Title

Neutrophilic dermatoses as a manifestation of a systemic lupus erythematosus flare.

Authors

Wang, Yingxue

Chen, Eugenia

Iyer, Priyanka

Publication Date

2024-01-18

DOI

10.1177/09612033231226350

Case Report

Neutrophilic dermatoses as a manifestation of a systemic lupus erythematosus flare

Lupus
2024, Vol. 0(0) 1–5

DOI: 10.1177/09612033231226350
journals.sagepub.com/home/lup
Sage

Yingxue Wang[1], Eugenia Chen[2] and Priyanka Iyer[2]

Abstract

Neutrophilic dermatoses (NDs) refer to a group of cutaneous conditions histologically characterized by the dense accumulation of neutrophils in the skin in the absence of infection. NDs have been associated with underlying autoimmune connective tissue disorders (CTDs) such as systemic lupus erythematosus (SLE), Sjogren's syndrome, and dermatomyositis. We describe a case of neutrophilic dermatoses as a manifestation of a SLE flare.

Keywords

Systemic lupus erythematosus, pregnancy, cutaneous lupus

Date received: 19 September 2023; accepted: 28 December 2023

Introduction

Neutrophilic dermatoses (NDs) refer to a group of cutaneous conditions histologically characterized by the dense accumulation of neutrophils in the skin in the absence of infection. Several types of NDs have been described, with Sweet syndrome (acute febrile neutrophilic dermatosis) being the classic example. NDs have been associated with a number of different systemic conditions such as inflammatory bowel disease, hematologic malignancies, and autoimmune CTDs.[1] Our case focuses on the association of NDs with autoimmune disorders, namely, SLE.

SLE is a chronic autoimmune CTD that presents with a variable constellation of symptoms outlined by the American College of Rheumatology (ACR). Cutaneous manifestations defined as SLE classification criteria include alopecia, oral ulcers, acute cutaneous lupus, and subacute cutaneous or discoid lupus.[2] As SLE is a disorder of the adaptive immune system, histologic examination of skin lesions typically reveals lymphohistiocytic infiltrate. Neutrophilic infiltrates in the context of SLE tend to be associated with bullous LE or vasculitic disease.[3,4] This case report describes a pregnant patient with a nonbullous, nonvasculitic neutrophilic dermatosis as a cutaneous presenting symptom of new-onset SLE. The patient underwent skin biopsies, received systemic steroids, and ultimately chose to terminate her pregnancy. This case discusses the course of her diagnosis and highlights the importance of considering SLE as a differential when faced with atypical presentations.

Case presentation

A 33-year-old female, 12 weeks pregnant via in vitro fertilization (IVF), with a history of rheumatoid arthritis (RA) on hydroxychloroquine (HCQ) presented with 1 month of diffuse generalized body pain, joint stiffness, bilateral leg swelling, and a rash involving her face, nose, palms, and bilateral legs. She noted the onset of a lacy reticular rash 5 days after her RA medication regimen was changed by her rheumatologist from HCQ to sulfasalazine. Despite self-discontinuing the sulfasalazine, she noted no improvement in her complaints. The leg pain and swelling was severe enough to limit her ability to ambulate and she needed to use crutches. The pain also spread to the lower back, neck, and bilateral upper extremities with diffuse joint stiffness. She developed additional distinct rashes which appeared as erythematous papules on her hands and papular lesions on her face, nose, and neck. On the physical exam, she was tachycardic and noted to have pitting bilateral leg edema. The skin exam revealed a lacy reticular rash on her bilateral legs, crusted lesions on her face and nose, a papule present

[1]Department of Internal Medicine, UCI Medical Center, Orange, CA, USA
[2]Division of Rheumatology, UCI Medical Center, Orange, CA, USA

Corresponding author:
Yingxue Wang, Department of Internal Medicine, UCI Medical Center, 101 The City Drive S, Orange, CA 92868, USA.
Email: yingxw5@hs.uci.edu

over her right neck, and an erythematous papular rash on her palms and fingertips (Figures 1–4).

Relevant laboratory results showed positive ANA, positive ds-DNA (1:2560), positive ANCA (MPO/PR3 negative), positive rheumatoid factor but negative anti-CCP, positive anti-SSA/La, proteinuria 1.1 g (24-hour urine), negative lupus anticoagulant, negative anti-cardiolipin antibodies, and negative beta-2 glycoprotein antibodies. Dermatology was consulted and the patient underwent skin biopsies of her right neck, right hand, and right knee. Pathology of the right neck lesion revealed neutrophilic vascular reaction, right hand with leukocytoclastic vasculitis, and right knee with direct immunofluorescence positive for lupus band test. The density of neutrophils in the right neck biopsy was not as high as routinely seen in Sweet syndrome. The constellation of findings ultimately was consistent with a diagnosis of new-onset SLE with diffuse body pain and joint stiffness, bilateral leg edema, and neutrophilic dermatoses as the presenting symptoms. The patient was started on systemic high dose steroids with improvement of her rash and stiffness. The patient ultimately opted to terminate her pregnancy with an inpatient dilation and curettage and obtain an outpatient renal biopsy. She was concerned that her pregnancy could be contributing to the proteinuria.

The patient was discharged with a prednisone taper. She followed up with rheumatology outpatient 1 month later, and there was resolution of her bilateral leg edema, face and hand rash, and joint pain. She was then started on mycophenolate mofetil and advised to complete her prednisone taper. Repeat urine test showed 0.22 g proteinuria, and it was decided to hold off on the outpatient renal biopsy and monitor with serial urine protein measurements.

Discussion

SLE is a chronic autoimmune CTD with many presenting symptoms ranging from cutaneous features to multiorgan involvement. Laboratory results typically show hypocomplementemia, positive ANA, and positive ds-DNA or anti-Smith antibodies. Histology of cutaneous LE usually reveals lymphohistiocytic infiltrate as SLE is a disorder of the adaptive immune system. The presence of neutrophilic infiltrates in SLE, while uncommon, is well-described in literature.[4,5] Several terms are used to delineate different SLE-associated NDs, such as neutrophilic urticarial

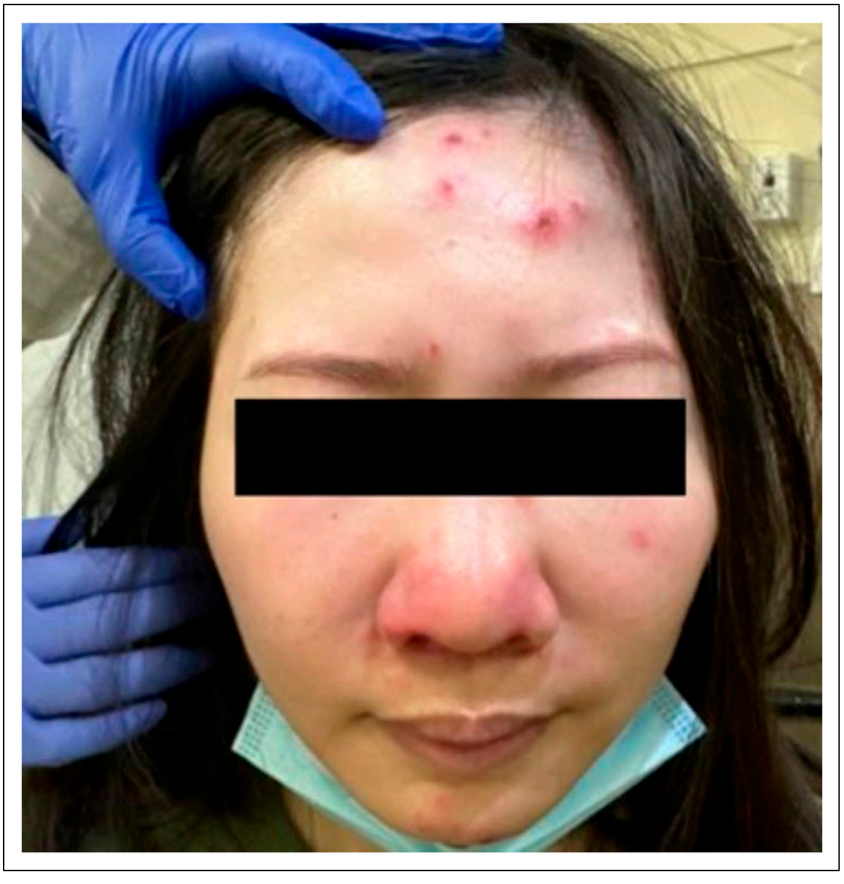

Figure 1. Papular lesions on the face and nose.

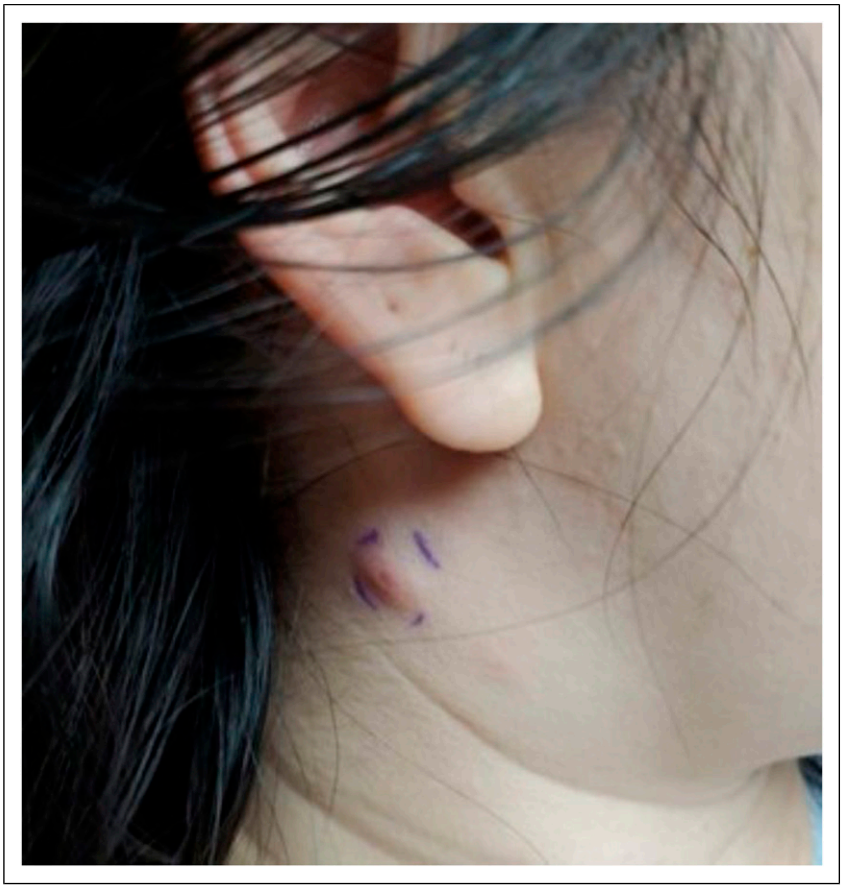

Figure 2. Papular lesion on the neck.

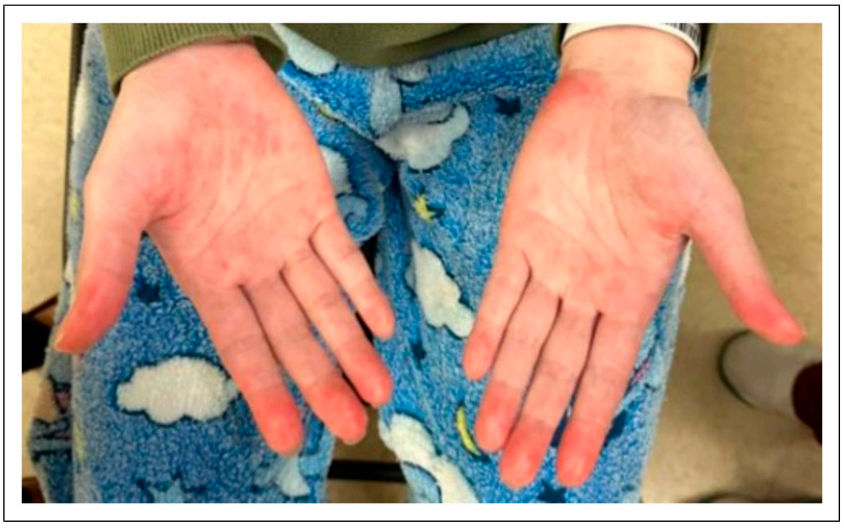

Figure 3. Erythematous papular rash on bilateral palms.

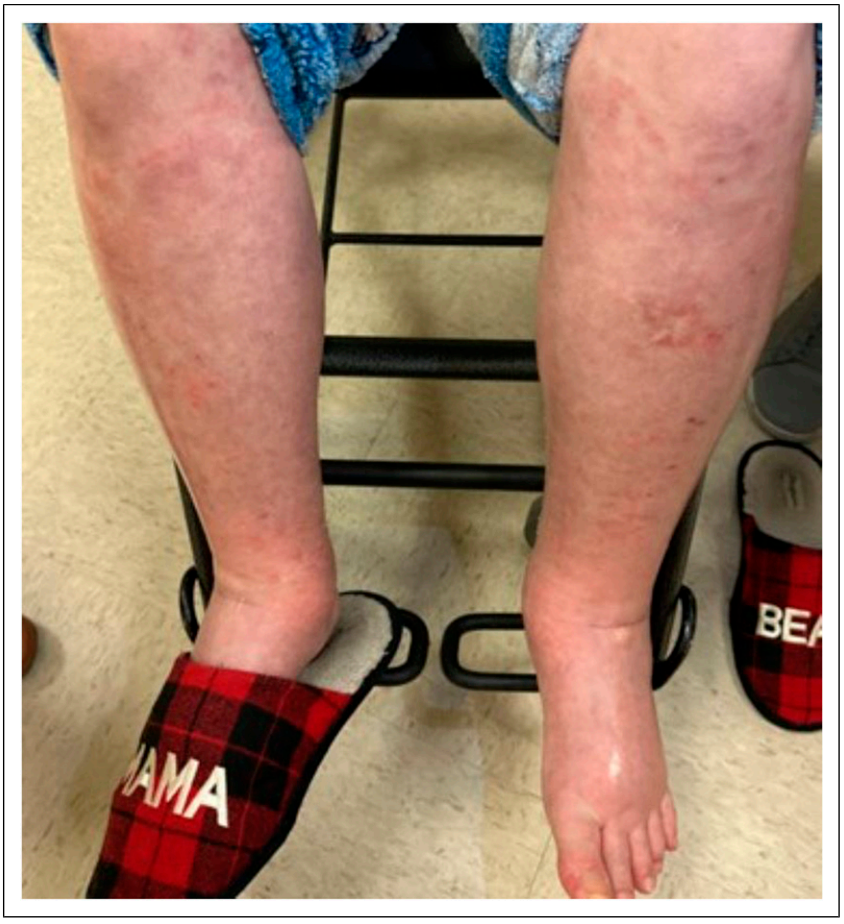

Figure 4. Reticular rash and edema on bilateral legs.

dermatosis (NUD), Sweet-like neutrophilic dermatosis (SLND), palisaded neutrophilic granulomatous dermatitis, and amicrobial pustulosis of the folds just to name a few.[6]

SLE-associated NDs tend to be seen with bullous or vasculitic disease.[3,4] However, there are case reports of nonbullous, non-vasculitic SLE-associated NDs, such as our patient's presentation as her right neck lesion manifested as a papule and had no evidence of vasculitis. Our hypothesis is that the patient likely had underlying SLE that was historically misdiagnosed as rheumatoid arthritis. Her initial presentation was joint pain without other typical manifestations of SLE per chart review. Her prior laboratory results had revealed a positive rheumatoid factor (which can appear in SLE) which led to the diagnosis of seropositive RA. Her disease was likely well controlled on HCQ but likely flared when she was switched to sulfasalazine during pregnancy. Additionally, the increase in sex hormones during pregnancy is associated with upregulation of Th2 cytokines and reduced expression of Th1 cytokines in order to support fetal tolerance in the mother.[7] This change in the Th1-Th2 cytokine profile may explain why Th2-mediated diseases such as SLE tend to flare during pregnancy. Conversely, Th1-mediated processes such as RA are likely to be quiescent during pregnancy. Female individuals who have been diagnosed with SLE are advised to have stable disease for 6 months before conceiving. HCQ is safe in pregnancy and should be continued.

Interestingly, our patient had conceived through IVF. Hormones such as estrogen and progesterone have been hypothesized to play a role in SLE given the increased prevalence of the disease in females.[8] Case reports have described previously healthy women with no physical symptoms of CTDs who developed SLE after undergoing IVF, but it is unclear if the patients may have had underlying "silent" disease, as there was no pre-IVF autoimmune laboratory data.[9] In patients with existing SLE who underwent IVF, the rate of complications such as SLE flares and venous thromboembolisms was 8%; these complications were seen in patients with poor adherence to treatment likely from lack of careful monitoring.[10] Our recommendation is that patients with SLE who wish to undergo IVF are advised to have stable disease for 6 months as mentioned prior and should be monitored closely by a multidisciplinary

team of clinicians including high risk obstetricians and rheumatologists.

In summary, the finding of NDs should prompt clinicians to evaluate the patient for an underlying systemic process. NDs may be the initial cutaneous presentation of SLE in one-third of patients.[3] We hope that as more cases are revealed and studied, this entity of neutrophilic skin lesions in the setting of SLE will become better defined so that clinicians can recognize this finding and direct patient care more effectively.

Declaration of conflicting interests

The authors declared no potential conflict of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical statement

Informed Consent

Written informed consent for patient information to be published was obtained from the patient.

ORCID iD

Yingxue Wang https://orcid.org/0009-0007-0342-5951

References

1. Weiss EH, Ko CJ, Leung TH, et al. Neutrophilic Dermatoses: a clinical update. *Curr Dermatol Rep* 2022; 11: 89–102.
2. Aringer M, Costenbader K, Daikh D, et al. 2019 European league against rheumatism/American college of rheumatology classification criteria for systemic lupus erythematosus. *Arthritis Rheum* 2019; 71: 1400–1412.
3. Quatrano NA, Criscito MC, Femia AN, et al.. Systemic lupus erythematosus–associated neutrophilic dermatosis with Palmoplantar involvement. *JAAD Case Rep* 2016; 2: 329–333.
4. Lee WJ, Kang HJ, Shin HJ, et al. Neutrophilic urticarial dermatosis and sweet-like neutrophilic dermatosis: underrecognized neutrophilic dermatoses in lupus erythematosus. *Lupus* 2018; 27: 628–636.
5. Larson AR and Granter SR. Systemic lupus erythematosus–associated neutrophilic dermatosis—an underrecognized neutrophilic dermatosis in patients with systemic lupus erythematosus. *Hum Pathol* 2014; 45: 598–605.
6. Hau E, Vignon-Pennamen MD, Battistella M, et al. Neutrophilic skin lesions in autoimmune connective tissue diseases: nine cases and a literature review. *Medicine (Baltim)* 2014; 93: e346–e346.
7. Zen M, Ghirardello A, Iaccarino L, et al. Hormones, immune response, and pregnancy in healthy women and SLE patients. *Swiss Med Wkly* 2010; 140: 187–201.
8. Bellver J and Pellicer A. Ovarian stimulation for ovulation induction and in vitro fertilization in patients with systemic lupus erythematosus and antiphospholipid syndrome. *Fertil Steril* 2009; 92: 1803–1810.
9. Ben-Chetrit A and Ben-Chetrit E. Systemic lupus erythematosus induced by ovulation induction treatment. *Arthritis Rheum* 1994; 37: 1614–1617.
10. Orquevaux P, Masseau A, Le Guern V, et al. In vitro fertilization in 37 women with systemic lupus erythematosus or antiphospholipid syndrome: a series of 97 procedures. *J Rheumatol* 2017; 44: 613–618.