

New study suggests cause of debilitating skin condition

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New findings from researchers at Wake Forest University Baptist Medical Center and colleagues suggest why some people with kidney failure can develop a rare tightening and swelling of the skin and other organs, including the lungs and heart.

Reporting in the October issue of the American Journal of Dermatopathology, the authors suggest a possible explanation for why some patients on kidney dialysis who are injected with a “contrast agent” during a magnetic resonance imaging (MRI) develop nephrogenic systemic fibrosis (NSF).

The U.S. Food and Drug Administration now requires a warning about the potential risk on the products’ labels. NSF leads to thickened, rough or hard skin usually on the arms, legs or trunk. In some cases, the limbs can become difficult or even impossible to move.

“The cause of this syndrome has been unclear,” said David C. Sane, M.D., senior researcher on the project. “Our research suggests both a potential cause and the possibility of preventing or treating NSF.”

Sane said the finding – that an enzyme known as transglutaminase-2 (TG2) may be involved – is the first to suggest how exposure to contrast agents may lead to NSF.

It has not been known what causes NSF, but a risk factor is exposure to gadolinium, an agent injected into patient’s veins during some MRI

procedures to help improve the visibility of internal organs during the test. The condition is relatively rare – it occurs in about 2 percent to 4 percent of kidney patients on dialysis who are exposed to gadolinium.

The researchers tested the hypothesis that TG2 may be involved in the response. The enzyme is found throughout the body and is involved in blood clotting and wound healing. They hypothesized that gadolinium may activate the enzyme and cause NSF.

The group obtained skin biopsies from five people with NSF and three healthy people. All NSF patients had renal failure and had previously had imaging procedures using gadolinium. The researchers tested for the presence of TG2 in the skin samples.

“Compared to the healthy subjects, there was a marked increase in TG2 in the subjects with NSF,” said Sane. “This suggests that activation of TG2 can produce the syndrome. TG2 is expressed in virtually all tissues and may explain why the fibrosis can occur in the heart and lungs, as well as the skin.”

Sane said the results also suggest a strategy for preventing or treating NSF – drugs such as cysteamine that inhibit the activation of TG-2.

“Our research is a pilot study, but we believe the results warrant further research into the use of TG-2 inhibitors in the treatment and prevention of NSF,” said Gil Yosipovitch, M.D., co-senior researcher, and a dermatologist. “Solving this puzzle might allow dialysis patients to take full advantage of the diagnostic capabilities of MRI.”

“This could be a general mechanism for a broad range of disorders that involve fibrosis, or tissue thickening,” said Sane.

Source: Wake Forest University

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