

# A case of paraneoplastic subacute cutaneous lupus erythematosus in a patient with metastatic melanoma



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## INTRODUCTION

Subacute cutaneous lupus erythematosus (SCLE) is a subtype of cutaneous lupus erythematosus characterized by photodistributed, nonscarring papulosquamous or annular skin lesions.<sup>1</sup> SCLE is most commonly idiopathic or drug-induced, although there have been rare cases of paraneoplastic subacute cutaneous lupus erythematosus (pSCLE) reported in the literature. Here, we describe a case of pSCLE associated with metastatic melanoma and review the previous cases of pSCLE.

## CASE REPORT

A 71-year-old man with a history of superficial spreading melanoma on the abdomen status post wide local excision two and a half years prior to presentation was seen in the dermatology clinic with a 5-month history of a pruritic rash. On physical examination, he was found to have scattered pink and red papules and plaques in a photodistributed fashion on his bilateral upper extremities, back, and chest, with some involvement of the abdomen and lower extremities (Fig 1, A and B), in association with hypo- and depigmented patches in these locations along with tan and brown hyperpigmentation on his scalp (Fig 1, C). A complete skin examination did not identify any new skin lesions concerning for malignancy. He reported no new triggers for cutaneous reactions such as new medications or supplements, personal care products, or recent illnesses. He was taking no medications or supplements at the time. He had been applying topical triamcinolone cream to the affected areas without improvement.

### Abbreviations used:

pSCLE:	paraneoplastic subacute cutaneous lupus erythematosus
SCLE:	subacute cutaneous lupus erythematosus

Concurrent with the development of his rash, the patient also noticed a firm mass in his left axilla, which was found to be an enlarged lymph node on physical examination. He reported a 4.53-kg weight loss over the previous 6 months but denied other systemic symptoms.

Laboratory evaluation, including a complete blood cell count, liver function tests, basic metabolic panel, and urinalysis, was unremarkable. Serologic studies were positive for antinuclear antibody at a titer of 1:640 with a homogeneous and speckled pattern, anti-Ro (SS-A) antibody of 76 (normal value,  $\leq 20$ ), and anti-smooth muscle antibody at a titer of 1:160 and negative for anti-double-stranded DNA, anti-La (SS-B) antibody, anti-Sm, and antiribonucleoprotein. A punch biopsy performed on one of the plaques showed vacuolar interface dermatitis with superficial perivascular lymphocytic infiltrate and mucin deposition. On the basis of the patient’s clinical, pathologic, and laboratory findings, he was diagnosed with SCLE. Fine needle aspiration of the enlarged lymph node demonstrated malignant cells, and subsequent immunohistochemistry was consistent with a diagnosis of metastatic melanoma. A subsequent positron emission tomography/computed tomography demonstrated intense fluorodeoxyglucose avidity in the left axillary node,

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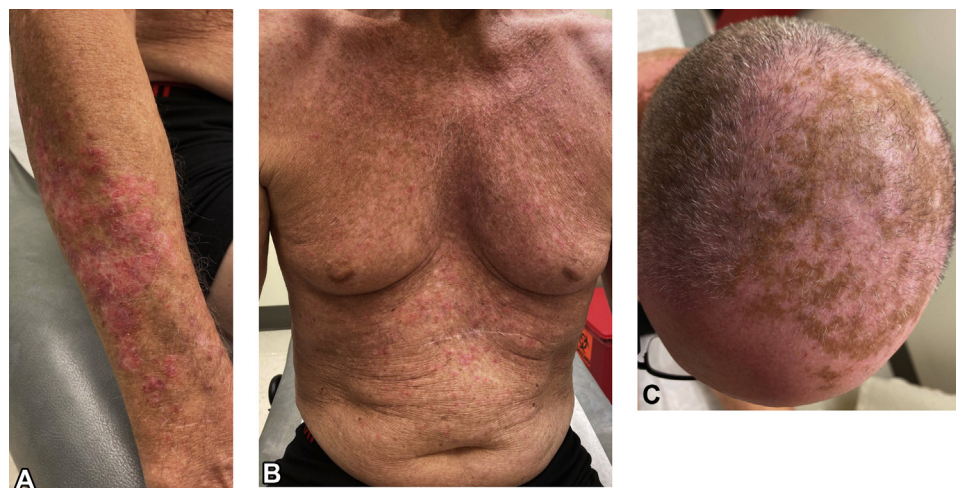
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**Fig 1.** A case of paraneoplastic subacute cutaneous lupus erythematosus in a 70-year-old man. Clinical images of pink and red papules and plaques on the (A) forearm and (B) chest, (B) confluent patches of hypo- and depigmentation on the chest, and (C) confluent patches of hyperpigmentation on the scalp.

consistent with the biopsy-proven metastatic melanoma, without other areas of abnormal uptake. The patient underwent left axillary dissection, in which 1 of the 19 lymph nodes removed was positive for melanoma via histopathology.

The patient was initially started on treatment with hydroxychloroquine for SCLE, which was discontinued 2 months after his lymphadenectomy due to significant improvement, with complete resolution of the rash by 5 months after surgery.

## DISCUSSION

This case highlights the occurrence of SCLE in association with metastatic melanoma. Diagnosis of SCLE is based on a combination of clinical, serologic, and histopathologic findings. In addition to the classic clinical findings (nonscarring, erythematous, papulosquamous/psoriasiform, or annular lesions in a photosensitive distribution), several serologic markers are helpful in diagnosis. In patients with SCLE, serologic findings are typically positive for anti-Ro (SS-A) antibody (70%-90%). Serologic findings are less frequently positive for antinuclear antibody (73%) and anti-La(SS-B) antibody (35%), whereas often negative for anti-double-stranded DNA, anti-Sm, and antiribonucleoprotein antibodies, found in only 10% of patients.<sup>1,2</sup>

The etiology for SCLE is classically drug-induced or idiopathic, with an estimated one-third of the cases likely attributable to drug exposures.<sup>3</sup> Thiazides, terbinafine, calcium channel blockers, angiotensin-converting enzyme inhibitors, tumor necrosis factor- $\alpha$  inhibitors, and proton pump inhibitors are common culprits.<sup>3</sup> SCLE as a

paraneoplastic phenomenon was first described in 1982, and subsequent case reports have found it to be associated with several types of malignancies (Table I). In 2020, the first case of melanoma-associated pSCLE was reported in a patient who experienced a recurrence of superficial spreading melanoma. Similar to our patient, the SCLE resolved with the removal of the patient’s melanoma.<sup>4</sup> A total of 33 pSCLE cases have been reported in the literature so far (Table I). Unlike SCLE, pSCLE does not demonstrate female predominance. The most common types of malignancies associated with pSCLE are lung (32.3%) and breast (20.5%). The wide range of malignancies associated with pSCLE suggests that the phenomenon can occur with most types of malignancies. Like SCLE, the pSCLE cases have a high frequency of anti-Ro (SS-A) antibodies (83.9%) and a low frequency of anti-La(SS-B) antibodies (36.8%) (Table I). Although classic SCLE frequently has positive direct immunofluorescence (with immunoglobulin deposits at the dermoepidermal junction),<sup>1</sup> this has been reported in a much lower percentage (34.8%) of pSCLE cases (Table I). In the majority of patients (59.4%), pSCLE was diagnosed before the initial diagnosis of malignancy or recurrence of disease, with an average of 5.8 months latency between rash onset and cancer diagnosis (Table I). In the remainder of patients, the onset of pSCLE typically coincided with the diagnosis of malignancy or recurrence, although in a few cases the onset of pSCLE occurred 1 to 3 years after the initial malignancy diagnosis.

Despite a growing body of pSCLE cases, the underlying pathophysiology is not understood.

**Table I.** Summary of the key features of reported cases of paraneoplastic subacute cutaneous lupus erythematosus

Clinical features and work-up	pSCLE	N*	SCLE	Reference
<b>Demographics</b>				
Median age, y	62	34	65	3
IQR <sup>†</sup> age, y	52-70	34	48-76	3
Mean age, y	60.9	34	51.5	2
Female	45.5%	33	75%, 77%	2,3
Male	54.5%	33	23%, 25%	2,3
Latency, <sup>‡</sup> mo	5.8	17 <sup>§</sup>	n/a	
pSCLE Dx first <sup>  </sup>	59.4%	32	n/a	
<b>Serology</b>				
Anti-Ro (SS-A)	83.9%	31	70%-90%	1
Anti-La(SS-B)	36.8%	19	30%-50%	1
ANA	76.9%	26	73%	2
<b>Histopathology</b>				
DIF	34.8%	23	69%, 86%	1,2
<b>General type of malignancy</b>				
Lung	32%	11		6,10,11,17,19
Breast	21%	7		12,13,18
Gastric	9%	3		16,20
Melanoma <sup>¶</sup>	6%	2		4
H/N SCC	6%	2		5
Esophageal	6%	2		15,19
Cholangiocarcinoma	6%	2		14
Uterine	3%	1		5
Prostate	3%	1		9
Lymphoma	3%	1		5
HCC	3%	1		7
Colon	3%	1		8

ANA, Antinuclear antibody; DIF, direct immunofluorescence; Dx, diagnosis; H/N, head and neck; HCC, hepatocellular carcinoma; IQR, interquartile range; n/a, not available; pSCLE, paraneoplastic subacute cutaneous lupus erythematosus; SCC, squamous cell carcinoma; SCLE, subacute cutaneous lupus erythematosus.

\*Number of total cases or tests where measurement had been reported.

<sup>†</sup>Interquartile range from 25th to 75th percentile.

<sup>‡</sup>Latency refers to time (in months) from the onset of paraneoplastic subacute cutaneous lupus erythematosus to the initial diagnosis of malignancy or diagnosis of recurrence.

<sup>§</sup>Paraneoplastic subacute cutaneous lupus erythematosus was first diagnosed in 19 of the 32 cases; however, latency duration was reported only in 17 of the 19 cases.

<sup>||</sup>Frequency of cases in which the onset of paraneoplastic subacute cutaneous lupus erythematosus occurs prior to the initial diagnosis of malignancy or diagnosis of recurrence.

<sup>¶</sup>Our new case has been included in the dataset.

Since most patients with SCLE have anti-Ro (SS-A) antibodies, it has been suggested that an autoreactive tumor antigen similar to the Ro (SS-A) antigen could be responsible for the paraneoplastic phenomenon.<sup>5</sup> Based on the literature, it does not seem that patients in whom pSCLE develops have or develop other autoimmune diseases. However, patients' medical histories are typically not reported in full in case

reports, and their family history, eg, of autoimmune diseases, is also generally not provided.

In summary, this case and the growing body of literature on pSCLE suggest that though very rare, malignancy can be a trigger for SCLE and thus one should have a high index of suspicion for malignancy in cases where the patient is elderly, is male, has a prior history of malignancy, does not have classic triggers or risk factors, or is refractory to the initial therapy. Appropriate diagnostic steps should be initiated in these cases to evaluate for an associated neoplastic disease.

#### Conflicts of interest

None disclosed.

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