

Forum Spotlights Venous Drainage/MS Link

BY AMY ROTHMAN SCHONFELD

TORONTO — The National Multiple Sclerosis Society is assuming a leadership role in disseminating information and mobilizing research on the role of chronic cerebrospinal venous insufficiency in the etiology and treatment of multiple sclerosis. The move comes in response to mounting pressure from patients and the scientific community questioning the hypothesis.

The society and the American Academy of Neurology jointly organized a Web forum during the annual meeting of the AAN that was open to thousands of off-site patients, family members, researchers, and members of the press.

The forum featured two of the investigators whose research on chronic cerebrospinal venous insufficiency (CCSVI) has sparked so much interest. In addition, the society has implemented an expedited research program to see whether scientific results can be replicated and further avenues explored.

"I know the MS Society shares the public's sense of urgency in advancing any lead that may help us understand the cause, provide the cure, or change the course of MS," said Dr. Aaron E. Miller, the society's chief medical officer. Dr. Miller, who is also professor of neurology and director of the MS Center at the Mount Sinai School of Medicine, New York, participated in the forum.

"The MS Society suggested holding a cosponsored educational Web forum on the CCSVI and MS ... because of the extent of misinformation and general confusion we were observing both on the Internet and in the media. We also felt the timing to be apropos because of the number of experts who would be [at the AAN meeting]," Arney Rosenblat, the society's vice president of public affairs, said in an interview.

More than 5,000 people were prereg-

istered for the forum, and more than 1,000 questions were submitted.

The speakers included Dr. Paolo Zamboni, director of the Vascular Diseases Center at the University of Ferrara, Italy, whose team was instrumental in hypothesizing a link between cerebrovascular insufficiency and MS.

In June last year, he and his colleagues described evidence of slowed and ob-



Dr. Zivadinov (left), Dr. Miller (third from left), and Dr. Zamboni (standing) discuss CCSVI in a forum held at the AAN meeting.

structed drainage in cerebrospinal veins in 100% of patients with MS, a condition that they called CCSVI (*J. Neurol. Neurosurg. Psychiatry* 2009;80:392-9). They also suggested that blood flow is detoured around obstructions and that reversed blood flow might initiate the inflammation and immune-mediated brain damage characteristic of MS.

The investigators had used advanced ultrasound techniques to evaluate blood outflow in 65 people with MS and in 235 controls who were either healthy or had other neurologic disorders.

Later last year, in December, the group reported on the safety and preliminary outcomes of surgical intervention using percutaneous transluminal angioplasty in 35 patients with relapsing-remitting, secondary progressive, and primary pro-

gressive multiple sclerosis (*J. Vasc. Surg.* 2009;50:1348-58).

Some positive effects were described—significant reduction of relapses and active lesions, improved function and quality of life, and less fatigue—although a high rate of restenosis was reported. The group issued a call for larger, controlled trials.

Dr. Robert Zivadinov, director of the Buffalo (N.Y.) Neuroimaging Analysis

Center, was another featured speaker. He and his group are exploring the prevalence of venous obstruction in 1,700 children and adults with MS, healthy controls, autoimmune-vascular disorders, and other neurologic diseases using a combination of transcranial and extracranial ve-

nous Doppler methods.

They released their preliminary results earlier this year, and Dr. Zivadinov unveiled the results of phase I of the Combined Transcranial and Extracranial Venous Doppler Evaluation Study during the forum. In these first 500 patients, 62.5% of MS patients met CCSVI diagnostic criteria, compared with 25.5% of healthy controls and 45.8% of those with other neurologic diseases. Although there was an increased likelihood that MS patients would meet the criteria for CCSVI (odds ratio, 4.85; *P* less than 0.001), compared with healthy controls, CCSVI seemed to be present in a proportion of healthy controls as well—in contradiction to Dr. Zamboni's hypothesis.

By late 2009, patients and their fami-

lies began asking for more information about CCSVI as a possible cause of MS, and endovascular stent treatment as a possible cure. At Stanford (Calif.) University, vascular specialist Dr. Michael D. Dake embarked on a program to insert stents into the internal jugular veins of MS patients based on Dr. Zamboni's reports—a program that was terminated in December because the procedure was deemed experimental.

Complications included the death of one of Dr. Dake's patients who had been on coumadin and a dislodged stent that required surgical removal in another patient.

With research reports published in reputable medical publications and calls from patients for more information, the MS Society decided to take an active role in evaluating "this interesting hypothesis that needed to be further explored: whether there is an association between CCSVI and MS," said Patricia A. O'Looney, Ph.D., the vice president of biomedical research for the society.

She cited previous research programs in gender differences in MS, genetics, and myelin repair mechanisms, as examples of the society's role in encouraging research in "underexplored" areas.

On Dec. 16, 2009, the society invited researchers worldwide to submit applications for funding and proposals for further research on CCSVI in MS. The deadline for submissions was Feb. 9, and decisions are expected mid-June.

In an interview, Dr. O'Looney declined to specify how much money has been allocated by the society. She said that she expects more than one project to be funded and that the hope is that definitive information about the CCSVI-MS association would be available within 2 years.

"We felt that answering this question was critical before patients underwent interventional treatment, which carries its own risks," Dr. O'Looney said. ■

Office-Based Questionnaires Flag Fall Risk in MS Patients

VITALS **Major Finding:** The number of falls in MS patients seen at an outpatient neurology clinic was strongly correlated with higher scores on the Expanded Disease Severity Scale ($r = 0.64$) and lower scores on the Activities-Specific Balance Confidence scale ($r = -0.77$).

Data Source: A study of 50 consecutive MS outpatients aged 16-68 years.

Disclosures: Dr. Cameron has served as a speaker or consultant for Teva Neurosciences, California Education Connection, and Mettler Electronics. This study was sponsored by a grant from the National Multiple Sclerosis Society.

BY HEIDI SPLETE

TORONTO — Poor scores on questionnaires related to balance confidence and disease severity were significant predictors of falls in adults with multiple sclerosis, based on data from a study of outpatients at a single facility.

Previous European studies have suggested an association between multiple sclerosis (MS) disease severity and the frequency of falling, but data on similar as-

sociations in U.S. patients are limited, said Dr. Michelle Cameron, a postdoctoral fellow at Oregon Health & Science University, Portland.

Dr. Cameron used two questionnaires to assess fall frequency in 50 consecutive MS patients during a clinical visit. Patients completed the Activities-Specific Balance Confidence (ABC) Scale and the self-report-

ed Expanded Disease Severity Scale (EDSS). The patients' EDSS scores ranged from 1 to 5, with an average score of 3.

The patients ranged in age from 16-68 years, with a mean age of 46 years, and 74% were women. A total of 31 patients (62%) reported falling at least once in the year prior to the study, and 14 (28%) reported falling at least six times in the year prior to the study. In addition, three of the patients (6%) reported falling

at least six times during the 2 months prior to the study.

The number of falls was strongly correlated with higher scores on the EDSS ($r = 0.64$) and lower scores on the ABC scale ($r = -0.77$). The number of falls over a 12-month period was strongly correlated with lower ABC scale scores ($r = -0.74$).

Patients who have lower balance confidence tend to fall more often, so if clinicians can identify at-risk patients early on, they can work with them to improve their balance confidence.

The results suggest that a majority of MS patients fall and more than one-fourth of them fall frequently, said Dr. Cameron, who presented her study in a poster at the annual meeting of the American Academy of Neurology. "Falls occur more often in those with lower balance

confidence," she said.

The ABC scale and a simple questionnaire about falls can easily be administered in a clinical setting, Dr. Cameron noted, and clinicians who identify patients at risk for falls can work with them to improve balance confidence. ■