THE MOST SUITABLE SURROGATE MARKER OF MS PROGRESSION? NO

Uroš Rot
Department of Neurology, University Medical Centre, Ljubljana, Slovenia

Although multiple sclerosis (MS) is an inflammatory and demyelinating diesase of the central nervous system, neurodegeneration is present from the beginning of the disease and often leads to irreversible neurological deficit. Clinical measures of disease progression, such as EDSS are inaccurate because they vary between relapses and remissions and have limited intra and inter-rater reliability.

Brain atrophy measured by MRI has been suggested as a promising tool for objective monitoring of disability progression. Longitudinal studies showed that the rate of brain volume loss is 0,5-1,35% per year in patients with MS compared to 0,1% in healthy individuals. A number of cross-sectional studies revealed that brain volume loss correlates with disability progression. For example, brain volume loss was found to be greater in patients with CIS who developed MS than those who did not and in patients with MS who progressed compared to patients who remained stable. Several studies also showed a correlation between brain volume reduction and cognitive impairment.

Is than the measurement of brain atrophy the most suitable surrogate marker of MS progression? I do not think so. MRI techniques of atrophy measurement are sensitive and reproducible but they are time-consuming, costly and not routinely available in clinical practice. Furthermore, factors such as alcohol consumption, smoking, Apolipoprotein E status and concomittant diseases, such as diabetes and cardiovascular risk factors adversely affect brain volume studies. Moreover, brain volume loss also progresses with age and is even more pronounced in patients with the mentionted risk factors. In addition, anti-inflammatory treatment for MS was shown to decrease brain volume within the first 6 months to 1 year. The phenomenon is named pseudoatrophy and reflects the resolution of edema and inflammation at the initiation of disease modifying drugs.

How can a clinical neurologist make a treatment decision in an individual patient based on MRI volmetric studies when the majority of disease modifying drugs did not show significant or showed inconsistent effects on brain volume? Even for one of the most powerful drugs we have, natalizumab, some of the studies demonstrated and some did not show the effect on brain volume.

Markers of the disease progression should be cheap, reproducible, non-invasive and well tolerated. Optical coherence tomography with different retinal layer measurements was demonstrated to correlate with the disease progression and could easily be a part of routine monitoring in patients with MS. Traditional and widely available methods used in the diagnosis of MS were also shown to be useful for monitoring of the disease process. For example, amplitude measurements of multimodal evoked potentials and motor evoked potentials correlated with clinical measures of the disease progression.

It would be even better if instead of longitudinal results of sophisticated technology studies, such as brain MRI volumetrics, management decisions could be guided by basic clinical and paraclinical data gained at the diagnosis or at the follow-up examinations. We have some useful prognostic data available for the treatment naive and treated MS patients. For example, high number of T2 lesions, presence of oligoclonal bands or IgM oligoclonal bands at the diagnosis and absence of immunomodulatory treatment indicate more severe late disability in patients with CIS. In patients who are already treated with immunomodulatory drugs relapses in first year and presence of Gd enhancing or new T2 lesions predict unstable disease and poor long-term prognosis which again help clinicians to tailor the treatment in an individual patient.