A 44-YEAR-OLD WOMAN with end-stage liver disease presents with a painful, ischemic, necrotic lesion on her right lateral and medial thigh (FIGURE 1). Several months ago, while being evaluated in the hospital for liver transplantation, she developed bacteremia, anion-gap metabolic acidosis, hepatorenal syndrome, and acute renal failure. She began continuous hemodialysis, which lasted for about 1 month, ending 35 days after the renal failure resolved.

Current laboratory values:
- Serum calcium concentration 7.8 mg/dL (reference range 8.5–10.5)
- Phosphorus 6.4 mg/dL (2.5–4.5)
- Corrected calcium-phosphorus product 55
- Parathyroid hormone 275 pg/mL (10–60)
- 25-hydroxyvitamin D 7.4 ng/mL (31–80).

Q: Given the patient’s history, which of the following does her skin lesion likely represent?
- Necrotizing fasciitis
- Calciphylaxis
- Disseminated intravascular coagulation
- Anticoagulant-induced skin necrosis

A: Calciphylaxis, or calcific uremic arteriolopathy, is the most likely. It is rare in people with normal renal function, and still rare but somewhat less so in end-stage renal disease patients undergoing chronic hemodialysis.

WHAT CAUSED IT IN OUR PATIENT?

The cause of calciphylaxis is unknown. Theories have focused on protein C and parathyroid hormone. Putative precipitating factors include acute tubular necrosis, albumin infusion with paracentesis, deficiency of protein C or S, hyperparathyroidism, hyperphosphatemia, hypercalcemia, vitamin D supplementation, steroids, trauma, and warfarin use.
**FIGURE 2.** Histologic study of the biopsied skin lesions. (A) A low-power image of the punch biopsy shows necrotic epidermis (arrow) that has physically separated from the underlying unhealthy hemorrhagic dermis (arrowhead). (B) A higher-power view of the hemorrhagic dermis shows scattered foci of deeply basophilic material (arrowheads). A reasonable differential diagnosis for this finding is atypical hyperchromatic fibroblastic and endothelial nuclei vs calcium deposits. (C) Von Kossa stain was performed to evaluate for the presence of calcium deposits; brown-staining areas indicate calcium deposition. (D) A section of the same tissue seen in C. (E and F) Calcium deposits within the wall of the centrally placed small- to medium-sized vessel.
Our patient had a history of hypothyroidism, ulcerative colitis, and end-stage liver disease due to primary sclerosing cholangitis, but no previous history of renal disease.

At the time of her acute renal failure, her calcium-phosphorus level was 55, parathyroid hormone level 274 pg/mL (normal 10–60), and protein C level 26% (normal 76%–147%). At the time the skin lesions were discovered, her protein C level had dropped to 14%; her parathyroid level had returned to normal.

Her home medications included furosemide (Lasix), levothyroxine (Synthroid), mesalamine (Pentasa), azathioprine (Imuran), ursodiol (Actigall), spironolactone (Aldactone), and omeprazole (Prilosec).

■ NONHEALING LESIONS

The skin lesions are characteristically erythematous and tender, with mottling of the skin early in the course. As the lesions progress, they develop central necrosis and deep ulcerations with eschar formation. The ulcers have irregular borders and do not heal. Histopathologic study typically shows epidermis with ischemic necrosis and calcium deposition along elastic fibers on Von Kossa calcium stains (FIGURE 2).

The skin lesions of calciphylaxis usually occur in areas of increased adipose tissue. The lesions may not manifest until several weeks after the initial insult (ie, the elevated calcium-phosphate level). Skin biopsy is recommended if a necrotic skin lesion is identified in a patient with an elevated calcium-phosphate level or in a patient with risk factors for renal, liver, or parathyroid disease.

■ PROGNOSIS IS POOR

Treatment is supportive. Intensive wound care (with surgical evaluation for skin grafting), hyperbaric oxygen, and possibly tissue plasminogen activator (if there is evidence of a hypercoagulable state and occlusive vasculopathy) may be the most beneficial. Identifying the underlying cause and regulating the calcium-phosphorus product level with diet, phosphate binders, bisphosphonates, and sodium thiosulfate are also important in wound healing. Cinacalcet (Sensipar) and parathyroidectomy should be considered in cases of secondary hyperparathyroidism.

Calciphylaxis is important to recognize early in its course and may require a multidisciplinary approach to treatment. Its prognosis is poor, with death rates ranging from 40% to 60%.

Our patient developed recurrent hepatorenal syndrome and sepsis and eventually died of septic shock.

■ REFERENCES


■ SUGGESTED READING


ADDRESS: Christopher R. Newey, DO, MS, Department of Neurology, S90, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail neweyc@ccf.org.