IVIG Is Safe, Effective for Scleromyxedema Lesions

BY MIRIAM E. TUCKER
Senior Writer

BALTIMORE — Intravenous immunoglobulin appears to be a safe and effective treatment for scleromyxedema, Dr. Francesco Boin said at a conference on rheumatic diseases sponsored by the Johns Hopkins University.

Scleromyxedema is a rare—though probably underrecognized—disorder that mimics scleroderma. It is characterized by widespread thickened skin and multisystem disease caused by mucinous deposition in the skin and internal organs. It has been described worldwide, with males and females equally affected, and both black and white patients reported in the United States. Mean age of diagnosis is about 55 years, ranging from 30 to 80.

PHOTOS COURTESY DR. LAURA HUMMERS

One scleromyxedema patient received IVIG 2 g/kg once monthly for 6 months and then every 8 weeks for 1 year.

Patients typically present with waxy, bumpy skin, initially in patches but later becoming confluent and generalized and eventually thickened and pendulous. Skin changes behind the ears are almost always present. "The buzzword is the ear … It's a very important spot to check if you're suspicious for this entity," said Dr. Boin, of the division of rheumatology at Johns Hopkins.

The patient's face will often have a "leonine" appearance. The hands may appear scleroderma-like, with flexion contractures of the fingers. Some patients have microstomia.

Findings from an incisional biopsy will show a distinct infiltrative process with massive amounts of mucin deposition. Patients will have a low-level monoclonal gammopathy, with no specific distribution of subtype. As with most fibrosing skin disorders, punch biopsy is not generally helpful in the diagnosis and is often not necessary.

Aside from the skin, scleromyxedema affects the neurologic, hematologic, gastrointestinal, and cardiopulmonary systems. Neurologic symptoms may include encephalopathy, seizures, stroke, psychosis, aphasia, gait disturbance, vertigo, and tinnitus. Cardiopulmonary involvement includes pulmonary hypertension in approximately 50% of patients, as well as pericardial effusion. Gastrointestinal symptoms can include dysphagia and esophageal dysmotility, Dr. Boin said.

Less commonly, some scleromyxedema patients will experience proximal muscle weakness or frank myopathy, with biopsy showing inflammation, atrophy, necrosis, and mucin deposition.

Without treatment, progressive disease and a poor prognosis are typical. Currently, there is no consistent therapeutic approach and few available long-term data. Treatments that have been investigated in small studies include thalidomide, cyclosporine, autologous stem cell transplants, prednisone, isotretinoin, intravenous immunoglobulin (IVIG), dermabrasion, extracorporeal phototherapy, radiation therapy, plasmapheresis, and psoralen-ultraviolet-light therapy.

Findings from a review of nine scleromyxedema patients who were referred to The Scleroderma Center at Johns Hopkins between 1996 and 2005 showed the mean patient age at diagnosis was 53.6 years (range 33-74), and the mean disease duration prior to referral was 2.1 years (range 0-6). Eight of the patients were white, and one African American. The majority (seven of nine) were female. Monoclonal gammopathy was present in eight patients, but none had evidence of multiple myeloma.

Clinical manifestations mimicking scleroderma included Raynaud's phenomenon in five (another had "cold sensitivity"), sclerodactyly (five), pulmonary hypertension (three), and gastroesophageal reflux disease (two). Encephalopathy was present in one patient, dysphagia in four, elevated creatine phosphokinase in two, and rhabdomyolysis in one. The only autoantibody detected was an antinuclear autoantibody in two patients, Dr. Boin's Hopkins associates Dr. Laura K. Hummers and Dr. Frederick M. Wigley reported in a poster at the 2005 American College of Rheumatology meeting.

Four of the patients with severe symptomatic skin involvement were treated with IVIG at a dose of 2 g/kg daily for 5 days. All patients tolerated the full course of IVIG, and all experienced dramatic improvement in their papular mucinosis skin lesions. Of those four, one also experienced rapid resolution of severe neurologic involvement after just one IVIG course, and another received six monthly treatments and continued without flare 4 months later.

The other two patients, followed for 31 and 34 months, respectively, postinitial treatment, both responded to six monthly treatments, reflared after 4 months, and are now continuing to respond to low-dose infusions at regular intervals—every 4-6 weeks in one patient, every 8 weeks in the other—to maintain control. Indeed, while IVIG appears to produce dramatic and rapid response, with "a softening in a matter of days," it may be necessary to continue therapy long term, he noted. ■

Statins Aid Vasculopathy, Stymie Ulcers in Sclerosis

Raynaud's patients treated with atorvastatin had less pain and fewer ulcers than controls.

BY NANCY WALSH
New York Bureau

BARCELONA — Statin therapy may ameliorate the vascular dysfunction that can lead to Raynaud's phenomenon and digital ulcers in systemic sclerosis, Dr. Anna Abou-Raya said at the annual European Congress of Rheumatology.

Systemic sclerosis is characterized by widespread vascular pathology, with initial events involving endothelial cell damage, loss of normal vasodilatory mediators, and excessive vasoconstriction. Within 4 years of diagnosis, up to 65% of patients have digital ulcers, which are painful and disabling and can be associated with infection, gangrene, and amputation, Dr. Abou-Raya said. Effective treatment remains elusive for many patients.

Aside from their well-documented lipid-lowering properties, statins display pleiotropic effects including effects on endothelial function that may be of benefit in slowing or preventing vascular damage.

"The appearance of endothelial cell abnormalities can be considered the crucial, and maybe the initial event in the pathogenesis of systemic sclerosis," Dr. Abou-Raya said.

"Furthermore, endothelial activation and damage are primary events not only at the initiation but throughout the course of disease," she added.

To evaluate the potential for statin therapy to retard or prevent vascular damage in systemic sclerosis, Dr. Abou-Raya and associates undertook a controlled study that randomized 40 patients with persistent Raynaud's phenomenon to receive atorvastatin, 40 mg/day, or placebo for 4 months.

The mean age of the patients was 49.7 years, and the mean duration of Raynaud's phenomenon was 8 years. The mean number of digital ulcers existing at baseline was 3.3, and all of the patients fulfilled the American College of Rheumatology criteria for having systemic sclerosis with Raynaud's phenomenon, despite ongoing vasodilator therapy.

Exclusion criteria included diabetes; hypercholesterolemia; hypertension; and cardiac, hepatic, and renal disease.

A mean of 1.6 new ulcers developed in patients in the statin group, compared with a mean of 2.5 new ulcers in the placebo group, which was a statistically significant difference, said Dr. Abou-Raya of the department of rheumatology at the University of Alexandria, Egypt.

Patients were also evaluated for functional status, with statistically significant improvements being seen on the modified Scleroderma Health Assessment Questionnaire Disability Index and on visual analog scale scores for pain and for physician global assessment.

Moreover, biomarkers of endothelial damage, such as intercellular adhesion molecule 1 (ICAM-1) and sE-selectin, as well as acute phase reactants, also improved significantly among patients in the atorvastatin group, Dr. Abou-Raya reported.

The drug was well tolerated, and there were no study dropouts.

The results of this study suggest statins can be beneficial in alleviating vascular dysfunction and improving patient functioning in systemic sclerosis.

"These drugs are relatively inexpensive, even in developing countries, and with our very limited therapeutic arsenal, any drug that leads to any improvement is a welcome addition," said Dr. Abou-Raya.

Larger studies will be needed to confirm these results, she added. ■