Thalidomide Treatment: Close Monitoring Urged

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ABANO TERME, ITALY — Thalidomide offers an effective option for the treatment of refractory cutaneous lupus, but close monitoring is needed so the drug can be stopped at the first sign of peripheral neuropathy, Dr. Chiara Briani said at a congress on skin, rheumatism, and autoimmunity.

This drug is being used increasingly for cutaneous lupus erythematosus that does not respond to conventional therapy, but its use is limited by adverse effects, in particular a sensory, axonal peripheral neuropathy.

Retrospective investigations of thalidomide in cutaneous disorders have suggested that the incidence of peripheral neuropathy can range from less than 1% to 70%.

Close electrophysiologic follow-up is recommended so the drug can be reduced or withdrawn as soon as signs of neuropathy appear.

It's not clear whether neuropathy is related to cumulative thalidomide dose, Dr. Briani said.

To address these concerns, 14 patients who had not responded to antimalarial agents were followed prospectively, undergoing regular biochemical, dermatologic, rheumatologic, and neurologic evaluations. All were women and ranged in age from 23 to 56 years. The teratogenic effects of thalidomide can be avoided among women of childbearing age with proper contraceptive measures, and strict regulations in this regard are in place in Europe, she said.

A 50% decline in sural sensory nerve action potential (SNAP) amplitude, with relative conservation of sensory nerve conduction velocity, was considered indicative of sensory axonal peripheral neuropathy. Whenever a patient reached a 50% decline in SNAP, the thalidomide dose was lowered, and the drug was stopped when a decline of 70% was reached.

The baseline dose was 100 mg/day of thalidomide, and after 1 month the dose was tapered to 50 mg/day and subsequently to 50 mg every other day, unless peripheral neuropathy developed.

At baseline one patient already had lupus-related peripheral neuropathy, and another patient also had diabetes, said Dr. Briani of the department of neurosciences, University of Padua (Italy).

The median follow-up was 14 months, and the mean cumulative thalidomide dose was 23 g.

All patients showed "dramatic improvement" in their cutaneous symptoms within 1-2 months of starting therapy, she said.

Neuropathy occurred in two-thirds (10) of the patients during the course of treatment as demonstrated on electrophysiologic testing, but only 6 complained of sensory symptoms.

Moreover, in patients who became symptomatic, the electrophysiologic changes often preceded the clinical symptoms, heightening the significance of monitoring in patients undergoing treatment with thalidomide, she said.

"We did not find a correlation between total thalidomide dose or duration of therapy and the occurrence of neuropathy," she said.

One patient had no signs of neuropathy after 23 months and a total dose of 30 g, while another developed peripheral neuropathy after only 4.5 months and a cumulative dose of 9.5 g.

Nor was there a clear association with underlying risk factors: The patient with diabetes did not develop a 50% decrease in sural SNAP until 14 months of treatment, and the patient who had signs of neuropathy already present at baseline showed only a 31.6% decrease. Pharmacogenetic susceptibility or other individual factors may contribute (Autoimmunity 2005;38:549-55).

In four patients the neuropathy resolved completely, in one patient partial improvement was seen, but in five patients there were no sural SNAP changes 15 months after thalidomide treatment was withdrawn.

For long-term treatment with thalidomide, therefore, close electrophysiologic follow-up is recommended so that the drug can be reduced or withdrawn as soon as subclinical signs of neuropathy appear, Dr. Briani said. ■