Paraneoplastic Subacute Cutaneous Lupus Erythematosus with Mucositis

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PII: S2352-5126(22)00086-8
DOI: https://doi.org/10.1016/j.jdcr.2022.02.001
Reference: JDCR 2243

To appear in: JAAD Case Reports

Received Date: 22 September 2021
Revised Date: 30 January 2022
Accepted Date: 1 February 2022

Please cite this article as: Abbott J, Westerdahl JS, Wada D, Klein S, Mathis J, Paraneoplastic Subacute Cutaneous Lupus Erythematosus with Mucositis, JAAD Case Reports (2022), doi: https://doi.org/10.1016/j.jdcr.2022.02.001.

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KEYWORDS: Paraneoplastic, non-small cell lung carcinoma, subacute cutaneous lupus erythematosus, SCLE

WORD COUNT: 1066
FIGURE COUNT: 3
REFERENCE COUNT: 10

ACKNOWLEDGEMENTS: None

DISCLOSURES: The authors have no conflict of interest to declare. This material has not been presented prior to this submission.

FUNDING SOURCES: This article has no funding source.

CONSENT: Patient consent was received from the patient.
Introduction:

Subacute cutaneous lupus erythematosus (SCLE) is a clinical phenotype of cutaneous lupus erythematosus (CLE) first described by Sontheimer et al. in 1979. This entity demonstrates characteristic clinical and serological findings with patients commonly developing non-scarring annular to arcuate polycyclic papulosquamous plaques on sun-exposed skin in the setting of mild systemic manifestations and the presence of Ro/SSA autoantibodies. Classically, SCLE has been associated with drug-related triggers; however, SCLE has also presented as a paraneoplastic phenomenon related to internal malignancies. Here we report a case of paraneoplastic SCLE with extensive mucositis due to small cell lung carcinoma.
Case:

A 62-year-old cachectic female with a 40-year smoking history, hypertension, diabetes mellitus type 2, and gastroesophageal reflux disease presented to dermatology clinic with a 3-month history of painful oral erosions and ulcerations affecting her gingiva, tongue, and oral mucosa. The patient initially developed white stuck-on lesions that became progressively more painful over 1 to 2 months, leading to erosions. Since the onset of the erosions, she had increasingly limited her oral intake and at the time of the visit could only tolerate thick liquids. Additionally, the patient reported developing a pruritic rash involving her upper extremities, chest, and back following the same timeframe. She had tried both medium-potency topical steroids and various over-the-counter (OTC) products without relief. She recently had been fitted for new dentures; however, she was unable to use them due to severe mouth pain. Otherwise, she denied any new occupational or social exposures or medications in the past six months. Her review of systems was positive for increased fatigue, weight loss, and a chronic cough.

Examination revealed extensive mucosal erosions and superficial ulcerations involving the tongue, buccal mucosa, hard/soft palate, and posterior oropharynx. In addition, the gingival mucosa demonstrated hypertrophy with a mild cobblestone appearance. Skin exam was notable for scattered erythematous to pink arcuate papules and plaques with mild scale (Fig 1). No regional lymphadenopathy was appreciated on physical exam.

Extensive serologic and laboratory testing was performed, which revealed the following notable findings: sodium 125 mmol/L (reference range 136-144 mmol/L), ANA 1:320 (speckled pattern),
SSA 52 Ab IgG 44 AU/ml (reference range 0-40 AU/ml), SSA 60 Ab IgG 93 (0-40 AU/ml). The following results were notably negative or within normal limits: serum protein electrophoresis (SPEP) test, HIV, hepatitis C, herpes simplex virus (HSV), Smith autoantibodies, histone autoantibodies, double-stranded DNA antibodies, and lactate dehydrogenase (LDH) levels.

A skin biopsy on the upper back demonstrated a vacuolar interface dermatitis with perivascular lymphocytic infiltrate and increased dermal mucin, and an oral mucosal biopsy revealed a robust lichenoid interface dermatitis (Fig 2A & 2B respectively). Direct immunofluorescence (DIF) showed grains of IgG around the basal and suprabasal epidermal cells. Indirect immunofluorescence was negative on monkey esophagus and rodent (mouse and rat) bladder substrates.

Chest X-ray (CXR) followed by a high-resolution CT scan demonstrated a 4.9 cm left perihilar mass that significantly compressed upon the left upper lobe bronchus, pulmonary vein, and artery (Fig 3). An endobronchial ultrasound-guided core needle biopsy was consistent with small cell lung carcinoma (SCLC).

Prior to the diagnosis of SCLC, the patient had been placed on a 1mg/kg prednisone taper of 4 weeks with marked improvement, although her symptoms rebounded several weeks after the taper was completed. After her malignancy was established, prednisone (1mg/kg) was restarted and tapered over six weeks concurrent with chemotherapy and radiation.
The patient completed four cycles of carboplatin and etoposide and radiation therapy of 45 Gy in 30 Fractions. Following treatment, the patient reported no recurrence of cutaneous or oral disease.
Discussion:

SCLE is a photosensitive dermatosis that is part of the cutaneous lupus spectrum with a reported incidence around 0.6-0.7 per 100,000 per year. It is commonly ANA and Ro/SSA positive, with the latter being small ribonucleoproteins (RNP) in the nucleus that translocate to the surface of keratinocytes on UV exposure. Mucous membrane ulceration is an uncommon finding in SCLE, with one series recording 24% of their cohort. Yet when present, mucosal involvement is more commonly associated with ANA, anti-DNA, anti-smith, and anti-RNP antibodies. Classically SCLE has been associated with medications (DI-SCLE) and this should be considered in every case. The most common culprit medications include proton pump inhibitors, thiazide diuretics, and antifungals. It should be noted that skin lesions of DI-SCLE are inseparable from non-drug-related SCLE. In the present case, drug etiologies were heavily considered however the patient denied taking any prescription or OTC medications prior to her mucocutaneous eruption.

Paraneoplastic SCLE is exceedingly rare with less than 20 cases reported in the literature. Although it has been associated with various malignancies, oroesophageal and lung carcinoma are most commonly reported and appearance of paraneoplastic SCLE may represent a late-stage manifestation. The pathogenesis of paraneoplastic SCLE is unknown but likely related to the expression of tumor antigens homologous to Ro antigen, with subsequent production of autoantibodies. For SCLE to be considered paraneoplastic, it should meet Mclean's criteria, wherein the dermatosis should develop after the malignancy but may be present before the diagnosis, and both dermatosis and malignancy follow a parallel course. Although rare,
paraneoplastic SCLE is likely underappreciated and clinicians should have a high degree of suspicion for a paraneoplastic etiology when patients present with atypical SCLE, such as cachexia or difficulty swallowing. We recommend performing basic laboratory (including LDH) and imaging studies (CXR) in suspected cases.

The histological findings in SCLE include vacuolar interface dermatitis with perivascular and periappendegeal lymphocytic infiltrate with extracellular mucin deposition. Distinctive staining patterns can be appreciated on DIF, where inter-epidermal deposition of IgG is present in the majority of patients. Remarkably, in our patient, this finding was appreciated on both cutaneous and oral mucous, helping to unify her clinical presentation.

Treatment for SCLE revolves around either identifying and removing suspicious medications or the treatment of underlying malignancy, with concurrent use of topical, intralesional, or systemic steroids for acute management in severe cases. Antimalarial agents such as hydroxychloroquine can be employed to help with recalcitrant disease. Regression of paraneoplastic SCLE generally occurs with treatment of the underlying malignancy; however, few recalcitrant cases are reported.

SCLE is classically related to drug-induced etiologies, however a paraneoplastic association should be considered in the appropriate clinical scenario (i.e. culprit medications are absence). Therefore, management of paraneoplastic SCLE should be coordinated in a multidisciplinary
approach with oncology as regression is to be expected with the treatment of the underlying malignancy.
ABBREVIATIONS USED: antinuclear antibodies, ANA; cutaneous lupus erythematosus, CLE; direct immunofluorescence, DIF; drug-induced subacute cutaneous lupus erythematosus, DI-SCLE; herpes simplex virus, HSV; lactate dehydrogenase, LDH; over-the-counter (OTC); subacute cutaneous lupus erythematosus, SCLE; small ribonucleoproteins (RNP); Chest X-ray (CXR)
FIGURE LEGENDS:

Figure 1:
Numerous scattered erythematous to pink papules and plaques with mild scale were seen throughout the neck, upper torso, and bilateral upper extremities (A). The extensive erosions and superficial ulcerations were noted through the oral mucosal extending into the posterior oropharynx (B).

Figure 2:
Punch biopsy from the upper back demonstrating an atrophic epidermis with vacuolar interface dermatitis, mild perivascular lymphocytic infiltrate with rare eosinophils, and increased dermal mucin deposition (A, 200x). Biopsy of the mucosal epithelium revealed hyperkeratosis, hypergranulosis, and a moderately dense, lichenoid infiltrate that focally obscures the basal layer of the epidermis; producing dyskeratotic keratinocytes and a few colloid bodies. (B, 100x).

Figure 3:
Chest CT revealed a left perihilar mass measuring 4.9 x 3.7 cm with significant narrowing of the left upper lobe bronchus and pulmonary vein and narrowing of the lingual pulmonary artery. The mass is abutting the left main pulmonary artery and the left atrial appendage.
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