

CALCIPHYLAXIS

Wilmer WA, et al. *Calciphylaxis: emerging concepts in prevention, diagnosis, and treatment. Semin Dial.* 2002;15(3):172-86.

Take home points:

1. A small vessel vasculopathy characterized by calcification of the medial vessel wall and intimal proliferation (unlike typical atherosclerosis which involves larger vessels and has intimal calcification)
2. Majority of patients have kidney disease, and most are on dialysis (for more than 1 year)
3. Presents typically as ischemia and necrosis of the skin (non-healing ulcer)
4. Carries a poor prognosis (difficult to treat, vasculopathy is extensive and most times irreversible)

Clinical features:

- Rare but now being detected with increasing frequency (present in 1-4% of dialysis patients)
- Calciphylaxis is a small vessel vasculopathy characterized by calcification of the medial vessel wall and intimal proliferation which can then lead to thrombosis
- In skin and subcutaneous tissues, ischemia leads to subcutaneous nodules and necrotizing skin ulcers.
- Predisposing factors: kidney disease, dialysis, obesity, warfarin therapy, protein C/S deficiency, hypercoagulable state, PUVA treatments, malnutrition
- Most frequently occur in areas with thicker subcutaneous adipose tissue (breast, abdomen, and thighs). Less commonly, occurs in an acral distribution.
- Can also present with ischemia to visceral organs and skeletal/cardiac muscle (can cause a myopathy).
- Carries a poor prognosis (difficult to treat, vasculopathy is extensive and most times irreversible)
- **Bottom line:** consider this diagnosis in your renal patients with a non-healing skin ulcer

Why is it called calciphylaxis? *Insights into pathophysiology...*

- Pure trivia for championship of the world: when this disorder was initially described in the 1960's animal experiments were carried out to figure out the pathophysiology. Rodents were *sensitized* with vit. D or PTH and then *challenged* with IV or intraperitoneal injections of iron or albumin. The rodents then developed vascular inflammation that resulted in calcification. Thus, it was thought that this disorder involved "anaphylactic" inflammation and calcification, hence the name: *calciphylaxis*.
- The term calciphylaxis is a not a good one because it isn't IgE mediated and has very little to do with true anaphylaxis. Just remember that this disorder probably relates to the fact that there is prior vascular sensitization → vessel trauma or some other vessel injury → calcium precipitation → end organ damage.
- A proposed new name is **calcific uremic arteriopathy** but this term is misleading because you don't have to be uremic to get it and it can involve venules as well as arterioles.

Does calcium, phosphorous or the $\text{Ca}^{++} \times \text{PO}_4$ product play a role?

- Studies comparing calciphylaxis patients (at the time of diagnosis of the disease) to ESRD controls show no difference in levels of calcium, phosphorous or the $\text{Ca}^{++} \times \text{PO}_4$ product
- However, this may be misleading because at the time of diagnosis, patients usually have very poor nutrition which affects these values. Time-averaged calculations have now shown that elevated calcium and phosphorous levels probably do play a role.
- **The magic number appears to be a $\text{Ca}^{++} \times \text{PO}_4$ product > 70.**

Does PTH play a role?

- Patients with calciphylaxis have an increased level of PTH as compared to ESRD controls
- However, parathyroidectomy doesn't help, likely because elevated PTH is a *sensitizer*. Once the damage is done, removing the elevated PTH won't help much.

Diagnosis and treatment:

- By the time tissue biopsies are taken, it's too late (though this is the definitive diagnostic test)
- Research is on-going regarding bone scan diagnosis and other studies
- Treatment options are scant. Preventive strategies are best: manage calcium, phosphorous, elevated PTH aggressively in your ESRD patients; prevent subQ trauma, reassess dialysis prescription (improve urea clearance).