Treat Neuropsychiatric Symptoms in SLE Patients

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ATLANTA – Neuropsychiatric manifestations are common in systemic lupus erythematosus, and although they are rarely directly attributable to SLE, they need to be addressed within the context of SLE management, according to Dr. John G. Hanly.

Data from the Systemic Lupus International Collaborating Clinics inception cohort indicate that nearly a third of SLE patients have neuropsychiatric manifestations, even very early in the course of disease. A study of the first 572 patients from that cohort showed that 172 had at least 1 of 19 neuropsychiatric syndromes, with nearly half having more than 1. The data from the cohort – which now includes more than 1,600 patients – have remained consistent over the years, and show that the most common neuropsychiatric manifestations were headache, mood disorder, and cognitive dysfunction.

"So the central nervous system is impacted in more than a single way for many of our patients," said Dr. Hanly of Dalhousie University in Halifax, N.S.

Patients from the cohort had a mean age of 35 years and mean disease dura-

tion of fewer than 6 months. When models developed to assess symptom attribution were applied, they showed that only 46-93 (depending on the model) of 242 neuropsychiatric events were attributable to SLE, and that those attributable to the disease were mainly seizures and cerebrovascular events (Arthritis Rheum. 2007;561:265-73).

However, regardless of attribution, the conditions consistently had an adverse effect on health-related quality of life, Dr. Hanly said.

The management of neuropsychiatric manifestations in SLE patients first requires establishment of diagnosis of neuropsychiatric SLE as robustly as possible. "For me, that means you first have to establish a robust diagnosis of SLE," he said.

Even if lupus is considered the primary reason for the neuropsychiatric event, it's still very important to look at non-SLE factors, including hypertension, infection, and metabolic abnormalities.

Indeed, the etiology of neuropsychiatric symptoms in SLE is multifactorial, and includes autoantibodies and anti-inflammatory mediators. Therefore, treatment options include symptom control, which works just as well in SLE patients as in non-SLE patients (particularly for seizures, mood disorders, and anxiety)

and also anticoagulation or immunosuppression, Dr. Hanly said.

Unfortunately, a paucity of data exists in regard to these latter treatments in SLE, and to a certain extent it is necessary (at least in regard to antiphospholipid antibodies) to draw on data from studies in antiphospholipid syndrome.

When it comes to secondary prevention of thrombotic events, those studies – which are mostly retrospective – show that aspirin is not helpful, and that standard antithrombotic treatment with warfarin is as good as high-intensity treatment with warfarin.

The warfarin findings remain somewhat controversial, as one meta-analysis showed some benefit of higher-intensity anticoagulation therapy, but with a higher degree of associated risks such as hemorrhagic complications.

When it comes to immunosuppression, there are several uncontrolled studies supporting the use of either oral corticosteroids at a high dosage (1 mg/kg per day), or pulse corticosteroids (250-1,000 mg/day) for nervous system disease. There is comparable evidence for pulse IV cyclophosphamide at either 0.75-1 g/m² per month or at 500 mg/week, he said.

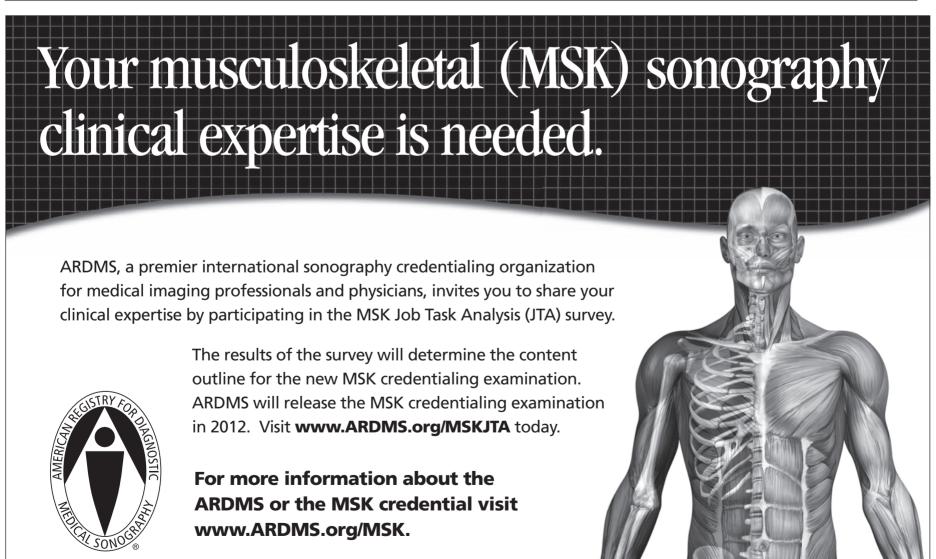
An open study in 13 patients showed that oral cyclophosphamide at 1-2 mg/kg

per day for 6 months, followed by azathioprine at 1-2 mg/kg per day indefinitely, was useful in patients with lupus psychosis. Complete resolution was seen in all patients after a mean of 44 days. Patients in that study also received prednisone at 1 mg/kg per day for the first 8 weeks, followed by a tapering of the dose. Four patients required pulse methylprednisone at 750 mg/day for other organ disease (Am. J. Med. 2003;115:59-62).

Another study showed that IV cyclophosphamide was superior to methylprednisolone alone in 32 patients with severe neurological disease (response rates, 95% vs. 46%). Mean response time was 5 months in both groups, and toxicity was comparable in both groups (Ann. Rheum. Dis. 2005;64:620-5).

Rituximab also has been studied, and in a Japanese study of 10 SLE patients with varied refractory CNS-related symptoms, treatment was associated with remission in 4 patients (Ann. Rheum. Dis. 2007;66:470-5).

Dr. Hanly has received grants from the Canadian Institutes of Health Research, Abbott, Roche, Schering, and UCB. He has also worked on clinical trials for Abbott and UCB and is on advisory boards for UCB, Roche, Genentech, and Glaxo-SmithKline.



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