

# Calciphylaxis Is 'Akin to a Myocardial Infarction'

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LAS VEGAS — An evolving understanding of the pathogenesis of calciphylaxis in hospitalized patients may lead to antithrombotic treatment strategies focused on vascular occlusion as well as dialysis- and parathyroid-specific interventions.

"Calciphylaxis is a therapeutic conundrum and also a nightmare," said Dr. Mark D.P. Davis, professor of dermatology at the Mayo Clinic, Rochester, Minn.

"We urgently need better treatment and preventive strategies," he stressed at a dermatology seminar sponsored by Skin Disease Education Foundation.

The condition's name, calciphylaxis, reflects an early belief that the introduction of a certain agent (likely during dialysis) induced calcification of vessels, a notion now disputed since the disease can occur in patients without renal insufficiency.

A more accurate name, first proposed by Dr. Patrick Dahl and his associates, is the vascular calcification-cutaneous necrosis syndrome (J. Am. Acad. Dermatol. 1995;33:53-8), which better characterizes calciphylaxis as "akin to a myocardial infarction," Dr. Davis said. Calcifications in

the walls of small arterioles supplying the skin are the first evidence of the disorder. The resultant clots trigger skin infarctions, just as a blockage of a vessel leads to an MI.

Treatment at Mayo focuses on vascular occlusion, along with management of hypercalcemia (with low-calcium dialysate and sodium thiosulfate in dialysis patients), hyperphosphatemia (with phosphate binding agents), hyperparathyroidism (with cinacalcet and bisphosphonates), and pain.

"It's very important to treat vascular occlusions and eliminate these luminal thromboses causing this cutaneous infarct," he said. "One way to treat an existing clot is to use thrombolytic agents."

Several Mayo Clinic patients have been treated with infused tissue plasminogen activator (tPA) at doses 1/10 of those used to treat an MI. Because of concern over bleeding, patients are admitted for the 2-week procedure. "We have had some success and are presently reviewing our experience with this approach," Dr. Davis said.

Anticoagulant medications, including heparin, low-molecular-weight heparin, and warfarin, are also employed so that calciphylaxis patients don't clot more.

Hyperbaric oxygen, which enhances tissue oxygenation and induces vascular

neogenesis (and may increase fibrinolytic activity within endothelial cells) also makes sense in the context of calciphylaxis as a disease of vascular calcification/cutaneous infarction.

Dr. M.R. (Pete) Hayden, a calciphylaxis researcher who has published several studies on sodium thiosulfate as a possible treatment, commented later that he is "looking forward excitedly to future papers" on the anticoagulant approach from Dr. Davis and Mayo researchers.

"Indeed, thrombolytic agents may be an important adjunctive intervention along with calcium-chelating agents and phosphate binding agents in appropriate patients because there are so many precipitating variables important to the development of calciphylaxis," said Dr. Hayden, research professor of internal medicine in the division of endocrinology, diabetes, and metabolism at the University of Missouri, Camdenton.

Other interventions have not fared as well. A comprehensive review of 64 patients treated at the Mayo Clinic failed to find any survival benefit with parathyroidectomy, despite case studies and series that have suggested the surgery is beneficial (J. Am. Acad. Dermatol. 2007;57:365-6).

Debridement was associated with a 1-year survival rate of 62%, versus 27% survival rates in patients who failed to undergo the procedure. Surgical and mechanical debridement are difficult to perform in patients with this "excruciatingly painful" disease, so painless debridement using maggots and ultrasound is being utilized at Mayo, to good effect, Dr. Davis said.

A population-based study conducted in the Rochester area found an incidence of 4.5 cases per million people, per year. About 1% of patients with chronic renal failure and 4% of dialysis patients reportedly have the disease.

Renal insufficiency characterizes the "vast majority" of patients with calciphylaxis, but many patients seen at the Mayo Clinic have underlying liver disease and no history of kidney failure, Dr. Davis noted.

Other findings in patients (with or without renal insufficiency) include hyper- or hypoparathyroidism, calcium-phosphate product greater than 70, obesity (body mass index greater than 30), systemic corticosteroid use, vitamin D deficiency, bone disease, systemic inflammatory state, and malignancy, especially bone metastasis.

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