

A recurrent ulcer over the left thigh: The Diagnostic Mimicry between lupus profundus and non-uremic calciphylaxis

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Abstract:

Calciphylaxis is a rare, life-threatening syndrome of vascular calcification and microvascular occlusion in the dermis and panniculus, leading to painful ischemic lesions. While historically tied to end-stage kidney disease, non-uremic calciphylaxis (NUC) has been increasingly recognized in patients with normal kidney function but with other risk factors, including systemic autoimmune diseases, hypercoagulable states or chronic steroid therapy. Diagnosing NUC in patients with such underlying autoimmune diseases is challenging. Its initial clinical presentation of indurated subcutaneous nodules and plaques closely mimic other conditions such as lupus profundus, a rare variant of lupus erythematosus characterized by lobular panniculitis. As the management for both conditions differ, misdiagnosis or delayed diagnosis can lead to inappropriate immunosuppression, delayed targeted therapy and worsening tissue ischemia. We present the case of a 34-year-old woman with previously known systemic lupus erythematosus (SLE) and prior biopsy-proven lupus profundus, who developed a chronic, non-healing thigh ulcer over the original lesion, subsequently diagnosed as NUC upon repeat biopsy.

Keywords:

Ulcer; Autoimmune disease; Lupus;
Calciphylaxis; Dermatopathology

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Introduction

Background Calciphylaxis is a rare, life-threatening syndrome characterized by systemic microvascular calcification and thrombosis, which leads to severe tissue ischemia, necrotic ulceration,

and high mortality rates [1]. While most frequently associated with end-stage renal disease, it is increasingly recognized in patients with normal kidney function—a variant known as non-uremic calciphylaxis (NUC). Patients with systemic

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autoimmune conditions, such as systemic lupus erythematosus (SLE), face an increased risk of NUC due to predisposing hypercoagulable states and frequent, long-term use of systemic corticosteroids [2]. Clinically, early-stage NUC closely mimics other conditions such as lupus profundus, a rare variant of SLE characterised by lobular panniculitis, creating a profound diagnostic dilemma. As management strategies for these two conditions are fundamentally different, misdiagnosis can introduce a dangerous therapeutic paradox that can accelerate tissue necrosis.

Case Presentation

A 34-year-old Chinese woman presented with a 1-year history of an indurated plaque over the left thigh since 2023 (Figure 1a). An initial biopsy performed in 2023 demonstrated histological features consistent with lupus profundus - superficial to deep perivascular and periadnexal chronic inflammatory infiltrate, small vessel fibrinoid necrosis and extension into the superficial lobular panniculus (Figure 2a, 2b and 2c). Direct immunofluorescence (DIF) showed granular IgM and C3 deposits along the basement membrane zone. She was simultaneously diagnosed with systemic lupus erythematosus (SLE) with positive antiphospholipid antibodies and was treated with hydroxychloroquine and prednisolone, which was subsequently tapered as her wound showed initial improvement. Despite ongoing maintenance therapy, her lesion deteriorated markedly two years later in November 2025 and a new painful ulcer developed over the original lesion. Examination revealed a 7 cm × 5 cm ulcerated plaque with necrotic borders and a sloughy base (Figure 1b).

Given the atypical progression, a repeat excisional biopsy over the new ulcer was performed. Histopathological findings revealed a distinct shift that was now diagnostic of calciphylaxis - superficial and deep perivascular infiltrate of lymphocytes and plasma cells with minimal inflammation within the fat. Small capillaries were seen within the area of inflammation, with calcium deposits within their vessel walls, highlighted on Von Kossa stain (Figure 3a and 3b). Direct immunofluorescence was negative. An extensive diagnostic workup including renal function, calcium metabolism and vascular studies were unremarkable – Creatinine 59μmol/L, adjusted Calcium 2.37mmol/L, ABPI on the right was 1.16

and 1.09 on the left, and a diagnosis of NUC was made.

She was subsequently treated multi-modally with intravenous antibiotics for secondary infection, surgical debridement, negative pressure wound therapy and thrice a week intravenous sodium thiosulfate 25g over four weeks. Immunosuppressants including Prednisolone 25mg was gradually tapered off over a month and Methotrexate 10mg/week was immediately stopped. The lesion showed excellent clinical response to the treatment over several months. (Figure 1c)

Discussion

This case highlights a profound diagnostic conundrum of NUC arising in a patient with pre-existing, biopsy-proven lupus profundus. NUC presents with tender, indurated subcutaneous nodules or plaques progressing to ulceration with histological findings of cutaneous microvascular calcification which tend to mimic other conditions [1] such as lupus profundus or subcutaneous panniculitis-like-T-cell lymphoma. Moreover, there is a lack of clear diagnostic criteria for calciphylaxis [3], which potentially delays its eventual diagnosis and treatment initiation. The pathogenesis of NUC in SLE patients is both multifactorial and synergistic. The hypercoagulable state in SLE and associated dystrophic calcification may predispose to calciphylaxis [4]. Systemic corticosteroids, the frontline treatment of lupus flare, is also an established independent risk factor for NUC [5], likely due to induced prothrombotic state [6] and promotion of vascular calcification [7]. This creates a dangerous therapeutic trap as escalating corticosteroid doses under the mistaken assumption of a "lupus flare" directly accelerates the pathophysiological cascade driving NUC.

Differentiating these entities relies on a low threshold for repeat biopsy on suspected lesions in high-risk patients that are worsening or not responding to treatment. Histologically, lupus profundus is characterized by lobular panniculitis with lymphocytic infiltrates and a hyaline necrosis of fat lobules [8], while NUC demonstrates calcification, fibrointimal hyperplasia and thrombosis in microvessels in subcutaneous adipose tissue and dermis best visualised via special staining [1].

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First-line treatment of lupus profundus is with immunosuppression such as hydroxychloroquine and glucocorticoids [9], while calciphylaxis is treated with a combination of wound care, sodium thiosulfate, cessation of calcification-promoting triggers like steroids and addressing predisposing conditions [3].

Conclusion

Non-uremic calciphylaxis is an important diagnostic mimic of lupus profundus in patients with systemic autoimmune diseases. Clinicians must maintain a high index of suspicion and pursue timely repeat biopsy when existing wounds fail to respond or continue to deteriorate with existing treatment. This enables timely initiation of appropriate therapy and can significantly change the clinical course for patients.

Take home messages

Lupus profundus and calciphylaxis can be clinical mimickers of each other

Timely repeat biopsy should be considered in high-risk patients presenting with rapidly progressive, painful lesions to rule out clinical mimickers such as calciphylaxis

Management of lupus profundus and non-uremic calciphylaxis differ vastly as the former mainly focuses on immunosuppressive therapy while the latter is treated with aggressive multimodal wound-directed therapy

Declarations

Author Contributions:

Li Cheng Ong contributed to the manuscript preparation, editing, and review of the final text

Wei Qiang Chng, Ding Yuan Wang, Michelle WT Liang and Yisheng Wong contributed to the editing, and review of the final text

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Figure Legends



Figure 1 (a) Clinical Picture of left thigh wound in 2023 during initial presentation (b) Clinical picture of left thigh wound in 2025 during subsequent presentation (c) Clinical picture of left thigh wound in February 2026 post treatment.

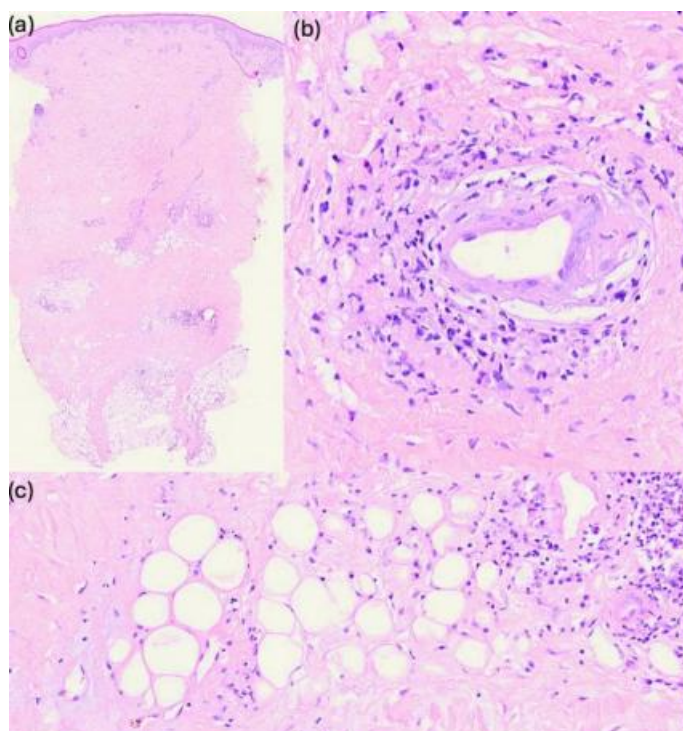


Figure 2 (a) There is a superficial and deep perivascular chronic inflammatory infiltrate of lymphocytes and plasma cells. (H&E, x40) (b) There is small vessel vasculitis with perivascular infiltrates of activated lymphocytes, nuclear dust and fibrinoid necrosis of vessels in the deep dermis and subcutis. (H&E, x400) and (c) There is a lobular panniculitis with infiltrates of lymphocytes, histiocytes and plasma cells. Hyaline fat necrosis can be seen. (H&E, x 400).

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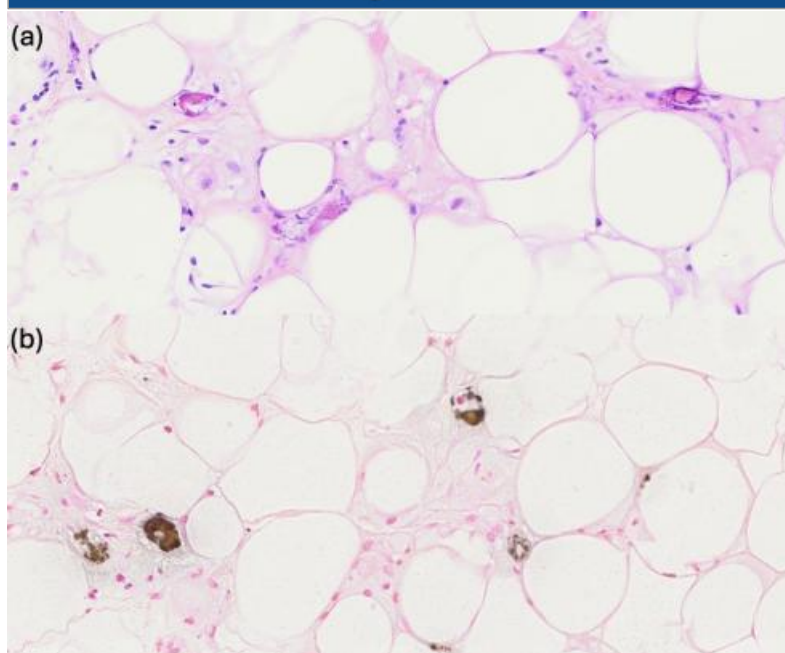


Figure 3 (a) and (b) Von Kossa positive deposits of calcium within small vessels in the subcutis. (Figure 3A: H&E, x 400; Figure 3B: Von Kossa, x 400).