Researchers lead committee to define the clinical course of multiple sclerosis

May 28 2014

Accurate clinical course descriptions (phenotypes) of multiple sclerosis (MS) are important for communication, prognostication, design and recruitment for clinical trials, and treatment decision-making. Researchers at Icahn School of Medicine at Mount Sinai, part of the International Committee on Clinical Trials of MS, collaborated to re-examine the standardized MS clinical course descriptions originally published in 1996 and recommend refined phenotype descriptions that include improved clinical descriptive terminology, MRI and other imaging techniques, analysis of fluid biomarkers and neurophysiology. The proposed 2013 revisions will appear in the May 28, 2014, online issue of *Neurology*, the medical journal of the American Academy of Neurology.

"Our goal for modifying the 1996 definitions is to better characterize patients with MS and provide a framework for both clinical research and ongoing clinical care," says Fred D. Lublin, MD, Director of the Corinne Goldsmith Dickinson Center for Multiple Sclerosis at The Icahn School of Medicine at Mount Sinai, and the article's lead author. "These revisions should make communication with patients and among physicians clearer and should also enhance the design, recruitment and conduct of clinical trials, which will further help us understand the disease."

Multiple sclerosis is a potentially debilitating disease in which the body's immune system eats away at the protective sheath (myelin) that covers the nerves. Damage to myelin causes interference in the communication

between the brain, spinal cord and other areas of the body and may result in deterioration of the nerves themselves. MS can be difficult to diagnose because symptoms often come and go, symptoms vary widely and there is no cure. However, treatments may help reduce MS attacks, manage symptoms and lessen disease progression.

The 1996 clinical course descriptions provided standardized definitions for four MS clinical courses, which included: relapsing-remitting (RR), secondary progressive (SP), primary progressive (PP), and progressive relapsing (PR). While these descriptions were believed to represent the spectrum of clinical subtypes of MS, it was recognized that the descriptions might change over time as a result of advanced imaging techniques and biological markers.

In reconsidering the prior MS disease course descriptors, the advisory group recommends that the core MS phenotype descriptions of relapsing and progressive disease be retained, with some modifications. The consensus is that disease activity detected by clinical relapses or imaging (gadolinium-enhancing lesions or new or unequivocally enlarging T2 lesions) as well as progression of disability can be meaningful additional descriptors of either relapsing or progressing disease. Evidence of disease activity and clinical progression, which by current understanding reflects ongoing inflammatory or neurodegenerative disease, may impact prognosis, therapeutic decisions and clinical trial designs and outcomes.

To assess disease activity, the group recommends at least annual clinical assessment and brain imaging for relapsing MS. For progressive MS, annual clinical assessment is recommended, but there was no consensus on the optimal frequency of imaging. They suggest that progression be determined annually by history or objective measure of change. Thus, the existing course descriptions should be sub-categorized based on activity or progression. For example a patient with relapsing-remitting (RR) MS who had a new gadolinium-enhancing lesion on a current MRI

would be considered to be RR-active. Conversely, "non-active" could be used the same way to indicate a patient with a relapsing course but no relapses or new MRI lesions during the assessment period. Inclusion of activity as a modifier of basic clinical course phenotype allows elimination of the progressive relapsing (PR) category because a PPMS patient who has an acute attack (thus fulfilling the prior criteria for PRMS) would be considered PP-active.

Another recommendation is that clinically isolated syndrome (CIS), which was not included in the initial MS clinical descriptors, but is now recognized as the first clinical presentation of a disease that shows characteristics of inflammatory demyelination that could be MS, be included in the spectrum of MS phenotypes. Prospective follow-up of most such patients should determine their subsequent disease phenotype. Radiologically isolated syndrome (RIS), where incidental imaging findings suggest inflammatory demyelination in the absence of signs or symptoms should not be considered a separate MS phenotype.

"Our understanding of multiple sclerosis has come a long way since the original phenotype classifications were standardized 18 years ago," says Dr. Lublin. "Future long-term longitudinal and cohort studies, imaging studies, prospective follow up and research is needed to better understand and define MS phenotypes, allowing us to continue to refine the framework for clinical research and care for the patients who turn to us for help."

Provided by The Mount Sinai Hospital