

New-onset systemic lupus erythematosus in a patient receiving risankizumab for psoriasis



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Key words: drug-induced lupus; risankizumab; severe plaque psoriasis; systemic lupus erythematosus.

INTRODUCTION

Systemic lupus erythematosus (SLE) and psoriasis are both chronic immune-mediated diseases, with the former caused by T-helper 1- (Th1-), Th2-, Th17-, and B-cell activation and the latter caused primarily by Th17 activation.^{1,2} Coexistent psoriasis and lupus erythematosus have been reported but is rare. In one retrospective study, 0.69% of psoriasis patients had SLE, and 1.1% of patients with SLE had psoriasis.³ Drug-induced lupus (DIL) is a well described phenomenon and has been reported with a number of medications, classically procainamide and hydralazine in slow acetylators. The presentation could be purely cutaneous, systemic, or both, depending on the medication.⁴ The onset of symptoms can be weeks to months after drug exposure and classically has been associated with the presence of antihistone antibodies.⁵ Reports on tumor necrosis factor- α inhibitor-induced lupus have become of particular interest, given the widespread use of tumor necrosis factor- α inhibitors in chronic immune-mediated disease.⁶ Currently, no other class of biologics have been implicated in drug-induced SLE. Herein, we report a case of new-onset SLE with a pan-positive lupus antibody profile, including antihistone antibodies, developing approximately 15 months after starting risankizumab for the treatment of psoriasis.

CASE REPORT

A 25-year-old woman presented to our clinic for evaluation of a widespread rash that was clinically consistent with psoriasis. Her psoriasis began after the delivery of her first child and involved the scalp, face, arms, legs, and trunk. She had no family history of psoriasis, lupus, or rheumatoid arthritis. Her psoriasis epidemiology screening tool test was

Abbreviations used:

DIL: drug-induced lupus
SLE: systemic lupus erythematosus

negative for psoriatic arthritis. Her estimated body surface area was 6%, with an investigator's global assessment score of 3. She was initially treated with clobetasol 0.05% solution, clobetasol 0.05% cream, ketoconazole 2% shampoo, and oral methotrexate 15 mg/week. After 6 months of combined treatment, the patient was not satisfied with her skin clearance and was subsequently switched to risankizumab 150 mg. At her 3-month follow up, the patient's skin was completely clear.

At the followup 16 months after starting risankizumab, the patient reported a 1-month history of increasing pain and swelling of her hands and knees associated with prolonged morning stiffness and fatigue. She did not have any appreciable rash, and on physical examination, she did not exhibit any signs of enthesitis or dactylitis. She was initially treated with indomethacin 50 mg thrice daily, which did not improve her symptoms, and she ultimately required a prednisone taper, which led to temporary relief. The patient was subsequently referred to rheumatology for further evaluation. Plain films of her hands and knees were unremarkable. Her laboratory test results were remarkable for high-titer antinuclear antibodies, as well as for the presence of anti-double stranded DNA antibodies, antichromatin, anti-Smith, antinuclear ribonucleoprotein, anti-SSA, and antihistone antibodies. She also tested positive for cyclic citrullinated peptide and rheumatoid factor. She had an elevated

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Table I. Initial laboratory results from the time of diagnosis of systemic lupus erythematosus

Laboratory test	Present case	Reference value/range
ANA	> 1:640	≤ 1:40
ESR	89 mm/h	Women: 0-20 mm/h Men: 0-15 mm/h
CRP	2.66 mg/dL	≤ 0.8 mg/dL
CCP	28 units	<20 units
Anti-dsDNA	238 IU/mL (high—salt- positive)	0-7 IU/mL
Antichromatin antibody	Positive	Negative
Anti-Smith antibody	Positive	Negative
Anti-RNP	Positive	Negative
Anti-Ro/SSA + SSB antibody	Positive	Negative
Antihistone antibody	Positive	Negative
Antiphospholipid antibody	Negative	Negative
Rheumatoid factor	Positive	Negative
C3	48 mg/dL	100-233 mg/dL
C4	5 mg/dL	14-48 mg/dL
Vitamin D	13.4 ng/mL	30-60 ng/mL
HCV	Negative	Negative
Platelets	542,000/ μ L	150,000-450,000/ μ L
Creatinine	0.52 mg/dL	Women: 0.50-1.10 mg/dL Men: 0.70-1.30 mg/dL

ANA, Antinuclear antibody; *anti-dsDNA*, anti-double-stranded DNA antibody; *Anti-RNP*, antinuclear ribonucleoprotein; *CCP*, anticyclic citrullinated peptide; *CRP*, C-reactive protein; *ESR*, erythrocyte sedimentation rate; *HCV*, hepatitis C virus.

sedimentation rate and a low complement level. Laboratory results are summarized in Table I. Based on her immunologic profile and clinical examination, the patient met the European League Against Rheumatism and the American College of Rheumatology SLE classification criteria.⁷

Given the patient's pan-positive lupus serology profile, including antihistone antibodies, drug-induced SLE was considered although pan-positive titers usually follow idiopathic SLE.⁵ Additionally, lower levels of complement, as seen in Table I, can be further indicative of an idiopathic cause of SLE. Notably, she had negative antiphospholipid antibodies, which ruled out antiphospholipid syndrome. After consultation with rheumatology, it was decided to discontinue risankizumab, initiate treatment with hydroxychloroquine 200 mg twice daily, and transition to ustekinumab 45 mg. Ten months after her diagnosis of SLE, the patient has maintained a Psoriasis Area and Severity Index score of 100 with good joint control and normalization of her complement levels while on ustekinumab 45 mg subcutaneously every 12 weeks and hydroxychloroquine 300 mg once daily.

DISCUSSION

While SLE is most likely due to a complex interplay between genetics and environmental

factors, one should always consider the possibility of a drug-induced phenomenon. DIL represents 6% to 12% of all lupus cases, with an annual incidence of 15,000 to 30,000 new cases per year in the United States. The distinction between DIL and SLE comes from the chronological relation of symptoms to new medication start as well as resolution with removal of the offending agent. Additionally, antibody tests can be used to help differentiate idiopathic SLE from DIL, as certain patterns have been established; however, these are not entirely exclusive. Antihistone antibody positivity has the highest correspondence to drug-induced systemic lupus, yet is not unique to DIL and can be found in cases of idiopathic SLE as well.⁵

In our patient, the onset of symptoms after starting risankizumab and her pan-positive lupus antibody profile raised the question of DIL. However, since the patient had concurrently began treatment with hydroxychloroquine, while discontinuing risankizumab and subsequently starting ustekinumab, the true timeline of the resolution of her symptoms may be difficult to establish. Furthermore, it is certainly conceivable that her SLE coincidentally developed after starting risankizumab. Interestingly, as ustekinumab is currently in clinical trials for use in patients with SLE, this case may add ancillary data to the possible effectiveness and safety in this population.^{8,9} As our case is just a single report of this potential association,

time will tell whether DIL is a true signal for risankizumab or just a mere coincidence.

Conflicts of interest

Barber has no conflicts of interest to report. Dr Song, has been a consultant, speaker or investigator for the following companies: AbbVie, Janssen, Amgen, Lilly, SUN, UCB, Incyte, Novartis, Sanofi & Regeneron, Castle Biosciences, Pfizer.

REFERENCES

1. Wong CK, Lit LC, Tam LS, Li EK, Wong PT, Lam CW. Hyperproduction of IL-23 and IL-17 in patients with systemic lupus erythematosus: implications for Th17-mediated inflammation in auto-immunity. *Clin Immunol*. 2008;127(3):385-393. <https://doi.org/10.1016/j.clim.2008.01.019>
2. Lowes MA, Suárez-Fariñas M, Krueger JG. Immunology of psoriasis. *Annu Rev Immunol*. 2014;32:227-255. <https://doi.org/10.1146/annurev-immunol-032713-120225>
3. Zalla MJ, Muller SA. The coexistence of psoriasis with lupus erythematosus and other photosensitive disorders. *Acta Derm Venereol Suppl (Stockh)*. 1996;195:1-15.
4. Ho CH, Chauhan K. Lupus Erythematosus. *Drug-Induced*. StatPearls Publishing; 2018.
5. Solhjoo M, Goyal A, Chauhan K. Drug-induced lupus erythematosus. In: StatPearls [Internet]. StatPearls Publishing; 2022.
6. Almoallim H, Al-Ghamdi Y, Almaghrabi H, Alyasi O. Anti-tumor necrosis factor- α induced systemic lupus erythematosus. *Open Rheumatol J*. 2012;6:315-319. <https://doi.org/10.2174/1874312901206010315>
7. Aringer M, Costenbader K, Daikh D, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. *Arthritis Rheumatol*. 2019;71(9):1400-1412. <https://doi.org/10.1002/art.40930>
8. ClinicalTrials.gov. A study of ustekinumab in participants with active systemic lupus erythematosus. Accessed February 17, 2022. <https://clinicaltrials.gov/ct2/show/NCT03517722>
9. van Vollenhoven RF, Hahn BH, Tsokos GC, et al. Maintenance of efficacy and safety of ustekinumab through one year in a phase II multicenter, prospective, randomized, double-blind, placebo-controlled crossover trial of patients with active systemic lupus erythematosus. *Arthritis Rheumatol*. 2020;72(5):761-768. <https://doi.org/10.1002/art.41179>