Cognition Impaired in 30% With ALS

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Cognitive impairment was found in 30% of patients with amyotrophic lateral sclerosis in a study designed to assess the prevalence of cognitive involvement in what used to be considered a disease restricted to the motor system, according to Dr. Gregory A. Rippon and his associates.

In an editorial comment accompanying this report, Dr. Michael J. Strong of the University of Western Ontario, London, said that the 30% prevalence of dementia found in this study may actually underestimate the prevalence in the general population.

These subjects were evaluated “long before the institution of detailed tests of frontotemporal lobe dysfunction,” which would likely have detected dementia in more of them. Moreover, subjects with a family history of neurodegenerative diseases were excluded from this study, which again may have led to an underrepresentation of dementia cases, he said.

Dr. Rippon agreed that estimates must be considered unreliable at best, since the studies from which they were derived were flawed by small sample sizes, selection bias, and varying definitions of cognitive impairment, and thus, different methods for assessing cognition.

As ALS is increasingly recognized as a multisystem neurodegenerative disorder, researchers have revised their estimates of cognitive involvement from 2% up to as much as 52%.

In what Dr. Rippon and his associates at Columbia University College of Physicians and Surgeons, New York, called one of the largest studies of the issue to date, the researchers assessed 40 consecutively treated patients with ALS seen in a 1-year period at the university’s Neurological Institute. These patients, along with 80 control subjects, underwent a battery of tests designed to evaluate learning and memory, executive function, attention and psychomotor speed, language comprehension, and visuospatial ability.

A small study of patients with classic amyotrophic lateral sclerosis found cognitive impairment in 30% of the patients and dementia in 23%.

Among the ALS patients, there was no difference between those with and without dementia in terms of age, sex, education level, site of symptom onset, emotional lability, subjective memory loss, or family history.

This finding is contrary to that of other researchers who suggested that patients with bulbar onset ALS are particularly susceptible to dementia, Dr. Rippon and his associates noted.

ALS symptom severity did not seem to affect test performance.

As a group, the ALS patients performed better than control subjects on most of the tasks tested.

Survival was the same in ALS patients with dementia as in those without dementia, but this study was underpowered to detect a survival difference of less than 3 years.

Previous studies have demonstrated a shorter survival time in ALS patients with frontotemporal dementia.

“Larger prospective studies with interval cognitive assessments would more fully address the possibility of differential survival,” they added.

In his editorial, Dr. Strong noted that the study’s findings may provoke controversy over the population or when treatment is continued for longer than 2 years, he noted.

Even with the program in place, other cases of PML are expected, including fatal cases, he said.

“This is balanced against the significant benefits that we believe the drug confers,” Dr. Katz said.

The main elements of the program are that Tysabri can be prescribed, distributed, and infused only by physicians, infusion centers, and pharmacies enrolled in the program, a process that is designed to “minimize the risk of PML, minimize death and disability due to PML, and promote informed risk-benefit decisions” regarding the use of Tysabri, according to the FDA.

A baseline MRI must be obtained in patients before treatment is started to help distinguish multiple sclerosis symptoms that may appear in the future from PML, and physicians are required to evaluate patients 3 and 6 months after receiving the first infusion, followed by every 6 months; information from these evaluations needs to be sent to the company regularly.

Infusion centers need to inform the company each time a patient has an infusion.

Prescribing physicians are required to be able to diagnose and manage opportunistic infections and PML, or to be prepared to refer patients to an appropriate specialty.

Tysabri was approved in November 2004, and withdrawn by the manufacturer in February 2005; no new cases of PML were reported. The FDA allowed clinical trials to resume earlier this year.

More information on Tysabri, including the new label and a summary of the risk-benefit information, is available at www.fda.gov/cder/drug/infopage/natalizumab/default.htm. Information on the program can also be obtained by calling the company at 800-416-2233.