Autoantibodies and neuropsychiatric events in lupus

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Systemic lupus erythematosus (SLE), commonly known as lupus, can affect nearly any part of the body, including the joints, skin, kidneys, heart, nervous system, and brain. Along with joint pain, muscle pain, unexplained fever, extreme fatigue, and skin rashes, neurologic and psychiatric events often accompany this autoimmune disease. Depending on the study, between 37 and 95 percent of SLE patients experience signs and symptoms of neuropsychiatric (NP) disease. Determining the correct attribution to NP events is a challenge when managing nervous system disease in individual SLE patients, as well as a critical factor in selecting the right treatment and evaluating progress. For guidance in these decisions, doctors need reliable biomarkers -- which, as dedicated researchers know, have proven difficult to find.

Generation of specific autoantibodies is one of the lupus-specific mechanisms underlying NP disease. Attempts to investigate their biomarker potential have been limited by the wide-ranging disease severity and duration of study patients, not to mention lack of standardization in both the classification of NP events and the methodology used for autoantibody detection. With the goal of overcoming these limitations, an international research alliance called the Systemic Lupus International Collaborating Clinics (SLICC) examined the association between a panel of autoantibodies and nervous system events at the time of diagnosis of SLE.

Their results, presented in the March 2008 issue of *Arthritis & Rheumatism* (http://www.interscience.wiley.com/journal/arthritis),

indicate two compelling links: one between anti-ribosomal P (anti-P) antibodies and psychosis attributed to SLE and the other between lupus anticoagulant (LAC) and cerebrovascular disease attributed to SLE.

Led by Dr. J.G. Hanly, a Rheumatologist at the Queen Elizabeth II Health Sciences Centre and Professor of Medicine at Dalhousie University in Halifax, Nova Scotia, and supported in part by grants from the Canadian Institutes of Health Research and the Lupus Foundation of America, the study focused on 412 SLE patients recruited from 18 treatment centers. Over 87 percent of the subjects were women, ranging in age from 34 to 58 and representing diverse ethnic backgrounds -- Hispanic, Asian, black, and white. At the time of enrollment, the mean disease duration was only 5 months.

Patients were evaluated to identify features of 19 NP syndromes, based on the American College of Rheumatology case definitions, within a 21-month window around the time of SLE diagnosis. Grouped into central and peripheral nervous system syndromes for analysis, the NP events included headaches, mood disorders, anxiety disorder, cerebrovascular disease, cognitive dysfunction, seizure disorder, acute confusional state, aseptic meningitis, movement disorder, Guillian-Barr syndrome, and psychosis. To determine the presence of telltale lupus autoantibodies, blood and plasma samples from each subject were analyzed in the research laboratory of Dr. Joan Merrill, a Rheumatologist and Chief of the Department of Clinical Pharmacology at the Oklahoma Medical Research Foundation and a co-investigator in the study.

Within the study window, 133 of the 412 patients (32.3 percent) had at least one NP event and 47 (11.4 percent) had two or more events. In total, the events encompassed 14 of the 19 recognized NP syndromes. The proportion of NP events directly attributed to SLE varied from 15 percent (32 of 214) to 36 percent (77 of 214), depending on the attribution model used. Testing for autoantibodies uncovered an

association between anti-ribosomal P antibodies and psychosis.

Seven patients had psychosis that was attributed to SLE and nearly half of these patients had anti-P antibodies. In addition, the presence of another lupus antibody called lupus anticoagulant was linked to cerebrovascular disease, particularly nonischemic stroke. There was no statistically significantly link with NP events and other lupus autoantibodies, including anticardiolipin, anti-A2-glycoprotein I and anti-NR2 glutamate receptor antibodies.

Source: Wiley-Blackwell