Calciphylaxis

Calcific uremic arteriolopathy · agonizing skin necrosis with roughly 50% one-year mortality, and sepsis is what kills

Stop the warfarin
start thiosulfate

RECOGNIZE IT *the pain arrives before the lesion looks like anything*

THE PAIN IS THE CLUE

Pain out of all proportion to what you can see, often before any visible lesion, and severe enough to need opioids. **In a dialysis patient, unexplained severe skin pain is calciphylaxis until proven otherwise.**

THE LESIONS

Progress from **livedo racemosa and retiform (net-like, angulated) purpura** to firm indurated plaques, then **black eschar and non-healing ulcers**. **Distribution is the giveaway: fatty areas**, thighs, buttocks, abdomen and breasts (proximal, worse prognosis), or distal legs.

WHO GETS IT

Classically **ESRD on dialysis**, though **non-uremic calciphylaxis exists** with primary hyperparathyroidism, malignancy, connective tissue disease and liver disease. More common in **women, obesity, diabetes** and rapid weight loss.

THE MODIFIABLE DRIVERS *read this as a list of things to stop today*

Driver	What to do about it
⚠ **Warfarin** the single most actionable	Warfarin inhibits vitamin K dependent **matrix Gla protein**, the natural inhibitor of vascular calcification, so it directly promotes the disease. **Stop warfarin and switch to an alternative anticoagulant** such as apixaban, or reassess whether anticoagulation is needed at all. Do this at diagnosis, not later
Calcium load	**Stop calcium-based phosphate binders** and switch to a non-calcium binder such as sevelamer or lanthanum. **Lower the dialysate calcium** and stop calcium supplements
Active vitamin D analogs	**Stop calcitriol and its analogs**, which raise calcium and phosphate absorption
Hyperphosphatemia	Aggressive dietary phosphate restriction and non-calcium binders. **Consider intensified dialysis**, more frequent or longer sessions, to lower calcium and phosphate burden
Hyperparathyroidism	**Cinacalcet** lowers PTH without the calcium load of other approaches, and is preferred. Parathyroidectomy is reserved for severe refractory hyperparathyroidism
Iron and steroids	IV iron and systemic corticosteroids are both associated with calciphylaxis and are reasonable to minimize where an alternative exists

TREATMENT *no single agent works, so run everything in parallel*

Pillar	Detail
Sodium thiosulfate	**Typically 25 g IV over the last 30 to 60 minutes of each hemodialysis session, three times weekly.** It chelates calcium, acts as an antioxidant and vasodilates. **The evidence is observational rather than randomized**, so be honest that it is widely used and biologically plausible rather than proven. Expect **nausea, volume load and a metabolic acidosis**, and monitor for it
Wound care and infection	**Sepsis from infected wounds is the leading cause of death**, so this is not a minor supportive detail. Specialist wound care, and **treat infection promptly**. **Debridement is debated**: it may help selected necrotic wounds but can also extend the injury, so it is a decision for a multidisciplinary team rather than a reflex
Pain control	The pain is severe and frequently under-treated. It usually needs **opioids with careful choice in renal failure**, avoiding morphine and codeine because of active metabolite accumulation, plus a neuropathic agent. **Involve palliative care early** for symptom control, and not only at the end
Diagnosis	**Usually clinical** in a dialysis patient with the classic picture. **Skin biopsy is controversial** because the biopsy site itself may ulcerate and fail to heal; if it is needed for uncertainty, take a **deep incisional or punch sample from the edge**, and expect calcification of small dermal arterioles with intimal fibrosis and thrombosis
The multidisciplinary team	Nephrology, dermatology, wound care, pain and palliative care, surgery and nutrition. **Outcomes are better where this is coordinated**, and no single specialty can manage it alone

THE DIFFERENTIAL *retiform purpura has a short list, and most of it is less painful*

Alternative	What points to it instead
Warfarin-induced skin necrosis	Occurs **within days of starting warfarin**, not years into it, classically in fatty areas too, and associated with **protein C or S deficiency**. The timing is the discriminator
Cholesterol embolization	Follows an **arterial procedure or anticoagulation**, with **livedo, blue toes with palpable pulses, eosinophilia and low complement**, plus renal decline. The peripheral distribution and the procedural history separate it
Antiphospholipid syndrome and other thrombotic states	Prior thrombosis or pregnancy loss, positive **lupus anticoagulant, anticardiolipin or anti-beta-2-glycoprotein I**. Worth screening in atypical or non-uremic cases
Vasculitis	**Palpable purpura** rather than retiform, systemic features, positive **ANCA** or cryoglobulins, and active urinary sediment
Cellulitis and pyoderma gangrenosum	Cellulitis is warm, spreading and responds to antibiotics. Pyoderma has an **undermined violaceous border**, shows **pathergy**, and is associated with IBD and hematologic disease. **Both are commonly diagnosed first, which is why calciphylaxis is typically recognized late**

Send these at diagnosis: calcium, phosphate and the calcium-phosphate product, **PTH**, alkaline phosphatase, 25-hydroxy vitamin D, albumin, and a coagulation screen including **protein C and S and antiphospholipid antibodies**, particularly in non-uremic disease. Imaging is not required to diagnose it, though **plain radiographs or mammography may show net-like vascular calcification** and can support the diagnosis when biopsy is being avoided.

PROGNOSIS & PEARLS

- **Mortality is roughly 50% at one year**, and higher with proximal and ulcerated lesions. **Say so honestly and start goals-of-care conversations early**, in parallel with active treatment rather than after it fails. This is a disease where aggressive treatment and palliative input belong together from the start.
- **Avoid subcutaneous injections into at-risk skin.** Insulin, heparin and other subcutaneous injections can trigger new lesions at the injection site through local trauma, so rotate away from affected and adipose areas.
- **The differential is wide and mostly less painful:** warfarin-induced skin necrosis, cholesterol embolization, vasculitis, antiphospholipid syndrome, nephrogenic systemic fibrosis, cellulitis and pyoderma gangrenosum. **Retiform purpura plus disproportionate pain in a dialysis patient is the combination that should stop you.**
- **Prevention is the only real win.** In dialysis patients, keep phosphate and calcium controlled, prefer non-calcium binders, **avoid warfarin where an alternative exists**, and treat hyperparathyroidism before it becomes severe.

References: KDIGO guidance on chronic kidney disease mineral and bone disorder · published reviews, registry data and consensus statements on calcific uremic arteriolopathy, including sodium thiosulfate use.

Educational aid; verify against current guidance, local formulary and patient factors.

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