plasmacytoid, lymphoid, and myeloid findings in 87 patients. 


**Mapping Biopsy Procedure on Management of Severe Buruli Ulcer Due to *Mycobacterium ulcerans*, Subspecies *shinshuense***

**Report of a Case** | A healthy male teenager presented with a 2-month history of eruptions on the dorsum of his left hand, which showed diffuse painful erythema and a 2-cm ulcer. Results of blood tests were normal but for slightly elevated C-reactive protein levels (0.46 mg/dL). Culture results from the ulcer were negative for any general bacteria. Computed tomography showed neither gas production nor abscess formation. Histologic examination of the erythematous lesion revealed diffuse necrosis, and Ziehl-Neelsen (Z-N) staining showed many acid-fast bacilli in the subcutis. We diagnosed cutaneous mycobacterial infection.

Despite treatment with oral clarithromycin, 800 mg/d, and levofloxacin, 500 mg/d, the lesion expanded. Therefore rifampicin, 450 mg/d, was added to the treatment regimen 7 days after the initiation of therapy. We performed debridement on day 8 (Figure, A). Although almost all the skin on the dorsum of his hand was debrided, the erythema further expanded. We performed a second debridement on day 25 and additionally excised the erythematous lesion toward the wrist, including the area labeled 8 in Figure, B, and debrided necrotic tissue. The lesion rapidly improved after the second debridement, although some finger extensor tendons gradually became necrotic, and reconstruction of tendons was needed. The patient showed no recurrence at 1-year follow-up.

At 4 weeks, growth of a yellow-white colony in Ogawa egg medium was observed. Analysis using DNA-DNA hybridization (Kyokuto, Japan) demonstrated *Mycobacterium marinum* bacteria. Polymerase chain reaction (PCR) analysis targeting insertion sequence IS2404 was negative. Pathogenic plasmid MUM001 gene sequences revealed Buruli ulcer caused by *Mycobacterium ulcerans* subsp *shinshuense*, a rare mycobacterium phenotypically close to *M ulcerans* that produces a toxin resembling mycolactone. We note that *M ulcerans* subspecies *shinshuense* can also affect tendons and muscles, as in our case and at least 1 other case. Recommendations concerning the duration of antibiotic treatment and timing of surgical intervention for Buruli ulcer have been offered in preliminary guidelines issued by the World Health Organization, but there is no reliable evidence to determine the extent of surgical excision.

**Discussion** | Using a 3-mm punch, we performed multiple biopsies from 13 erythematous sites on our patient’s hand and wrist (Figure, A-D) before first debridement at points 1 through 6 (Figure, A) and before second debridement at points 7 through 13 (Figure, B-D). We retrospectively examined the relationship among clinical presentations, histologic findings (hematoxylin-eosin [H-E] and Z-N stainings), and results of PCR analysis for IS2404 (Figure, G) to demonstrate the features of sites that needed debridement (Table). From the clinical course, we determined that all sites of first debridement (samples 1-6) and the area around sample 8 of the second debridement needed surgical resection. We performed the second debridement to address severe postoperative functional limitations and in-
flammation found on visual inspection, and significant improvement was achieved, even though other erythematous lesions were not surgically removed.

The histologic findings from H-E staining could be roughly categorized into 2 patterns: necrosis without granuloma formation (Figure, E) and granuloma formation without necrosis (Figure, F). The sites that needed resection necrosis without granulomatous reaction was observed (hematoxylin-eosin, original magnification ×100). F. Histologic findings from site 10 showed granulomatous reactions without necrosis (hematoxylin-eosin, original magnification ×100). G. Results of polymerase chain reaction (PCR) analysis for IS2404 using pu4f and pu7r primers. Samples 1, 2, 4, 5, 6, and 11 tested positive for IS2404. Gene markers 1 through 13 represent biopsy samples taken from sites 1 through 13, respectively; gene marker N, normal control; gene marker D, 100-bp DNA marker.

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Table. Mapping Biopsy Evaluated by PCR Analysis and Histologic Examinationa

<table>
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Abbreviations: H-E, hematoxylin-eosin stain; PCR, polymerase chain reaction; Z-N, Ziehl-Neelsen; +, positive finding; −, negative finding.

* Results of PCR analysis for IS2404 and histologic examination with Z-N staining and H-E staining of all mapping biopsy samples taken before first debridement (sites 1-6) and before second debridement (sites 7-13).
The mapping biopsy procedure to determine an adequate surgical margin has been performed in cases of malignant neoplasm such as extramammary Paget disease. We propose that if administration of recommended antibiotics for an adequate duration proves ineffective, the preoperative mapping biopsy procedure might be used to determine the extent of surgical excision in Buruli ulcer and to avoid unnecessary resection if pathologic services are available.

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Severe Nonuremic Calciphylaxis Due to Hyperphosphatemia Resolving With Multimodality Treatment Including Phosphate Binders

Calciphylaxis is a highly morbid disease with a 1-year mortality of approximately 80% that is usually associated with kidney disease. We report a case of nonuremic calciphylaxis in the setting of hyperphosphatemia that improved dramatically with phosphate binders and supportive care.

Report of a Case | A white woman approximately 60 years old presented with numerous painful subcutaneous plaques and cutaneous necrosis, ulceration, and eschars on her hips, thighs, buttocks, abdomen, and breasts. She had a history of diabetes mellitus, congestive heart failure, tobacco abuse (half-pack of cigarettes daily), and endocarditis with artificial aortic valve replacement 7 years previously, requiring long-term warfarin treatment. Additional medications included aspirin, atorvastatin, furosemide, glimepiride, lisinopril, and metoprolol.

Her physical examination was remarkable for obesity (BMI, 32.3 [calculated as weight in kilograms divided by height in meters squared]) with firm, painful subcutaneous plaques on the lateral hips, thighs, buttocks, breasts, and abdomen. Overlying the plaques were large, angulated ulcerations with firm adherent black eschars and peripheral dusky erythema (Figure 1A and B). Histopathologic analysis confirmed the diagnosis of calciphylaxis (Figure 2).

The patient had no history of renal dysfunction, but her serum phosphorus level was elevated, at 5.3 mg/dL (normal, 2.4-4.7 mg/dL). (To convert serum phosphorus to millimoles per liter, multiply by 0.323.) Findings from a complete blood cell count, comprehensive metabolic panel, extended antiphospholipid antibody panel, and assays for parathyroid hormone, vitamin D levels, protein C, and protein S were normal, with the exception of a hemoglobin level of 10.4 g/dL (normal, 12.0-16.0 g/dL). (To convert hemoglobin to grams per liter, multiply by 10.0.) Her prothrombin time and international normalized ratio were appropriate for valvular anticoagulation and had been stable for years. Her hyperphosphatemia in the absence of kidney disease prompted testing for fibroblast growth factor 23 (FGF23) level, which was elevated. Additionally, iron studies demonstrated iron deficiency, at 20 µg/dL (normal range, 28-170 µg/dL). (To convert iron to micromoles per liter, multiply by 0.179.)

Multimodality therapy was instituted, consisting of sevelamer, 800 mg, 3 times daily as a phosphate binder; hyperbaric oxygen, 6 days per week for 10 weeks; oral alendronate, 10 mg/d; and local care with topical collagenase and petrolatum dressings. After 2 months of these therapies, the patient had significant clinical improvement. Warfarin was replaced with dabigatran etexilate owing to reports of warfarin-associated calciphylaxis. The patient was counseled about tobacco cessation and quit smoking over 3 months. Surgical debridement was considered but ultimately avoided due to significant, continued clinical improvement (Figure 1C and D).

Discussion | Calciphylaxis most commonly occurs in the setting of end-stage renal disease and an elevated calcium-phosphate level. However, calciphylaxis in the absence of renal impairment has been described in the setting of obesity; liver disease; elevated calcium-phosphorus, phosphorus, and alkaline phosphatase; decreased albumin; diabetes; and treatment with systemic corticosteroids and warfarin. It has most commonly been described in white women.

Our patient’s risk factors for calciphylaxis included smoking, obesity, ethnicity, elevated phosphorus levels, and potentially warfarin treatment. She had substantial clinical improvement with multimodality therapy, with the most specific targeted intervention being treatment with phosphate bind-