# Contrast Agents May Pose Danger in Renal Disease

BY BRUCE K. DIXON
*Chicago Bureau*

Gadolinium-based contrast agents, when given to patients with renal disease, have been linked to a rare, potentially fatal, sclerodermalike skin disease called nephrogenic systemic fibrosis or nephrogenic fibrosing dermopathy.

In December, the Food and Drug Administration issued a public health advisory stating that the agency has received reports of 90 patients with moderate to end stage kidney disease who developed the new disease within 2 days to 18 months after they had magnetic resonance imaging (MRI) or magnetic resonance angiography (MRA) with a gadolinium-based contrast agent. Many—but not all—of these patients received a high dose of the contrast agent; some received only one dose, according to the FDA.

Nephrogenic fibrosing dermopathy (NFD) is marked by areas of tight, rigid skin and may progress to nephrogenic systemic fibrosis (NSF), which is associated with scarring of internal organs. Symptoms may include burning; itching; swelling; hardening and tightening of the skin; red or dark patches on the skin; yellow spots on the whites of the eyes; stiffness in joints, with trouble moving or straightening the arms, hands, legs, or feet; pain deep in the hip bones or ribs; and muscle weakness.

Worldwide, about 215 cases of NSF/NFD have been reported. The medical histories of 75 of these patients have been reviewed in detail, and all had received a gadolinium-based contrast agent.

The advisory recommends alternative imaging studies for patients with renal disease. When patients with renal disease must receive a gadolinium-based contrast agent, prompt dialysis following the MRI or MRA should be considered, the FDA statement said.

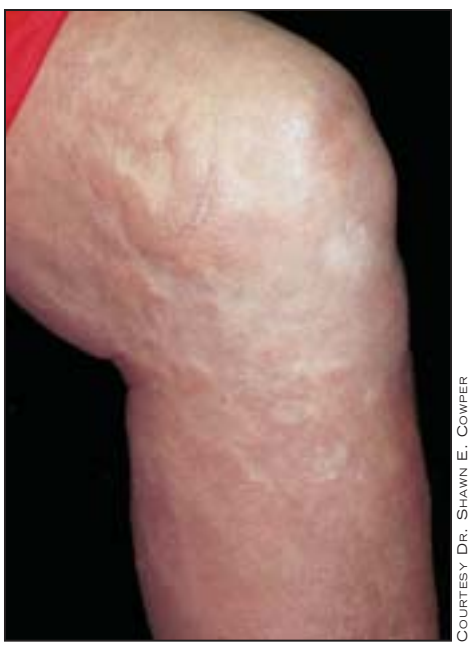
Reports of the new disease have been steadily increasing since April 2006, when two European hospitals reported 25 cases following Omniscan injection. These cases had accumulated over a period of 4 years. In June 2006, the FDA issued an initial advisory about the disorder. In its December advisory, the FDA said that cases have been associated with three of the five approved gadolinium-based contrast agents, but there is reason to believe that any of the approved agents could cause the disease. Currently, there are five FDA-approved gadolinium-based contrast agents: Magnevist, MultiHance, Omniscan, OptiMARK, and ProHance. These contrast agents are FDA approved for use during an MRI scan, but not for use during an MRA scan.

Dr. Emanuel Kanal, professor of radiology and neuroradiology at the University of Pittsburgh Medical Center, was one of several radiologists who reviewed concerns about the emerging disease at the annual meeting of the Radiological Society of North America in Chicago.

"Nearly 100% of the patients with known NSF were confirmed to have received a gadolinium-based MR contrast agent prior to the diagnosis being made. Of those, over 90% had received Omniscan, which is way out of proportion to Omniscan's market share," said Dr. Kanal, who also is director of MR services at the medical center.

Fewer cases of NSF have been reported in patients who had been scanned using OptiMARK or Magnevist, and no cases have been linked to the remaining licensed agents, ProHance and MultiHance.

In a statement, GE Healthcare said the company is "concerned by this trend of a higher incidence of NSF concurrent with gadodiamide use, and we continue to urge caution in using Omniscan in renally compromised patients, consistent with our prescribing information."



COURTESY DR. SHAWN E. COWPER

**Nephrogenic systemic fibrosis may induce joint stiffening as well as skin changes and bone pain.**

A revised guidance document for safe MRI practices is slated for publication early this year in the American Journal of Roentgenology and on the American College of Radiology Web site. ■

# Tissue Characterization Key

**Imaging** *from page 1*

so for imaging structures and is not very good at assessing function.

Its strengths are very specific metabolic information and strong prognostic value. Solid evidence shows that the extent of an ischemic lesion or perfusion deficit on nuclear imaging predicts the patient's prognosis.

Disadvantages include poor spatial resolution, radiation exposure, cost, poor assessment of flow, and uncertain availability of the tracer for PET scanning.

Some newer applications of nuclear cardiology may be more exciting, Dr. Friedrich said. Animal studies suggest that accumulation of a tracer may correlate with the activity of a plaque. Nuclear medicine may allow visualization of matrix metalloproteinases, an important component of plaque stability, or visualization of apoptosis. To overcome the poor spatial resolution, studies are underway to fuse CT and nuclear images to overlay anatomic images with metabolic details.

▶ **CMR.** Although not yet as good as nuclear medicine for assessing metabolism, CMR provides good structural images and is very good for assessing function. It is noninvasive, safe, and versatile. It is especially good at tissue characterization but also good for assessing function and flow. "It has the largest future potential because we have not started to exploit all the options in molecular imaging" with CMR, he said.

CMR is complex to perform, however, and costly because both image acquisition and evaluation take too long under current protocols. "We're working on getting evaluations done in a few minutes" instead of the typical half-hour, he said.

Experimental uses of CMR suggest that it could allow clinicians to assess cardiac pathophysiology directly instead of surrogate markers, Dr. Friedrich said. Recent, unpublished studies in animals report that CMR visualized ischemia-induced intracellular edema, which showed up before the irreversible injury of acute infarction.

Dr. Friedrich and his associates now are studying CMR for triage of emergency department patients with suspected acute coronary syndrome who don't have troponin levels or echocardiography results that warrant sending them straight to the catheterization lab.

"According to the guidelines, you have to wait a couple of hours and repeat the troponin. If you are unlucky, this was an infarct, and during those 4, 6, or 10 hours you have lost most of the myocardium you could have salvaged," he said.

Under their CMR protocol, intracellular edema can be identified quickly, and those patients are sent to the cath lab within minutes of intake. Patients with negative results in the multistep protocol are being sent home before ordering a second troponin test.

"This is [an] example where tissue characterization, without using a contrast agent, can be very, very helpful in a daily clinical setting," he said. ■

# Multislice CT and MPI Both Useful for Detecting CAD

BY JOHN R. BELL
*Associate Editor*

The information offered by multislice CT and myocardial perfusion imaging is sufficiently different that both tools are meaningful to the diagnosis of coronary artery disease—but evidence may predispose MSCT to becoming the first-line test, Joanne D. Schuijf of Leiden (the Netherlands) University Medical Center and colleagues reported.

They reported results from 114 patients (mean age 60 years) who underwent single-photon emission CT (SPECT) myocardial perfusion imaging (MPI) along with noninvasive coronary angiography with MSCT after presenting to either of two outpatient clinics with chest pain (J. Am. Coll. Cardiol. 2006;48:2508-14). Each patient underwent both tests within 30 days of the other.

**'Only half of the observed lesions on MSCT may be of hemodynamic significance.' And 50% of patients with CAD on MSCT had normal MPI.**

MSCT showed that 29% of the patients had nonobstructive coronary artery disease (CAD), with 35% diagnosed with at least one significant lesion. The remaining 36% of patients were determined by MSCT not to have CAD. Notably, of the patients with abnormal MSCT findings, 55% (40 patients) had normal results on MPI—a dichotomy illustrating that "only half of the observed lesions on MSCT may be of hemodynamic significance. Even among patients with obstructive CAD on MSCT, 50% had normal MPI," the investigators wrote.

Their study "is a first attempt to apply MSCT in patients with an intermediate likelihood of CAD," they noted. The consistency of MSCT findings with those of invasive coronary angiography indicated that "the high accuracy of MSCT demonstrated previously in patients with a high likelihood of CAD also applies to patients with an intermediate likelihood of CAD."

With the advent of MSCT and its greater diagnostic sensitivity over MPI, "a paradigm shift occurs in the definition of CAD, displacing the emphasis from inducible ischemia to atherosclerosis," Ms. Schuijf and colleagues wrote. "Based on the discrepancy between MSCT and MPI, one can argue that MSCT could be used as the first-line test. A normal MSCT excludes CAD, and the patient can be reassured."

In an accompanying editorial, Dr. Sharmila Dorbala of Brigham and Women's Hospital, Boston, and colleagues noted that although the consistency between the findings via MSCT and those via invasive coronary angiography was "excellent," the study—like its predecessors in the literature—showed a diagnostic inconsistency between MSCT and MPI.

However, their ultimate assessment of the study's findings seemed to indicate a diagnostic advantage to MSCT. "Except in patients with high-risk scan features, combined testing with [MSCT and MPI] may be an effective strategy to both diagnose extent of CAD and guide management to the appropriate vessel," they wrote. ■