

## BRIEF ARTICLE

## Histopathological Granuloma Formation in Subacute Cutaneous Lupus Erythematosus

Nattanicha Chairsiraneepan, MD<sup>1,2</sup>, Poonnawis Sudtikoonaseth, MD<sup>1</sup>

<sup>1</sup> Institute of Dermatology, Ministry of Public Health, Bangkok, Thailand

<sup>2</sup> Texas Tech University Health Sciences Center, Department of Medicine, Lubbock, Texas

### ABSTRACT

**Introduction:** Subacute cutaneous lupus erythematosus (SCLE) is one of the cutaneous lupus erythematosus subtypes. Being an autoimmune condition in nature, its diagnosis requires compatible clinical presentation with histopathological findings.

**Objective:** To present a case of subacute cutaneous lupus erythematosus with granuloma formation.

**Case report:** A 56-year-old woman presented with red plaques on her face, trunk, and extremities for 15 years. Two skin biopsies were performed during two different visits. The results showed tuberculoid leprosy and multiple granuloma annulare. She was treated accordingly for years with no improvement in her condition. Later, the third skin biopsy with CD123 immunohistochemical stain was done. The result was most consistent with cutaneous lupus erythematosus. Together with her clinical findings, she was finally diagnosed with SCLE. Her rashes resolved after being treated with hydroxychloroquine and topical steroid.

**Conclusion:** The diagnosis of SCLE must be made based on both clinical presentations and histopathological findings.

### INTRODUCTION

Subacute cutaneous lupus erythematosus (SCLE) is an autoimmune condition. It usually presents as scaly, erythematous annular plaques on photo-distributed areas. It typically affects young to middle-aged females. About 50% of SCLE patients can develop systemic lupus erythematosus<sup>1</sup>. Histopathologic findings include marked basal cell degeneration and mucin deposition. Granuloma formation is an unusual histopathological finding in SCLE that had never been described before.

### CASE REPORT

A 56-year-old woman presented at the dermatology outpatient clinic with reddish rashes on the upper and lower extremities for 10 years. There was no loss of sensation on skin lesions. Cutaneous lupus erythematosus was suspected at the time. However, the skin biopsy revealed tuberculoid granulomatous dermatitis suggesting borderline leprosy. Slit-skin smear for acid-fast bacilli (AFB) was negative. She was, however, diagnosed with borderline tuberculoid leprosy. A complete 2-year course of leprosy treatment with rifampicin (600 mg monthly), clofazimine (300 mg monthly and 50 mg daily), and

March 2024 Volume 8 Issue 2

dapsone(100 mg daily) was given without distinct improvement. Afterward, she was lost to follow-up.

Five years later, the patient returned to the clinic because of the progression of red rashes on the face, buttocks, and upper and lower extremities. A second biopsy was performed demonstrating granulomatous dermatitis at the superficial dermis. Further investigations included tissue AFB, Grocott's methenamine silver (GMS), and periodic acid-Schiff (PAS) special stains, all yielded negative results. Direct immunofluorescence was negative. PCR for mycobacterium was negative. The patient was diagnosed with multiple granuloma annulare. She was treated accordingly with oral metronidazole and topical 0.1% betamethasone cream. No significant improvement was achieved after several months of treatment. Therefore, on a regular follow-up visit in 2018, the third skin biopsy was done with suspicion of subacute cutaneous lupus erythematosus. Physical examination showed multiple scaly, erythematous, annular plaques distributed on the face, trunk, and upper (Figure 1) and lower extremities. KOH scraping was negative for fungus.

**Figure 1.** An erythematous scaly annular plaque on the right shoulder.



Histopathological findings showed focal interface dermatitis with superficial dermal granulomas comprising aggregates of histiocytes. There was sparse superficial and, most importantly, deep dermal perieccrine infiltration of mononuclear inflammatory cells (Figure 2), which were not present in previous histopathological results from our revision. Immunohistochemistry demonstrated numerous positive CD123 cells within the infiltrates (Figure 3). Direct immunofluorescent was positive for fibrinogen at the dermo-epidermal junction. Tissue AFB, GMS, and PAS stains were negative. Antinuclear antibody (ANA) showed positive titer 1: 160 with a speckled pattern, and anti-SSA(Ro) and anti-SSB(La) were negative. Complete blood count, blood chemistry panel, and urinary analysis were normal.

The review of other systems was unremarkable. The patient was diagnosed with subacute cutaneous lupus erythematosus. She was treated with hydroxychloroquine 200 mg BID initially for one month then 100 mg daily and topical 0.1% triamcinolone cream twice daily along with strict sun protection measures. Her lesions gradually improved and resolved with post-inflammatory hyperpigmentation.

## DISCUSSION

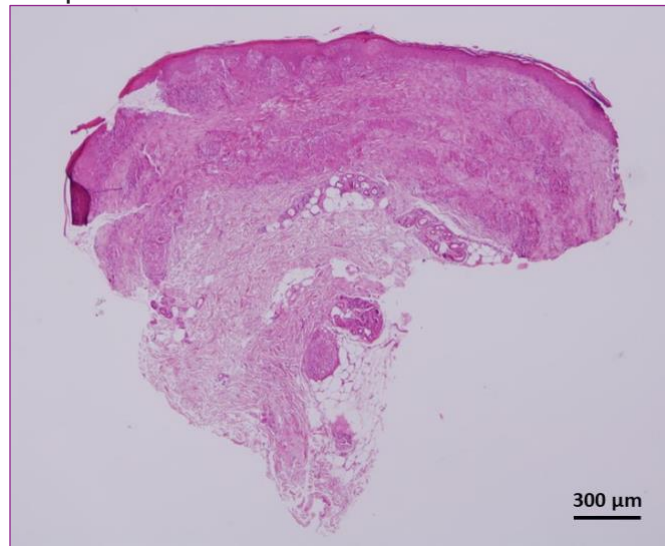
Granuloma formation is a skin inflammatory reaction that can be triggered by infection, foreign bodies, tumors, or systemic inflammation<sup>2</sup>. It involves dendritic cells, histiocytes, and T-cell lymphocytes. When granulomatous skin disease is suspected, it is vital to differentiate a patient's skin condition as infectious or non-infectious. In this patient, many tissue cultures and PCR for TB were completed with negative results. The slit skin smear was negative. However,

she had been initially treated with anti-leprosy drugs according to the report of histopathology which suggested tuberculoid granulomatous dermatitis.

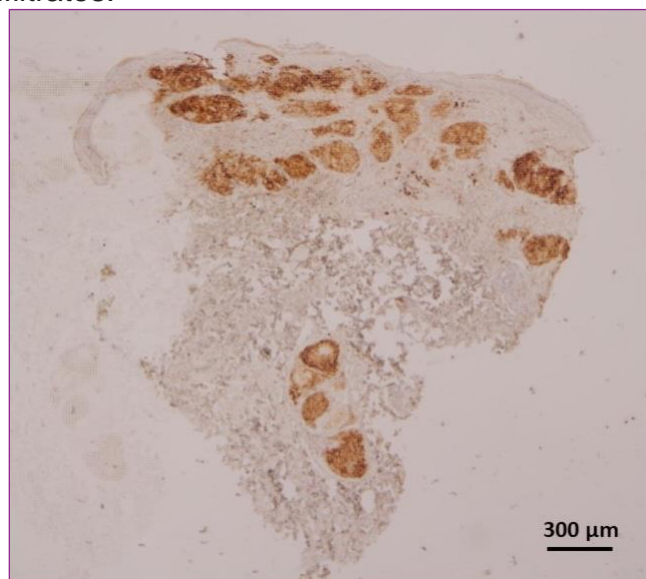
In subacute cutaneous lupus erythematosus (SCLE), histopathological findings typically show epidermal atrophy, basal vacuolization,

and mild to moderate mononuclear infiltrate restricted to superficial dermis inflammation. Interface dermatitis observed in SCLE lesions consists mainly of activated T cells and macrophages near apoptotic basal keratinocytes<sup>3</sup>. Follicular plugging and basement membrane thickening are usually absent<sup>4</sup>. Peri-adnexal lymphocytic infiltration

**Figure 2.** Skin biopsy with Hematoxylin and eosin staining 20X demonstrating focal interface dermatitis, superficial dermal granulomas comprising aggregates of histiocytes with sparse superficial and deep dermal peri-ecrine infiltration of mononuclear inflammatory cells.



**Figure 3.** Skin biopsy with CD123 immunochemical staining demonstrating numerous positive CD123 cells within the infiltrates.



can be observed<sup>5</sup>. Approximately 60% of SCLE cases show positive immunoglobulin or complement components at the dermo-epidermal junction<sup>3</sup>. Plasmacytoid dendritic cells, which express CD123, are usually increased in lupus erythematosus<sup>6</sup>. Many of the histopathological findings of the patient from the third biopsy together with her annular plaques pointed towards SCLE.

Half of SCLE patients meet the criteria for SLE<sup>3</sup>. ANA is positive in 70-80% of SCLE cases, anti-Sjögren's Syndrome A antibody (anti-Ro/SSA) is positive in 70% of the cases<sup>7</sup> and Anti-Sjogren's Syndrome B antibody (anti-La/SSB) is positive in 30-50% of the cases<sup>8</sup>. Serology and immunofluorescence provide supportive clues to the diagnosis of SCLE. Still, negative serology cannot be used to exclude disease and positive serology is not always diagnostic<sup>9</sup>. Our case was positive for ANA and negative for anti-Ro and anti-La, but no other clinical manifestations fulfilled the latest EULAR/ACR classification criteria for SLE. From a thorough literature review, no granuloma formation was reported in SCLE. However, there was a report of sebaceous granuloma formation in discoid lupus erythematosus lesions in which the authors proposed that lipids from disrupted sebaceous glands caused foreign body giant cell granuloma. Some other reports of SLE patients with granuloma formation in lymph nodes and internal organs<sup>10,11</sup>. The granuloma formation in SCLE is unusual and needs to be elucidated.

Treatment of SCLE includes the use of topical therapies, systemic agents, and sun protection<sup>12</sup>. Topical therapies include corticosteroids and calcineurin inhibitors. Oral antimalarial drugs are first-line systemic therapy for SCLE. Other systemic treatments in SCLE that have been reported are methotrexate, azathioprine, thalidomide,

mycophenolate mofetil, and oral retinoids<sup>12</sup>. Our patient resolved with the treatment of hydroxychloroquine and a topical steroid. Regular follow-up is crucial in lupus erythematosus cases due to the chronic or recurrent course of the disease and the tendency to develop systemic lupus erythematosus in the future.

## CONCLUSION

The histopathological finding in our patient with the diagnosis of SCLE is not typical. Some evidence of cutaneous lupus erythematosus in histology and clinical presentation of the patient directed toward SCLE. CD123 immunohistochemistry can also aid in diagnosing cutaneous lupus erythematosus. Nonetheless, the diagnosis of SCLE must be based on both clinical and histological findings.

**Conflict of Interest Disclosures:** None

**Funding:** None

**Corresponding Author:**

Nattanicha Chairsrimaneepan  
3601 4th St, Lubbock, TX 79430  
Phone: 806-999-3691  
Email: [nattanicha5.13@gmail.com](mailto:nattanicha5.13@gmail.com)

**References:**

1. Ribero S, Sciascia S, Borradori L, Lipsker D. The Cutaneous Spectrum of Lupus Erythematosus. *Clin Rev Allergy Immunol*. 2017;53(3):291-305.
2. Terziroli Beretta-Piccoli B, Mainetti C, Peeters MA, Laffitte E. Cutaneous Granulomatosis: a Comprehensive Review. *Clin Rev Allergy Immunol*. 2018;54(1):131-146.
3. Stavropoulos PG, Goules AV, Avgerinou G, Katsambas AD. Pathogenesis of subacute cutaneous lupus erythematosus. *J Eur Acad Dermatol Venereol*. 2008;22(11):1281-1289.
4. Moatasim A, Haque UI A. The value of individual microscopic features in diagnosis

- of cutaneous lupus erythematosus [LE]. *Int J Pathol.* 2005; 3 (2): 76-80.
5. Parodi A, Caproni M, Cardinali C, et al. Clinical, histological and immunopathological features of 58 patients with subacute cutaneous lupus erythematosus. A review by the Italian group of immunodermatology. *Dermatology.* 2000;200(1):6-10.
  6. Chen SJT, Tse JY, Harms PW, Hristov AC, Chan MP. Utility of CD123 immunohistochemistry in differentiating lupus erythematosus from cutaneous T cell lymphoma. *Histopathology.* 2019;74(6):908-916.
  7. Okon LG, Werth VP. Cutaneous lupus erythematosus: diagnosis and treatment. *Best Pract Res Clin Rheumatol.* 2013;27(3):391-404.
  8. Grönhagen CM, Nyberg F. Cutaneous lupus erythematosus: An update. *Indian Dermatol Online J.* 2014;5(1):7-13.
  9. Callen JP. Cutaneous lupus erythematosus: a personal approach to management. *Australas J Dermatol.* 2006;47(1):13-27.
  10. Shrestha D, Dhakal AK, Shiva RK, Shakya A, Shah SC, Shakya H. Systemic lupus erythematosus and granulomatous lymphadenopathy. *BMC Pediatr.* 2013;13:179.
  11. Bharti A, Meena LP. Systemic lupus erythematosus with hepatosplenic granuloma: a rare case. *Case Reports Immunol.*
  12. Walling HW, Sontheimer RD. Cutaneous lupus erythematosus: issues in diagnosis and treatment. *Am J Clin Dermatol.* 2009;10(6):365-381.