

CALCIPHYLAXIS:

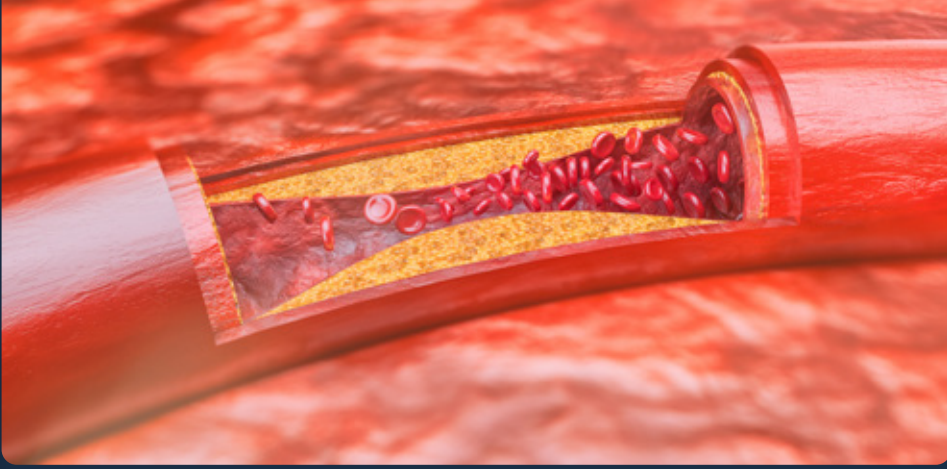
A Rare Disorder That Can Be Deadly for Kidney Patients

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Calciphylaxis is a rare disorder that affects the smallest of arteries that supply blood to the skin. These vessels, called arterioles, become blocked by deposits of calcium, fibrous tissue and blood clot, leading to a loss of



delivery of oxygen to the skin. As a result, the skin becomes necrotic (dead, black) and may develop ulceration (open sores). Many of these areas of compromised skin then become infected, which can be life-threatening and difficult to treat. Although the process of calciphylaxis is poorly understood, there are risk factors that appear to be common to its development.



Many of us think of the primary function of the kidneys as removing waste and excess fluid from the blood. In addition, the kidneys play important roles in controlling blood pressure, stimulating formation of new blood cells in the bone marrow, and maintaining normal body chemistry by regulating the balance of sodium, potassium, phosphorous, calcium, and numerous other elements and compounds. As kidney function worsens, the normal handling of calcium and phosphorous is impaired. The kidneys cannot eliminate phosphorous normally, and elevated phosphorous levels in the blood lead to a rise in parathyroid hormone (PTH) in response. The elevated PTH levels cause calcium to be released from bone, resulting in thinning of the bones and making calcium available to form deposits in other tissues, such as blood vessels. This cycle of impaired handling of calcium and phosphorous forms the basis of what is called metabolic bone disease (MBD). Uncontrolled MBD may significantly increase the risk of developing calciphylaxis.

Factors that are believed to contribute to the development of calciphylaxis include kidney failure with the associated calcium and phosphorous abnormalities of MBD, elevated PTH levels, treatment with certain preparations of vitamin D, treatment with warfarin (a blood thinning drug), certain inflammatory conditions and high body fat content. Other risk factors include number of years on dialysis, diabetes mellitus, and low blood albumin (protein) levels. Unfortunately, there are very few studies that define the degree to which each of these may increase the risk of developing calciphylaxis.

An important component of the diet of a dialysis patient is minimizing the

intake of dietary phosphorous. This is achieved by avoiding foods that are high in phosphorous and by treatment with oral phosphate binders, medications that are taken with a meal to absorb the phosphorous in the food and prevent its absorption into the bloodstream as food is digested. Controlling blood phosphorous levels may be important in preventing the development of calciphylaxis.

Calciphylaxis first appears as a web-like rash and painful nodules or plaques in the skin, most commonly in the thigh area or other areas of increased body fat. As the condition progresses, open sores and blackening of the skin may occur. Diagnosis may be made by skin



biopsy, although no specific criteria for making the diagnosis have been established. Typically, the diagnosis will be made based upon the clinical suspicion of the physician and the exclusion of other diagnoses related to diseases of the blood vessels, such as vasculitis or other diseases caused by the body's immune system.

Treatment for calciphylaxis may be quite varied, and the optimal treatment is unknown. Perhaps the most commonly used treatment is sodium thiosulfate, which is a compound administered by infusion at dialysis three times per week for three months. Unfortunately, there have been no clinical trials to evaluate the effectiveness of this treatment, although one study demonstrated improvement in approximately 75 percent of 53 patients.¹ Other important considerations in treating the condition include wound care and pain management regimens. The biochemical abnormalities of metabolic bone disease should be corrected as much as possible, controlling blood phosphorous, calcium, and PTH levels. For persistently elevated PTH levels unresponsive to medication, parathyroidectomy (surgical removal of the parathyroid glands) may be necessary. Medications believed to contribute to the risk of calciphylaxis should be discontinued, such as Vitamin D, oral calcium, warfarin and iron.

Calciphylaxis may be fatal if infection becomes widespread. Close attention to and prompt treatment of open wounds are essential in managing the condition. Although it is difficult to determine which patients will develop calciphylaxis, aggressive management of serum phosphorous and PTH levels may dramatically reduce risk.

Dr. Mahoney is the Chief Medical Officer for Lifeline Vascular Care and a member of the DPC Education Center Advisory Council.

Reference

1. Nigwekar, S U *et al.* Sodium thiosulfate therapy for calcific uremic arteriopathy, *CJASN* 2013; 8:1162.