

SHORT COMMUNICATION

Subacute Cutaneous Lupus Erythematosus Associated with Ramucirumab Therapy

Elise Hogan, BS¹, Kelsey Nusbaum, BS¹, Anne Householder, MD¹

¹University of Cincinnati College of Medicine, Cincinnati, OH

Lupus erythematosus is an autoimmune inflammatory condition with a constellation of clinical findings including fever, malaise, myalgias, and loss of appetite/weight.¹ Subsets of this disease are numerous, with subacute cutaneous lupus erythematosus (SCLE) demonstrating cutaneous manifestations. While the etiology of SCLE is often multifactorial, drugs can induce SCLE in up to 30% of cases. Drug-induced SCLE was first documented in 1985 in association with hydrochlorothiazide, and has since been described in association with numerous medications.² Hydralazine, procainamide, isoniazid are the three highest risk medications for lupus erythematosus, while SCLE associated medications are primarily hydrochlorothiazide, calcium channel blockers, and ACE inhibitors.³ There has been increasing discussion surrounding chemotherapeutic agents inducing SCLE, with highest risk medications of docetaxel, paclitaxel, fluorouracil, capecitabine, tamoxifen citrate, and doxorubicin.³

Ramucirumab is a fully human monoclonal antibody that targets VEGFR2, indicated in patients with hepatocellular carcinoma with prior treatment of sorafenib. Common side effects include thrombocytopenia, hypoalbuminemia, hyponatremia, neutropenia, fatigue, edema, and

hypertension.⁴ There have been no known associations between ramucirumab and SCLE.

A 64-year-old male with a history of hepatitis C, hepatocellular carcinoma, and cirrhosis recently started on ramucirumab presented to clinic with a three-month history of worsening pruritic eruption. The patient received three cycles of ramucirumab. His medications included insulin glargine and lispro, levothyroxine, losartan, nadolol, prochlorperazine, and sildenafil, all stable prior to beginning ramucirumab. The patient had received nivolumab infusions with a resolved dermatitis and sorafenib earlier in disease progression that was discontinued for fatigue.

Physical exam revealed an annular erythematous eruption with scaling patches on bilateral upper extremities in a photosensitive distribution clearly demarcated by clothing lines (Figure 1), clinically suspicious for SCLE. The differential included systemic lupus erythematosus (SLE), dermatomyositis, nummular atopic dermatitis, and lichen planus. The skin biopsy revealed



Figure 1. Clinical photo of presenting rash

parakeratosis with loss of the granular layer, dyskeratosis, disorganized and crowded basal layer solar elastosis and a moderate perivascular lymphocytic infiltrate in the papillary and available superficial reticular dermis (Figure 2). The anti-nuclear antibody (ANA) panel was significant for Anti-SSA (Ro) antibodies greater than 8.0 AI (standard range 0-0.9AI).

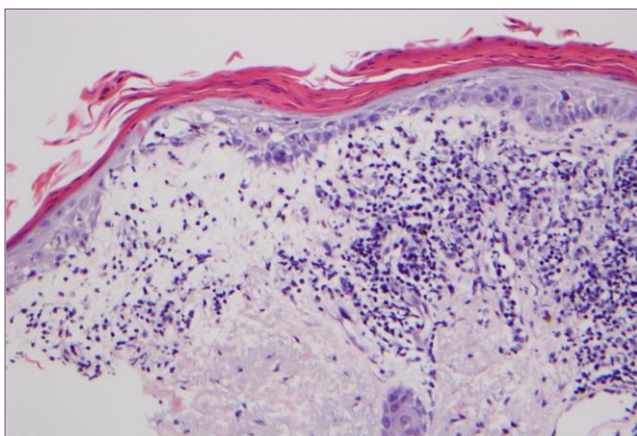


Figure 2. Histopathologic section of patient specimen, showing cytotoxic dermatitis. H&E stained at 20x magnification.

The biopsy findings are highly consistent with cytotoxic dermatitis. This, in combination with the presence of anti-SSA antibodies, supported clinical suspicions of SCLE. Anti-Ro antibodies are present in 80% of patients with proven SCLE.⁵ Conditions such as dermatomyositis and SLE are less likely due absence of systemic symptoms. The authors are not aware of other reports of SCLE due to ramucirumab monotherapy. There have been reports of

other VEGF biologic therapies that developed SCLE, such as bevacizumab and ranibizumab.⁶ However, these medications are humanized antibodies against VEGF-A. There were no other confounding medications on his list. Cases of nivolumab causing a SCLE eruption have been reported; however, was associated with concurrent use and not after discontinuation. There is the potential that previous nivolumab therapy could have contributed to this eruption; however, the only significant medication change in the past year was ramucirumab which likely caused the exanthem.

In conclusion, ramucirumab can be associated with subacute cutaneous lupus erythematosus.

Conflict of Interest Disclosures: None

Funding: None

Corresponding Author:

Elise Hogan, BS
231 Albert Sabin Way
Cincinnati, OH 45229
Email: hoganes@mail.uc.edu

References:

1. Cojocaru, M., Cojocaru, I. M., Silosi, I., & Vrabie, C. D. Manifestations of systemic lupus erythematosus. *Maedica*, (2011), 6(4), 330–336. [PMID: 22879850]
2. Reed BR, Huff JC, Jones SK, et al. Subacute cutaneous lupus erythematosus associated with hydrochlorothiazide therapy. *Ann Intern Med*. 1985 Jul;103(1):49-51. [PMID: 3873891].
3. Bolton C, Chen Y, Hawthorne R, et al. Systematic Review: Monoclonal Antibody-Induced Subacute Cutaneous Lupus Erythematosus. *Drugs R D*. 2020 Dec;20(4):319-330. [PMID: 32960413].
4. Zhu AX, Kang YK, Yen CJ, et al. REACH-2 study investigators. Ramucirumab after sorafenib in patients with advanced hepatocellular carcinoma and increased α -fetoprotein concentrations (REACH-2): a

- randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol.* 2019 Feb;20(2):282-296. [PMID: 30665869].
5. Cleaver N, Ramirez J, Gildenberg S. Cutaneous lupus erythematosus in a patient undergoing intravitreal bevacizumab injections: case report and review of the literature. *J Drugs Dermatol.* 2013 Sep;12(9):1052-5. [PMID: 24002156].
 6. Andric M, Dixit S, Robaei D, Watchorn R, Verma N. A case of subacute cutaneous lupus erythematosus as a result of ranibizumab (Lucentis) treatment. *Indian J Ophthalmol.* 2013 Dec;61(12):752-4. [PMID: 24212210].