Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

New diagnosis of systemic lupus erythematosus after COVID-19 vaccination: A case report and review of literature

Urmi Khanna, MD,[a] Yasmine Oprea, BA,[b] Adnan Mir, MD, PhD,[c] and Caroline Halverstam, MD[a]

Key words: connective tissue diseases; COVID-19; inflammatory skin diseases; mRNA vaccines; systemic lupus erythematosus.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) mRNA vaccines are highly effective against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and provide immunity by stimulating host cells to produce viral spike proteins which eventually lead to protective antibody formation.[1] The immediate adverse effects following the administration of these vaccines include myalgia, headache, fatigue, chills, and fever. The commonly reported cutaneous side effects include injection site reactions, morbilliform rashes, and urticaria or hypersensitivity reactions.[2] There is no definite data proving causality between administration of mRNA vaccines and immune-mediated inflammatory diseases (IMID).[1] However, this association between autoimmunity and mRNA vaccines is an area of ongoing research and is thought to occur due to similarities between SARS-CoV-2 spike protein and human proteins.[1,2] Herein, we describe a case of new-onset systemic lupus erythematosus (SLE) following the administration of a COVID-19 vaccine.

Abbreviations used:

COVID-19:	Coronavirus disease 2019
SARS-CoV-2:	severe acute respiratory syndrome coronavirus 2
IMID:	immune-mediated inflammatory diseases
SLE:	systemic lupus erythematosus
CRP:	C-reactive protein
SLICC:	Systemic Lupus International Collaborating Clinics

CASE REPORT

An 18-year-old female with a history of autism presented with a rash of 1-month duration. A week before the onset of the rash, the patient had received the first dose of the Pfizer-BioNTech (BNT162b2) mRNA vaccine. The patient initially developed facial swelling accompanied by red, painful, persistent bumps involving the face and extremities. There was no history of photosensitivity, oral ulcers, Raynaud's phenomenon, previous COVID-19 infection, and no known family history of autoimmune conditions. The patient denied taking any medications or herbal supplements. Examination showed ill-defined, erythematous, tender plaques and nodules on the face, arms (Fig 1, *A* and *B*), frontal scalp, legs, and chest. The patient also developed scarring alopecia with scalp lesions clinically consistent with discoid lupus erythematosus (Fig 1, *C*). Laboratory workup revealed leukopenia (white blood cell, 2520/μL), elevated C-reactive protein of 5.1 mg/L, positive anti-nuclear (1:2560) antibodies, positive anti-ribonuclear protein antibodies, positive anti-Smith antibodies, low complement levels (C3 of 62.3 mg/dL; C4 of 11.8 mg/dL), an elevated urine

From the Division of Dermatology, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, New York[a]; Albert Einstein College of Medicine, Bronx, New York[b]; and Dermpath Diagnostics, New York, New York.[c]

Funding sources: None.

IRB approval status: Not applicable.

Statement on prior presentation: This work has not previously been presented or published.

Consent statement: Consent for the publication of all patient photographs and medical information was provided by the authors at the time of article submission to the journal stating that all patients gave consent for their photographs and medical information to be published in print and online and with the understanding that this information may be publicly available.

Correspondence to: Caroline Halverstam, MD, Division of Dermatology, Albert Einstein College of Medicine, 3411 Wayne Ave, 2nd Floor, Bronx, NY 10467. E-mail: chalvers@montefiore.org.

JAAD Case Reports 2022;30:30-4.

2352-5126

https://doi.org/10.1016/j.jdcr.2022.09.026

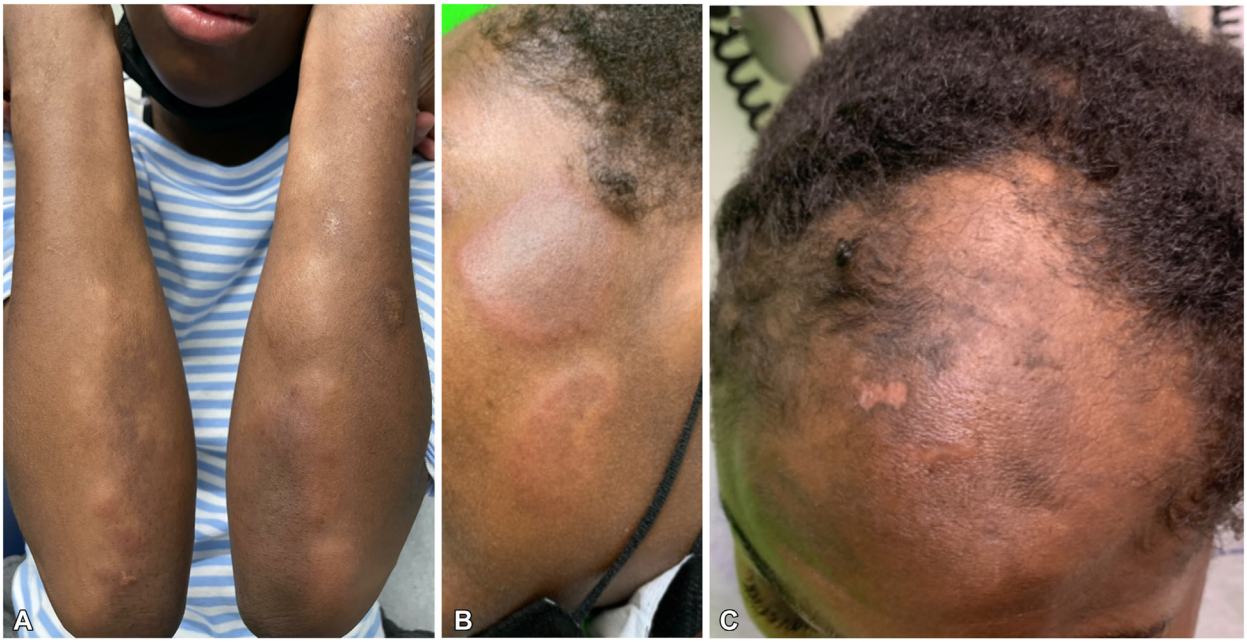

Fig 1. A, Erythematous, tender, indurated plaques on extensor surfaces of bilateral upper extremities and; (**B**) face. **C,** Scalp lesions.

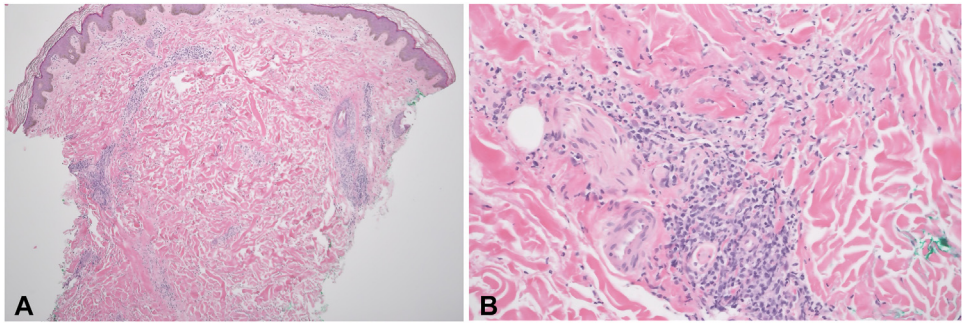

Fig 2. A, Skin biopsy demonstrated a superficial and deep, perivascular and periadnexal inflammatory infiltrates with minimal epidermal change (40×, hematoxylin and eosin [H&E]). **B,** The inflammatory infiltrate consists of lymphocytes with occasional neutrophils and neutrophilic debris (200×, H&E).

protein level (54.2 mg/dL), and an elevated urine protein to creatinine ratio (237 mg/gm). A biopsy from a plaque on the thigh revealed a superficial and deep perivascular and periadnexal infiltrate comprised of lymphocytes, with occasional neutrophils and neutrophilic debris (Fig 2, *A* and *B*). These features were consistent with a neutrophilic urticarial dermatosis, which can often be associated with SLE, and thus, pointed to a diagnosis of SLE given the dermatologic and laboratory findings. The scalp lesions were unable to be biopsied due to patient refusal. The patient fulfilled the Systemic Lupus International Collaborating Clinics criteria, and a diagnosis of SLE was established. She was initially treated with a prolonged taper of systemic steroids, beginning at 50 mg oral prednisone. However, once tapered down to 10 mg of prednisone, the patient experienced a flare of new erythematous plaques occurring on the face and elbows. This prompted addition of oral hydroxychloroquine and increasing the prednisone with a slower taper. At 3 months follow-up, the patient's rash resolved with brown macules and atrophic plaques.

DISCUSSION

Studies have reported that COVID-19 infection may be associated with subsequent flares of autoimmune conditions, including systemic lupus erythematosis.[3] In addition to infection by the SARS-CoV-2 virus itself, it has been reported that COVID-19 vaccination may also be associated with flares of existing autoimmune diseases.[4] Furthermore, there

Table I. Reported cases of systemic lupus erythematosus after COVID-19 vaccination

Authors	Age of patient	Sex of patient	PMH of patient	Vaccine received	Timeline of symptom onset	Symptoms and clinical findings	Affected organs	Laboratory findings	Treatment	Outcome
Lemoine et al[1]	68	Female	No history of autoimmune conditions	Pfizer (BNT162b2)	2 d after first dose	Bilateral proximal upper and lower extremity muscle weakness, stiffness, pain	Joints, skin	• ANA positive 1:640 • Anti-dsDNA positive 221 IU/mL • ESR 68 mm/h • CRP 149.3	Methotrexate 20 mg weekly, prednisone 5 mg daily	Improvement of symptoms
Molina Rios et al[2]	42	Female	None	Pfizer (BNT162b2)	2 wk after first dose	Inflammatory polyarthralgia of the hands and feet, bilateral synovitis of joints of the upper extremities, bilateral Achilles tendon enthesopathy, coagulopathy (anti phospholipid syndrome)	Joints	• ANA positive 1:1280 • Anti-dsDNA positive 1:160 • CRP 91 mg/dL • ESR mm/h	Sulfasalazine 500 mg twice daily	Treated and discharged
Mousa et al[5]	22	Female	None	Pfizer (BNT162b2)	1 wk after first dose	Erythematous non-blanching maculopapular rash on extremities and ears, epigastric pain associated with nausea and vomiting	Skin, GI	• ANA positive 1:1200 • Anti-dsDNA positive 1:160 • ESR 65 mm/h	Methylprednisone 500 mg 3 d Oral prednisone starting at 40 mg and tapered over 4 wk 200 mg hydroxychloroquine daily 50 mg azathioprine daily	Symptoms (rash and abdominal pain/ nausea) were resolved in 3 d
Patil and Patil [6]	22	Female	Infective jaundice	AstraZeneca (AZD 1222; ChAdOx1-s)	2 wk after the first dose	Pain in right knee, bilateral cervical lymphadenopathy, mild hepatomegaly, pedal edema, petechiae, rash	Joints, skin	• ANA positive 1:320 • Anti-dsDNA positive • ESR 92 mm/h • CRP 2.8 mg/L	Prednisolone 50 mg daily Hydroxychloroquine 400 mg daily Mycophenolate mofetil 2 g daily Furosemide 20 mg daily Telmisartan 20 mg daily	Improvement in symptoms after 1 mo
Nune et al[7]	24	Male	None	Pfizer (BNT162b2)	2 wk after the second dose	Polyarthralgia, joint stiffness, fever, fatigue, synovitis in metacarpophalangeal joints	Joints	• ANA positive 1:2560 • Anti-dsDNA positive 379 IU/mL • CRP 54 mg/L	Prednisone 60 mg daily Methotrexate 15 mg weekly	Improvement of symptoms after 2 mo
Zavala-Miranda et al[8]	23	Female	None	AstraZeneca (AZD 1222; ChAdOx1-s)	1 wk after first dose	Anasarca, hair loss, pitting edema of lower extremities	Kidneys	• ANA positive 1:1280 • Anti-dsDNA positive 17.1 IU/mL • Kidney biopsy showed secondary membranous nephropathy with diffuse thickening of the basement glomerular membrane and mild mesangial expansion	High dose glucocorticoids Hydroxychloroquine Diuretics Mycophenolate mofetil	Improved symptoms after 3 wk

Kaur et al[9]	54	Male	Sjogren syndrome	Pfizer (BNT162b2)	2 wk after the second dose	Fatigue, weight loss, shortness of breath, burning and pain on bilateral feet, non-pruritic erythematous maculopapular palpable purpuric lesions on the dorsal and plantar surface of bilateral feet	Skin, systemic	• ANA positive 1:1280 • Anti-dsDNA positive >300 IU/mL • ESR 59 mmHg	Prednisone 60 mg daily Mycophenolate mofetil 1 g daily	Symptoms improved after initiation of treatment
Baez-Negron et al[10]	27	Female	Type 1 diabetes mellitus	Moderna (mRNA-1273 vaccine)	2 wk after the second dose	Symmetric polyarthralgia of the proximal interphalangeal joints, metacarpophalangeal joints, wrists, knees, and ankles	Joints	• ANA positive 1:160 • Anti-dsDNA positive 46 IU/mL • ESR 88 mm/hg	Prednisone 20 mg daily Mycophenolate mofetil 2 g daily	Polyarthritis symptoms subsided
Current case	18	Female	Autism	Pfizer (BNT162b2)	1 wk after the first dose	Erythematous, tender plaques on the frontal scalp, face, arms, legs, and chest	Skin	• ANA positive 1:2560 • Anti-Smith antibodies positive	Hydroxychloroquine Systemic steroids	Rash resolved with brown macules and atrophic plaques

ANA, Antinuclear antibody; *Anti-dsDNA*, anti-double stranded DNA; *CRP*, C-reactive protein; *ESR*, erythrocyte sedimentation rate; *PMH*, past medical history.

are emerging concerns about new-onset development of vaccine-associated IMIDs such as myasthenia gravis, sarcoidosis, immune thrombotic thrombocytopenia, autoimmune liver disease, rheumatoid arthritis, and SLE.[5] The underlying mechanism of vaccine-associated onset or flares of IMIDs are hypothesized to be alteration of immune responses due to molecular mimicry, interferon-gamma production via stimulation of toll-like receptors, mRNA-induced alteration of post-translational transcription of proteins, and/or vaccine adjuvants triggering inflammasomes.[5,6] In the case of COVID-19 vaccines, it has been suggested that the level of immunogenicity of the vaccine administered may be correlated with the rate of autoimmune disease flares. Highly immunogenic COVID-19 vaccines that produce greater spike protein-specific antibody levels and T cell responses may be more likely to cause immune dysregulation, and therefore, produce a potential autoimmune disease flare.[4]

At least 8 cases (Table I) of new-onset SLE triggered by COVID-19 vaccination have been reported in the literature to date.[1,2,5-10] The majority of patients were female (75%), with 63% patients in their third decade of life. Besides the skin, the musculoskeletal system was most commonly affected, followed by renal and gastrointestinal involvement. Of these cases, 63% occurred after the first vaccine dose and 37% occurred following the second vaccine dose. Interestingly, the onset of SLE after the first dose of the vaccine ranged from 2 to 14 days, whereas, onset of SLE after the second vaccine dose was noted 2 weeks following vaccination in these reported cases. Previous studies examining the exacerbation of existing autoimmune conditions have noted that symptom severity was increased following the second dose of the COVID-19 vaccine or with prior COVID-19 infection.[4] This may indicate that the increased immune response following repeated exposure to either the vaccine or the virus itself corresponds to an increased autoimmune response, raising the possibility that autoimmune exacerbations may be increased with booster shots as well.

In light of this scientific data, we believe that in our patient, the administration of the mRNA vaccine may have disrupted the immune balance to cause the previously asymptomatic disease to flare and present for the first time. Given our patient's recurrence of lesions upon near-completion of the steroid taper as well as the need for continued treatment with hydroxychloroquine to prevent flares several weeks post-vaccination suggest that this is likely a true development of SLE requiring chronic therapy rather than a transient immune activation.

Amidst the ongoing COVID-19 pandemic, there is an increased use of mRNA vaccines, and it is important for physicians to be aware of the potential for these vaccines to induce exacerbations of existing autoimmune disorders or potentially unmask de novo autoimmune diseases in predisposed individuals. This case does not question the safety or efficacy of COVID-19 vaccines, since vaccination is the single most effective intervention to prevent COVID-19 infection and the development of severe illness from it. In conclusion, in patients with persistent systemic signs or symptoms after COVID-19 vaccine administration, clinicians should consider a thorough evaluation for new-onset or flare of IMIDs.

Conflicts of interest

None disclosed.

REFERENCES

1. Lemoine C, Padilla C, Krampe N, et al. Systemic lupus erythematous after Pfizer COVID-19 vaccine: a case report. *Clin Rheumatol*. 2022;41:1597-1601. https://doi.org/10.1007/s10067-022-06126-x
2. Molina Rios S, Rojas Martinez R, Estévez Ramirez GM, Medina YF. Systemic lupus erythematosus and Antiphospholipid syndrome after COVID-19 vaccination. A case report. *Mod Rheumatol Case Rep*. 2022:rxac018. https://doi.org/10.1093/mrcr/rxac018
3. Gracia-Ramos AE, Martin-Nares E, Hernández-Molina G. New onset of autoimmune diseases following COVID-19 diagnosis. *Cells*. 2021;10(12):3592. https://doi/10.3390/cells10123592
4. Sprow G, Afarideh M, Dan J, et al. Autoimmune skin disease exacerbations following COVID-19 vaccination. *Front Immunol*. 2022;13:899526. https://doi.org/10.3389/fimmu.2022.899526
5. Mousa N, Saleh AM, Khalid A, Alshaya AK, Alanazi SMM. Systemic lupus erythematosus with acute pancreatitis and vasculitic rash following COVID-19 vaccine: a case report and literature review. *Clin Rheumatol*. 2022;41(5):1577-1582. https://doi.org/10.1007/s10067-022-06097-z
6. Patil S, Patil A. Systemic lupus erythematosus after COVID-19 vaccination: a case report. *J Cosmet Dermatol*. 2021;20:3103-3104. https://doi.org/10.1111/jocd.14386
7. Nune K P Iyengar, Ish P, Varupula B, Musat CA, Sapkota HR. The Emergence of new-onset SLE following SARS-CoV-2 vaccination. *QJM*. 2021;114(10):739-740. https://doi.org/10.1093/qjmed/hcab229
8. Zavala-Miranda MF, González-Ibarra SG, Pérez-Arias AA, Uribe-Uribe NO, Mejia-Vilet JM. New-onset systemic lupus erythematosus beginning as class V lupus nephritis after COVID-19 vaccination. *Kidney Int*. 2021;100(6):1340-1341. https://doi.org/10.1016/j.kint.2021.09.009
9. Kaur I, Zafar S, Capitle E, et al. COVID-19 vaccination as a potential trigger for new-onset systemic lupus erythematosus. *Cureus*. 2022;14(2):e21917. https://doi.org/10.7759/cureus.21917
10. Báez-Negrón L, Vilá LM. New-onset systemic lupus erythematosus after mRNA SARS-CoV-2 vaccination. *Case Rep Rheumatol*. 2022;2022:6436839. https://doi.org/10.1155/2022/6436839