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Case Report

Appraising SARS-CoV-2 infections after full mRNA COVID-19 vaccination in patients with systemic lupus erythematosus (SLE)☆

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A R T I C L E   I N F O

A B S T R A C T

The 2019 Coronavirus disease (COVID-19) vaccine is a major weapon in the fight against the severe acute respiratory syndrome brought about by coronavirus 2 (SARS-CoV-2). The vaccine significantly reduces the risk and severity of infection by SARS-CoV-2. Patients with systemic lupus erythematosus (SLE) need protection from vaccine-preventable diseases including COVID-19. SLE patients have higher rates of severe infections due to immunosuppressive therapies and multiple immunologic defects – both of which are capable of blunting the immune responses after vaccination. In the management of COVID-19, recommendations have been developed to guide adjustments and/or continuation of immunosuppressive therapies for an effective immune response following vaccination with mRNA-based or viral vector-delivered vaccines. Monoclonal antibodies have also become available since December 2021. Here we present three cases of SLE patients who contracted COVID-19 after vaccination. One was managed in ambulatory settings and two required hospital admission.

Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease associated with abnormal production and clearance of autoantibodies. The etiopathogenesis of SLE is complex and has been linked to genetic, environmental, and hormonal factors [1].

SLE pathogenesis appears to involve antigen-independent and antigen-dependent mechanisms. The former may include the engagement of Toll-like receptors (TLR) on antigen-presenting cells with microbial molecules, and the latter can include self-antigens or, possibly, cross-reactive exogenous trigger antigens [2]. Clinically, the course of SLE is variable but usually characterized by episodic flares that can affect different organs/tissues. Immunosuppressive medications that include steroids, disease-modifying anti-rheumatic drugs (DMARDs) and biologic DMARDs are used in SLE to suppress autoimmune reactivity and limit disease progression and organ damage yet they increase the risk of infection [3]. In all, infections represent a major cause of morbidity and mortality globally [4,5].

Two mRNA COVID-19 vaccines namely the Moderna (mRNA-1273) and Pfizer/BioNTech (BNT162b2) were granted emergency use authorization and are being used globally to prevent COVID-19 infections. The efficacy rates of the Moderna and Pfizer vaccines were 94.1% and 95.0%, respectively with low percentages (< 0.1%) of serious adverse effects reported during phase III trials of both vaccines [6,7]. Notably, patients on immune-modifying medications or immunosuppressants were excluded from all phases of the Moderna vaccine trials (NCT04470427) [7] as well as from phases I to III of the Pfizer/BioNTech vaccine trials [6,8].

Consequently, there is some ambiguity about the effects of COVID-19 mRNA vaccines in patients with SLE [9]. As reduced immunogenicity has been reported with influenza vaccination in SLE patients [10], there is a knowledge gap about the response to vaccines in SLE patients, notwithstanding the American College of Rheumatology provides guidance about COVID vaccination for patients with rheumatologic diseases [11].

Case presentation

Case 1

A 27-year-old female with chronic thrombocytopenia, SLE (diagnosed in 2013 and not on any immunosuppressants) with SLEDAI-2K...
score of 6 in 2013, polyarthralgia, and suspected undifferentiated connective tissue disease was fully vaccinated with the mRNA Moderna vaccine on 1/22/21 and 2/25/21. However, she was found to be COVID positive on 4/21/21 via PCR testing at the outpatient clinic after presenting with flu-like symptoms. Her vital signs were stable and she was not significantly short of breath, therefore not requiring supplemental oxygen. She did not require inpatient admission. Lab results were significant only for thrombocytopenia (Platelet count was $104 \times 10^9$/L). She was discharged from the clinic to complete her quarantine at home without any further complications. COVID-19 spike total antibody test was eventually obtained 11 days after receiving her booster on 1/13/22 and was positive at > 250 U/ml.

Case 2

A 43-year-old female with a past medical history significant for lupus nephritis (SLEDAI-2 K score 11 points in June 2020) and antiphospholipid syndrome on Hydroxychloroquine 200 mg once daily, Mycophenolate mofetil 360 mg twice daily and Sirolimus 1 mg daily. She had previously been on Belimumab (Benlysta) 800 mg weekly injections from March 2021 but this was stopped in July due to diarrhea and nausea that resolved after Benlysta was stopped. The patient also had history of hypertension, chronic kidney disease stage 3, pulmonary embolism and a prior stroke secondary to antiphospholipid syndrome and was on Coumadin 2.5 mg daily. She presented to the hospital on 01/17/22 with a 2-day history of headache, cough, right collarbone pain, chills, fevers, chest pain, myalgias, fatigue, diarrhea, and generalized weakness. Vital signs were within normal limits and a physical exam was most significant for dehydration. She had been fully vaccinated for COVID-19 with the Pfizer mRNA vaccines in March and April 2021 with a booster dose in September 2021. She was admitted for COVID-19 gastroenteritis diagnosed via PCR and a pre-renal acute kidney injury (AKI). She received IV fluids, two 6 mg doses of dexamethasone, and a 200 mg dose of Remdesivir. SARS-CoV-2-S (Spike) total antibody levels were elevated (> 250 U/ml). She improved significantly after two days and was discharged to follow up with her primary care provider and rheumatologist.

Case 3

A 32-year-old man with a past medical history of type 1 diabetes mellitus on insulin, end-stage renal disease (ESRD) secondary to diabetic nephropathy and on hemodialysis (HD), SLE, antiphospholipid syndrome (APS) with a history of splenic infarct on warfarin (SLEDAI-2 K score of 20 in January 2022), peripheral arterial disease (PAD) with balloon angioplasty of right anterior and posterior tibial arteries, hypothyroidism and asthma, who presented to the hospital on 1/14/22 with fatigue, malaise, myalgias and cough productive of clear sputum. The patient had been fully vaccinated for COVID-19 with the Pfizer mRNA vaccine on 3/9/21 and 3/30/21. The vital signs were essentially normal with respiratory rate of 14/min and SPO2 96% on room air. The lab results were significant for a positive COVID-19 PCR test, neutrophilic leukocytosis of $14.6 \times 10^9$/L, hyperglycemia with blood glucose 471 mg/dL. For SLE, the patient was on hydroxychloroquine 200 mg daily, prednisone 5 mg daily, and COVID was managed with a 3-day course of Remdesivir (200 mg on day one, then 100 mg daily). SARS-CoV-2-S (Spike) total antibody levels were elevated (> 250 U/ml) and he was discharged after an uncomplicated hospital course.

Key: CKD – BMI – Body mass index; Chronic kidney disease; URI – Upper respiratory infection; TIDM – Type 1 Diabetes mellitus; ESRD – End stage renal disease; APS – Antiphospholipid syndrome; PAD – Peripheral arterial disease

| Patient | S.N. | Specific Comorbidities | COVID-19 Vaccination Dose | COVID-19 Infection | Symptoms of COVID-19 Infection | Treatment |
|----------|------|------------------------|--------------------------|-------------------|-------------------------------|-----------|
| Patient 1 | 1    | Overweight (BMI > 25)  | First and second dose 80 and 56 days prior to infection, respectively | 257 days after the second dose | Headaches, fever, myalgia, chest pain, fatigue, diarrhea, Remdesivir | Dexamethasone and Remdesivir, | |
| Patient 2 | 2    | Stroke, CKD, 3. Hyper tension, history of ESRD (PAD), APS, SLE | First and second dose 285 and 267 days prior to infection, respectively | 267 days after the second dose | Headaches, fever, myalgia, chest pain, fatigue, diarrhea, Remdesivir | Dexamethasone and Remdesivir, | |
| Patient 3 | 3    | Overweight (BMI > 25)  | First and second dose 111 and 260 days prior to infection, respectively | 290 days after the second dose | Headaches, fever, myalgia, chest pain, fatigue, diarrhea, Remdesivir | Dexamethasone and Remdesivir, | |
Discussion

The viral upper and lower respiratory infections caused by the COVID-19 pandemic have overwhelmed the health system and caused many hospitalizations and deaths. In the fight against COVID-19, both the Moderna and Pfizer vaccines stimulate active immunity, while monoclonal antibodies offer passive immunity to the virus. We report the case of three SLE patients, some on chronic immunosuppressive medications, who developed COVID-19 after being vaccinated against COVID-19 (Table 1).

Guidelines do exist for administering vaccines to certain populations of patients [12]. According to the American College of Rheumatology (ACR) guidelines on COVID-19 vaccination, persons with autoimmune diseases were not found to have any greater incidence of symptoms consistent with inflammation or disease flare-ups when compared to the placebo group [13]. Therefore, persons with autoimmune diseases are recommended by the Center for Disease Control and Prevention (CDC) to receive any authorized COVID-19 vaccine [14].

Various levels of antibody protection can develop in response to vaccination and in COVID-19; the emphasis is on high-affinity neutralizing antibodies. Other protective antibody mechanisms include antibody-dependent cytotoxic cell killing, opsonophagocytosis and complement fixation [15]. These antigen-specific antibodies can be measured by enzyme-linked immunosorbent assay (ELISA).

Interestingly, primary vaccine failure may occur in some immunosuppressed individuals who fail to develop the anti-spike IgG antibodies after COVID-19 vaccination and instead produce autoantibodies against phospholipids [16]. It is possible that vaccine failure, i.e. COVID-19 infection after vaccination, may be due to infection with COVID-19 variants including the highly infectious Delta (B.1.617.2) and Omicron (B.1.1.529) SARS-CoV-2 variants, which have been associated with breakthrough infections. Of note, our third patient subsequently received preventative protection with a combined treatment of long-acting monoclonal antibodies tixagevimab and cilgavimab that were authorized by the FDA on December 8, 2021. This preventative treatment was well tolerated by our patient and we have utilized this antibody cocktail for patients who failed to develop antibodies due to their immunosuppressed state or treatment with B-cell depleting therapies, such as rituximab.

For vaccine failure, there may be two reasons likely involved: vaccine-related and host-related. Vaccine-related reasons can be mitigated by enforcing strict vaccination protocols, ensuring the cold chain and vaccine route, administration and schedule. Host-related aspects, i.e., vaccine nonresponsiveness, are more complicated. Healthy individuals may fail to generate antibodies in response to routine vaccines in 2–10% of cases [17]. Additional factors can also be implicated (regulatory T and B-cells, interleukin 10 (IL-10), elderly age (> 65 years) and obesity) [18,19].

Conclusion

The immunosuppressive therapies that are often required to manage SLE tend to alter immune responses including those that follow vaccination. Consequently, SLE patients represent a population of individuals with inflammatory and immunosuppressive features that may include larger groups of potential vaccine non-responders. Identifying those individuals would lead to the monitoring for the development of protective antibodies against the virus after COVID-19 vaccination, possibly helping with better management of the patient’s condition and associated clinical risks.

Declaration of Competing Interest

None.

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