Various Gadolinium-Based Agents May Up NSF Risk

BY BRUCE JANCIN

SAN FRANCISCO — Less than 5% of patients in severe renal failure who are exposed to gadolinium-based contrast agents will develop the disabling, often fatal condition called nephrogenic systemic fibrosis. So what other predisposing factors might be involved?

Analysis of a single-center series of 12 biopsy-confirmed cases of nephrogenic systemic fibrosis (NSF) suggests a number of commonalities: concomitant use of erythropoiesis-stimulating agents, a heightened inflammatory state at the time of the imaging procedure, metabolic acidosis, and more than a 24-hour gap between the imaging procedure and the next dialysis session, Dr. Anne Laumann reported at the annual meeting of the American Academy of Dermatology.

The literature, which through May 2008 included close to 400 cases of NSF, most often implicates exposure to gadodiamide. However, all 12 patients in this series were instead exposed to a different contrast agent—gadopentetate dimeglumine—at a mean cumulative dose of 65.5 mL. Only 2 patients were additionally exposed to gadodiamide, according to Dr. Laumann, director of the collagen vascular disorders clinic at Northwestern University, Chicago.

The mean interval between exposure to a gadolinium-based contrast agent and symptom onset was 21 days, with a maximum of 65 days. Time from symptom onset to diagnosis of NSF averaged 190 days, with a maximum of 5 years.

NSF is a scleromyxedema-like disease characterized by subcutaneous induration and dermal fibrosis with thickened collagen bundles. The clinical features include rock-hard skin, severe burning pain, muscle involvement, fixed joint contractures, impaired mobility, pseudo-clubbing of the fingers, gadolinium-containing scleral plaques, and periocular papules. Five of the 12 Northwestern patients have died.

No new cases of NSF have been diagnosed at the medical center in the past year, when radiologists became attuned to the danger posed by magnetic resonance imaging using gadolinium-based contrast agents in patients with low renal function, the dermatologist noted.

Seven of the 12 patients were on hemodialysis and 3 were on peritoneal dialysis at the time of their imaging procedures; the other 2 patients were also in severe renal failure, with estimated glomerular filtration rates of 24 mL/min per 1.73 m^2 or less. The average time lag between gadolinium exposure and the next dialysis treatment was 32 hours.

Ten of the 12 patients were on erythropoiesis-stimulating agents. Seven had experienced an inflammatory event less than 24 hours prior to gadolinium exposure. The median anion gap was 10 mmol/L and the mean serum albumin was 2.5 mg/dL, indicative of systemic inflammation.

Treatment was unsatisfactory. All 12 patients received physical and/or occupational therapy aimed at helping them adapt to their limitations. Two of three patients who received imatinib showed slight improvement in mobility. One of two on intravenous sodium thiosulfate experienced some pain relief. One patient underwent live-donor kidney transplantation with subsequent improvement in glomerular filtration rate, but he remains severely immobilized. ■

Risks Outweigh Benefits of Using HGH for Antiaging

BY SHERRY BOSCHERT

SAN FRANCISCO — Growth hormone therapy might help adults with a deficiency, but there's no evidence that it helps normal elderly adults or athletes.

Illegal use in antiaging clinics probably accounts for the largest use of growth hormone in the United States today, Dr. Andrew R. Hoffman said.

The therapy is indicated for adults for the treatment of growth hormone deficiency caused by pituitary disease, hypothalamic disease, surgery, radiation, or trauma. It is the only drug in the U.S. that cannot legally be prescribed off label, he said at a meeting on diabetes and endocrinology sponsored by the University of California, San Francisco.

What's more, its use in normal elderly people may cause harm by inducing glucose intolerance or increasing the risk for cancer, "although we do not know that" for sure, said Dr. Hoffman, professor of medicine at Stanford (Calif.) University and the Veterans Affairs Palo Alto Health Care System.

Interest in treating normal age-related declines in growth hormone secretion and insulin-like growth factor 1 (IGF-1)—dubbed the "somatopause"—zoomed after a 1999 study reported that giving growth hormone injections to male veterans aged older than 60 years for 6 months increased lean tissue mass by 9%, skin thickness by 7%, and lower-back vertebral density by 2%, while decreasing fatty tissue by 14% (N. Engl. J. Med. 1990;323:1-6). The authors described the effects as equivalent in magnitude to the changes that occur during 10-20 years of aging. "This set up a lot of excitement and was the basis for all the antiaging clinics you can find," Dr. Hoffman said.

It also generated multiple animal studies by the National Institutes of Health, every one of which showed that longevity is associated with lower growth hormone levels, not higher ones. A systematic review of randomized, controlled trials of growth hormone injections in healthy elderly humans reported small changes in body composition and high rates of adverse events (Ann. Intern. Med. 2007;146:104-15).

One of the potential side effects with growth hormone overtreatment is increased edema. "You can't say it increases muscle," Dr. Hoffman said. "Much of it might be fluid retention."

The medical literature suggests that treatment probably is helpful for patients with growth hormone deficiency syndrome, Dr. Hoffman said. Treatment produces significant and durable changes in cardiac effects. Bodily fat mass, LDL cholesterol, and total cholesterol levels decrease but insulin and glucose levels tend to increase.

In general, patients treated for growth hormone deficiency syndrome become more physically active, increase their strength and exercise capacity, and slightly increase bone mineral density.

Other data suggest, however, that high levels of IGF-1 over long periods of time could increase the risk for prostate cancer or premenopausal breast cancer.

Dr. Hoffman has received research support, owned stock, or been a consultant to companies that market growth hormone or related products, including Ambryx, LG Life Science, Tercica, Merck Serono, Pfizer, Novo Nordisk, and Teva Pharmaceutical Industries. ■

After Heart Attack, SLE Patients at Higher Risk Than Diabetics

BY DENISE NAPOLI

Systemic lupus erythematosus conferred a greater risk for adverse outcomes following acute myocardial infarction than did diabetes mellitus, according to an analysis of more than 900,000 patients from the U.S. Nationwide Inpatient Sample.

Based on that finding, "a person with SLE presenting to the [emergency department] with an acute MI must be considered as a high-risk MI and triaged accordingly," Dr. Mansi A. Shah and associates wrote (J. Rheumatol. 2009; 36:570-5).

Furthermore, in an interview, coauthor Dr. Eswar Krishnan said physicians should lobby organizations like the American Heart Association to "take up this issue [and] issue recommendations, and disseminate information" to emergency department physicians and on-call specialists, who are largely unaware of this increased risk profile for SLE patients.

According to the authors, only one study has previously assessed the risk of postacute MI mortality in SLE patients. That study did not find that the risk of in-hospital mortality was similar between patients with and without SLE; however, neither did that study look at morbidity, or compare outcomes of SLE patients with those of patients who have other diseases.

In the SLE group without diabetes who were hospitalized with acute MI, in-hospital mortality was 8.3%, with an adjusted OR of 1.7.

Nevertheless, said Dr. Krishnan of the division of immunology and rheumatology at Stanford (Calif.) University, "given the rarity of SLE, and MI in SLE, a repeat study is perhaps not feasible. My opinion is that until proven otherwise, let us triage lupus patients as high risk."

The survey that was done by Dr. Krishnan, Dr. Shah, and Dr. Amber Shah looked at a total of 906,638 patients who were hospitalized with acute MI in 1993-2002. Of these, 667,956 patients had neither SLE nor diabetes mellitus, based on hospitalization discharge codes; they served as controls. Of the remaining patients, 2,192 had SLE without diabetes; 236,016 had diabetes without SLE; and 474 had both SLE and diabetes. All patients were 18-70 years of age.

Overall among the study population, in-hospital mortality was 5.1%. In the control group alone, it was 4.7%; in the diabetes-only group, it was 6.2% (adjusted odds ratio, 1.00, equal to that of controls), and—highest of all—in the SLE-only group, it was 8.3%, with an adjusted OR of 1.7.

Because the diabetes-with-SLE group was so small, there were too few in-hospital deaths to have "a robust estimate of rate difference" in this population.

After the data were broken out by race and gender, black men in the SLE-only group had the highest mortality (15.2%, compared with mortality less than 6% in all other groups and races).

The researchers also looked at the length of hospitalization. After the data were adjusted for age, sex, race, income, and heart failure upon admission, they found that the SLE group had an OR of 1.5 for prolonged hospitalization (defined as longer than 6 days), compared with the controls. For comparison, the diabetes-only group had an OR of 1.2.

The SLE with diabetes group's adjusted OR for a prolonged hospital stay was 1.3; in the diabetes-only group, it was 1.2.

According to Dr. Krishnan, it is up to physicians to educate their lupus patients about the increased coronary risks associated with the disease. She also said that physicians should refer patients with SLE to preventive services.

Dr. Krishnan said that none of the study's authors had any competing interests to disclose. ■