Cognition May Improve After Lupus Diagnosis

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — The first prospective, longitudinal study of how cognition in patients with newly diagnosed lupus changes over time produced two surprising findings—that cognitive function is impaired in most patients at the time of diagnosis, but improves dramatically in the 3-4 years after diagnosis.

The study of 113 patients diagnosed at three institutions failed to identify variables to help explain why cognitive function improved over time. Several factors, however, were associated with cognitive dysfunction at baseline—most notably depression, Dr. Michelle Petri said at the annual meeting of the American College of Rheumatology.

"It begs the question of whether we should be doing depression intervention in early lupus," said Dr. Petri, professor of medicine at Johns Hopkins University, Baltimore. "I can't tell you that depression causes this. It's just as likely that lupus causes depression and lupus causes cognitive dysfunction."

Several previous prospective studies that looked at patients with established lupus reported that 10 years after diagnosis 80% of patients had measurable cognitive dysfunction. Those studies also reported surprising improvements over time, except perhaps in patients who are persistently anticardiolipin-positive, in whom cognitive function appears to decline over time, Dr. Petri said.

Dr. Petri followed the 113 patients in quarterly visits for 3-4 years. Patients underwent a brain magnetic resonance imaging (MRI) and positron emission tomography (PET) scan at the first and last visits, and were assessed yearly using the ACR neuropsychiatric battery. Every visit included assessments of disease activity, depression, and fatigue; laboratory tests including measures of antiphospholipid antibodies; and measures of nine areas of cognitive function using a computer-assisted battery of tests called Automated Neuropsychological Assessment Metrics (ANAM).

Results showed that 60% of patients at the time of lupus diagnosis had ANAM scores one standard deviation below control patients, and 19% had ANAM scores two or more standard deviations below controls, she said.

ANAM scores improved significantly over time in eight of nine categories—all except simple reaction time, which neither improved nor declined. Gains were seen in vigilance/sustained attention, visual scanning and learning, nonverbal immediate memory, nonverbal delayed memory, visual perception and mental rotation, sustained attention and working memory, simple mental arithmetic, and visuospatial perception and working memory.

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DR. PETRI

The analysis estimated significant improvements in ANAM at 18 and 36 months and significant improvements in results on the ACR neuropsychiatric battery at 12 and 36 months after diagnosis.

Autoantibodies were not associated with changes in cognitive function over time. Neither was smoking status nor the use of prednisone or aspirin at baseline.

Depression at baseline (measured by the Calgary Depression Scale) was associated with problems in visual scanning and learning, vigilance and sustained attention, visuospatial perception and working memory, and sustained attention and working memory.

"This appears to be the most important construct," she said, though several other baseline measures were associated with smaller numbers of cognitive problems.

The cohort was 97% female, with an average age of 38, and comprised 56% whites, 20% Hispanics, 15% blacks, 5% Asian Americans, and 4% others.

ANAM was developed by the military to assess the effects of chemical agents, extreme environments, and fatigue.

The investigators reported having no conflicts of interest. ■

Lupus, RA Cardiovascular Risk Equivalent to That of Diabetes

BY NANCY WALSH
New York Bureau

FORT LAUDERDALE, FLA. — Patients with systemic lupus erythematosus and rheumatoid arthritis should be considered in a cardiovascular risk category equivalent to that of patients with diabetes, with aggressive management of risk factors, particularly dyslipidemia, according to experts.

It is not yet clear whether the increased incidence of coronary artery disease (CAD) in patients with lupus and RA is a result of rheumatic factors that drive the atherosclerotic process, or if risk factors in the milieu of rheumatic disease cause patients to be more vulnerable, said Dr. Daniel Edmundowicz.

"But in any case, the process is driven by dyslipidemia," he said. "We are born with LDL cholesterol levels around 35-40 mg/dL, and a lab result that says you are normal at 130 mg/dL is wrong—that's average but it's abnormal for homo sapiens, and if you are vulnerable you are in trouble."

Because of this vulnerability, "many of us feel that patients with rheumatologic diseases should be considered CHD [coronary heart disease] risk equivalents," said Dr. Edmundowicz, director of preventive cardiology at the University of Pittsburgh Medical Center's Cardiovascular Institute.

"CHD risk equivalent" is the designation given by the National Cholesterol Education Program (NCEP) to people with diabetes and conditions such as peripheral arterial disease who have a high prevalence of CAD events like fatal and nonfatal myocardial infarction.

Currently, NCEP practice guidelines suggest that patients who are CHD risk equivalents be treated aggressively with regard to their risk factors such as cholesterol. "Patients with rheumatologic diseases should be reaching the same aggressive risk factor goals, which would mean non-HDL cholesterol less than 130 mg/dL or less than 100 mg/dL for patients who already have CAD, and LDL cholesterol of less than 100 mg/dL or less than 70 mg/dL if they already have CAD," he said.

For many patients, meeting these goals will require statins, Dr. Edmundowicz said at a meeting sponsored by RHEUMATOLOGY NEWS and Skin Disease Education Foundation.

"Over the past 20 years, we have demonstrated that statin therapy is safe, and there now are effective and inexpensive generic lipid-lowering drugs," he said.

But with aggressive statin therapy it is important to realize that titration of the drugs provides minimal additive benefits and can increase toxicity. "If you start your patient on 40 mg of simvastatin and then raise it to 80 mg, you are probably only going to get an additional 5% of lowering of lipoproteins but you are much more likely to get myalgias," he said.

Additive or combination lipid therapy is now becoming much more popular, utilizing agents that have different mechanisms of action. For example, blocking cholesterol uptake with ezetimibe and absorbing biliary cholesterol with bile acid sequestrants can provide very effective lowering of LDL, he said.

Attention also must be paid to lowering blood pressure, smoking cessation, and increasing physical activity. Of course, these patients have considerable limitations, with restricted joint range of motion and deconditioning, but even small inroads can be very beneficial, he said.

Dr. Edmundowicz consults for GNC, Merck & Co., Schering Plough, and Takeda. SDEF and this newspaper are owned by Elsevier. ■

Atherosclerosis Is Not Common in Early SLE

BY SALLY KOCH KUBETIN
Publication Editor

SAN FRANCISCO — The majority of vascular events that occur early in the course of systemic lupus erythematosus cannot be attributed to atherosclerosis, judging from the results of an ongoing multinational study.

The inception cohort included 1,249 patients who enrolled in the study within a year of receiving a diagnosis of SLE. During the first 8 years of follow-up, 72 patients had 97 vascular events. Among these were 24 cases of heart failure, 23 strokes, 15 cases of angina, 13 MIs, 13 transient ischemic accidents (TIAs), and 9 cases of peripheral vascular disease (PVD).

Of these 97 events, 31 were attributable to atherosclerosis, said Dr. Murray B. Urowitz, who presented the findings at the annual meeting of the American College of Rheumatology. An event was attributed to atherosclerosis if it occurred when SLE was inactive or if atherosclerotic changes were identified on imaging or pathology.

The events that could not be attributed to atherosclerosis occurred during a phase of active lupus in 50 cases; the remaining 16 vascular events had known causes such as fluid overload, pregnancy, or coagulation disorders. The 31 events attributable to atherosclerosis occurred in 22 of the lupus patients and included 12 cases of angina, 8 MIs, 5 cases of heart failure, 4 PVDs, and 2 TIAs.

The 22 patients who developed symptomatic early atherosclerosis during the first 2 years of follow-up were more likely to be male, be older at lupus diagnosis, have hypertension, and be obese than were the 661 cohort members who did not have symptomatic atherosclerosis, said Dr. Urowitz, a rheumatologist at Toronto Western Hospital and a participant in the Systemic Lupus International Collaborating Clinics.

The 22 participants with atherosclerosis were also more likely to have high serum cholesterol levels and/or diabetes, be smokers, and have a family history of coronary artery disease, but these were not significant.

The participants were enrolled between 2000 and 2008; 89% were women. Whites accounted for 49%; 15% were black, 16% Hispanic, 16% Asian, and 4% other. Mean age at lupus diagnosis was 34; disease duration at the end of follow-up was 5.5 years. About 70% had been on steroid therapy, 40% had taken immunosuppressants, and 63% had used antimalarials. ■