# Subacute cutaneous lupus erythematosus following abemaciclib therapy for metastatic breast cancer

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## INTRODUCTION

Subacute cutaneous lupus erythematosus (SCLE) is a subtype of cutaneous lupus erythematosus that can be differentiated based on clinical, immunologic, and histopathologic features; however, features between idiopathic and drug-induced SCLE may be indistinguishable. With the recent development of novel cancer therapies, an increasing number of drugs are being implicated in the development of SCLE. Here, we report a case of SCLE in association with abemaciclib, a CDK4/6 inhibitor, which is a treatment used for metastatic breast cancer.

## CASE REPORT

A 74-year-old woman presented to the clinic with a 6-month history of a recalcitrant pruritic eruption of the head, neck, and upper portion of the trunk. She had a history of intraductal carcinoma of the right breast with lung metastasis in April 2019. She was undergoing treatment with palbociclib and fulvestrant, but metastatic brain lesions found in November 2019 prompted the transition from palbociclib to abemaciclib. Her cutaneous eruption began 4 months later. Prior to her presentation to dermatology, she tried over-the-counter non-sedating antihistamines and 1% hydrocortisone, which provided minimal relief.

On examination, annular erythematous plaques with a focally polycyclic pattern were seen in a primarily photo distributed distribution. A complete review of systems was negative, except for gastrointestinal symptoms related to her cancer treatments. Shave and punch biopsies of left side of the chest and upper left portion of the back, respectively, were performed (Figs 1, *A, B* and 2, *A, B*).

*Abbreviations used:*

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|---|---|
| CDK: | cyclin-dependent kinase |
| SCLE: | subacute cutaneous lupus erythematosus |
| SLE: | systemic lupus erythematosus |

Histologic examination of both biopsies revealed vacuolar changes of basal keratinocytes associated with lymphocyte exocytosis, focal epidermal atrophy, and dyskeratotic keratinocytes scattered at the dermoepidermal junction (Fig 2). The dermis demonstrated a moderately dense superficial and deep perivascular and periadnexal lymphocytic infiltrate in association with interstitial mucin deposition. Laboratory findings were as follows: positive for antinuclear antibody (no titer reported), anti-Ro/SS-A, and anti-histone antibody and negative for anti-dsDNA and anti-La/SS-B antibodies. Taken together, the clinical and histologic findings were supportive of SCLE and given the lack of evidence for systemic lupus erythematosus (SLE), the drug-mediated disease was suspected.

The patient's metastatic lesions were stable on abemaciclib and fulvestrant, and her side effect profile of diarrhea and constipation was tolerable. Therefore she elected to continue with her current treatment. Her cutaneous symptoms were managed with high potency topical steroids, with significant improvement. Later hydroxychloroquine was added but discontinued after a few weeks due to nausea. Four months after the presentation, the decision was

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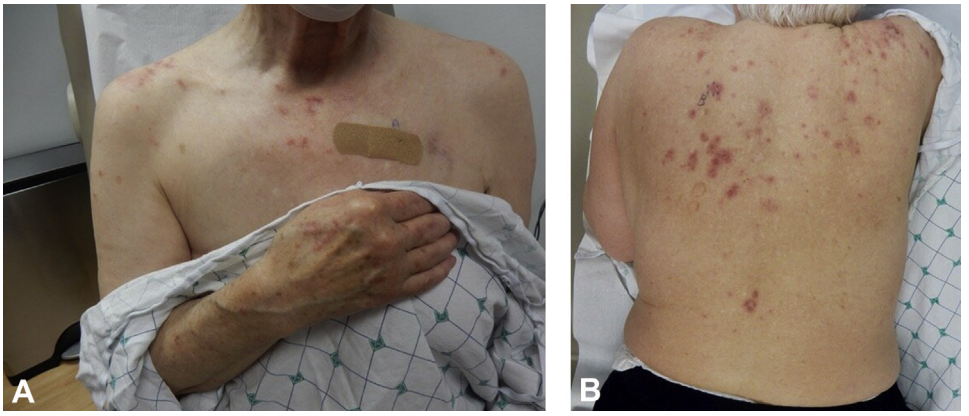


**Fig 1.** Physical examination. **A**, Annular pink thin scaly plaques on the chest and dorsal extremities. **B**, Pink to red scaly papules and plaques in the central and upper portion of the back.

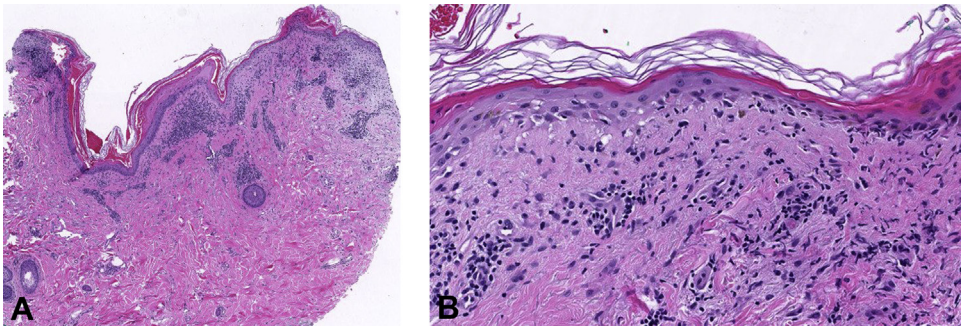


**Fig 2.** Histopathology. **A**, Vacuolar changes of basal keratinocytes, focal epidermal atrophy, dyskeratotic keratinocytes, and a moderately dense superficial and deep perivascular and periadnexal infiltrate, with an increase in interstitial mucin. **B**, Focal epidermal atrophy, basilar vacuolization, and dyskeratotic keratinocytes. (Original magnifications: **A**, ×100; **B**, ×400.)

made to discontinue abemaciclib, which resulted in the resolution of her symptoms, further supporting the diagnosis.

## DISCUSSION

Drug-induced SCLE was first documented as an adverse effect to hydrochlorothiazide in 1985; since then, over 10 drug classes have been implicated.[1] Most cases are seen in women, with an average age of 58 years.[2] Cutaneous findings are characterized by annular, polycyclic plaques or papulosquamous lesions in a photosensitive and often symmetric distribution appearing after drug exposure and resolving with discontinuation. Almost 50% of patients with SCLE meet the American College of Rheumatology criteria for SLE, but a subsequent study has revealed that only 10%-15% of patients develop severe clinical manifestations of SLE.[2] Systemic features classically seen in drug-induced SLE are also rare. Moreover, SCLE following medication exposure is not uncommon; more than one-third of SCLE cases were attributed to drug exposure in a population-based study.[3]

The presence of antinuclear antibody and anti-Ro/SS-A antibodies is highly suggestive of drug-induced SCLE and is seen in about 80% of cases.[2] Anti-La/SS-B$^{+}$ and anti-histone$^{+}$ antibodies are found in less than 50% and 33% of patients, respectively. Additionally, the classic histopathologic findings include an interface dermatitis with vacuolization of the basal cell layer associated with a perivascular dermal lymphocytic infiltrate and dermal mucin deposition.[4]

The cyclin-dependent kinases 4 and 6 (CDK4/6) are vital regulators of neoplastic growth as they are downstream of multiple signaling pathways leading to cellular proliferation. Abemaciclib and 2 other CDK4/6 inhibitors, ribociclib and palbociclib, have recently become, in combination with endocrine therapy, the standard of care based on prolonged progression-free survival in patients with estrogen receptor$^{+}$, human epidermal growth factor receptor 2-neu$^{-}$ metastatic breast cancer.[5] To date, 2 case

reports of SCLE induced by palbociclib have been published.[6,7] With the addition of this case report of abemaciclib induced SCLE, together, these findings suggest a possible class effect with CDK 4/6 inhibitors.

Targeted therapies like CDK4/6 inhibitors may help offer insight into the mechanisms of drug-induced SCLE. A study has shown that CDK6 inhibition leads to reduced tumor angiogenesis and proliferation.[8] The resultant increase in apoptosis and subsequent nucleosome release has been purported as a possible path toward increased autoimmunity.[6] However, it is important to note that given the large variety of pharmaceuticals implicated in drug-induced SCLE, the pathophysiology of drug-induced SCLE is not well understood. Further awareness and observation are important to evaluate whether such a pattern becomes evident in future research with CDK4/6 inhibitors, which may reveal novel information about the role of these kinases in dermatopathology.

**Conflicts of interest**

None disclosed.

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