Systemic Lupus Erythematosus and Critical Illness

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Hildy M. Schell-Chaple, PhD, RN, CCNS, CCRN-K

ABSTRACT

Systemic lupus erythematosus is a chronic autoimmune disorder that causes a wide range of mild to life-threatening conditions that require hospitalization and critical care. The morbidity and mortality of systemic lupus erythematosus are associated with the organ system damage caused by intermittent or chronic disease activity and with the complications of long-term and toxic immunosuppressant medication regimens. This article reviews the epidemiologic, clinical, diagnostic, and therapeutic information essential for critical care clinicians who provide care to patients with systemic lupus erythematosus. Key words: autoimmune diseases, critical care, systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is a chronic autoimmune connective tissue disease that affects many organ systems and has a broad range of clinical manifestations. Patients with SLE may initially present with abnormal skin or joint findings to the clinic or may present with life-threatening cardiac, renal, or hematologic conditions to the emergency department. Infection and cardiac disorders are the most common causes of hospitalization for patients with SLE.1 Intensive care unit (ICU) admission rates for hospitalized patients with SLE are as high as 37%, with sepsis as the leading ICU diagnosis.2 Over the past few decades SLE has surpassed rheumatoid arthritis as the most common autoimmune disease diagnosis among patients requiring ICU care.3 The wide range of clinical manifestations of SLE and the challenges of differentiating disease flares from associated secondary conditions can complicate the diagnosis and plan of care for ICU patients with SLE. This article summarizes the epidemiologic, clinical, diagnostic, and therapeutic information essential for critical care nurses to provide optimal care to patients with SLE.

Case Presentation

D.B. is a 20-year-old Hispanic female college student with no relevant medical history who developed fatigue and bilateral knee discomfort and swelling. Her pain partly responded to ibuprofen, and she believed she had overexerted herself during a hike with friends. Two weeks later she went to the student health center with dyspnea, palpitations, and mild chest pain. The clinic sent her to the emergency department, where she presented with a temperature of 38.1 °C, respiratory rate of 22/min, heart rate of 124/min, blood pressure of 95/70 mm Hg (mean, 78 mm Hg), and an abnormal electrocardiogram with ST-segment elevations.

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The authors declare no conflicts of interest.

DOI: https://doi.org/10.4037/aacnacc2020355
in all leads except V₁ and aVR. She received a diagnosis of pericarditis and cardiac tamponade and required ICU admission and pericardial drain insertion. Laboratory tests were conducted because her joint symptoms and presenting condition put an autoimmune disorder high on the differential diagnosis list. The diagnosis of SLE was made on the basis of D.B.’s clinical presentation and serologic test results, including an antinuclear antibody (ANA) titer of 1:89, low C3 and C4 complement component levels, and positive tests for anti–double-stranded DNA (anti-dsDNA) and anti-Smith antibodies. A pulse dose of methylprednisolone (1 g intravenously daily for 3 days) followed by a tapering dose of prednisone was the first-line treatment of D.B.’s new diagnosis of SLE with a significant cardiac presentation.

History and Epidemiology

Descriptions of a condition with facial skin lesions termed lupus (meaning wolf in Latin) have been traced back to the 13th century, when myths of werewolves were prevalent.¹ Not until the 19th century was the term lupus erythematosus coined for the disease because of the presentations of raised red skin lesions, mostly in young women.²³ In the early 1900s, Sir William Osler, a founding physician of Johns Hopkins Hospital, was the first to describe lupus erythematosus in a published case series as a systemic disease with involvement beyond the skin.⁴ During the 20th century, glucocorticoid treatment for SLE and serum antibodies involved in this autoimmune disease were discovered.⁵⁶ Ongoing research of this complex disease continues to improve our understanding of the pathogenesis of SLE, improve diagnostic tests, identify more precise treatment strategies, and reduce treatment-associated complications.

The global incidence and prevalence of SLE vary widely. The highest rates are in North America, Asia, and Australia, and the lowest rates are in Africa and Europe.⁷ Worldwide prevalence of SLE ranges from 6.5 to 241 per 100,000 persons, with the highest rate in the United States.⁸ The wide variations are associated with sex, age at diagnosis, race/ethnicity, genetic and epigenetic factors, and environmental factors. The incidence of SLE is highest in women of childbearing age, nonwhite populations, and persons of low socioeconomic status.⁹¹² Despite advances in treatment, including new biologics and combination drug regimens, the mortality of patients with SLE has not improved over the past 2 decades; the mortality hazard ratio is 2.12 (95% CI, 1.62-2.80).¹³ Both early and late morbidity and mortality of SLE are due to complications of the disease itself or of its treatments. Infection and cardiovascular events are leading causes of morbidity and mortality.¹⁴ Study of potential genetic variants associated with SLE may yield targeted biologic therapies that can mitigate treatment-related complications.

Pathophysiology

Although the cause of SLE is not fully understood, genetic predisposition and immunologic and environmental triggers are associated with the development and progression of this disease. In SLE, dysregulation of the body’s innate and adaptive immune responses leads to autoantibody production and complement deficiency. This dysregulation leads to activation of T cells, secretion of inflammatory cytokines, and stimulation of B-cell activity, resulting in autoantibody production.¹⁵ The increased number of antigen-antibody immune complexes from the production of autoantibodies contributes to the pathogenic response in SLE. Autoantibody production by specific B cells has been associated with the pathogenic mechanisms of SLE.¹⁶ Of the numerous autoantibodies reported in SLE, a select number, including antinuclear, antiphospholipid, and SLE-specific antibodies, are routinely used to diagnose and classify SLE.¹⁷ The specific antibodies from these autoantibody groups used to detect SLE include antichondroitin antibody, lupus anticoagulant, anti-β₂-glycoprotein I antibody, anti-dsDNA antibody, and anti-Smith antibody.¹⁸¹⁹ These autoantibodies combine with cell surface antigens to form immune complexes that deposit in tissues because of the altered clearance ability of the complement system. The skin and joints are common sites for accumulation of these deposits, which subsequently stimulate chronic inflammation. If not controlled, the chronic inflammation leads to necrosis, scar tissue formation, tissue damage, and manifestations of the disease in the skin, joints, and serous membranes and in the renal, cardiac, neurologic, and other organ systems.

The complement system is an essential part of the immune system that aids in the clearance
of foreign antigens and dead cells by antibodies and phagocytic cells. The ongoing activation of the complement system during the SLE autoimmune response leads to complement deficiency. Complement component C1q deficiency is associated with progression to SLE. A functioning complement system is essential to the body’s innate response to infection and injury. Complement proteins are important in the inflammatory response, in phagocytosis of targeted antigens and antigen-antibody complexes, and in production of membrane attack complexes that target cell death. Cell death occurs routinely under normal and pathologic conditions and does not cause chronic inflammation or injury when the clearance functions of the immune system are intact. Complement deficiency results in an insufficient inflammatory response to infection along with deposition of antigen-antibody complexes and cell debris into tissues because of altered phagocytosis and impaired clearance of membrane attack complexes. The chronic inflammation resulting from accumulation of cell debris and immune complexes is one of the main pathogenic mechanisms of SLE.

Diagnosis

The initial presentation of SLE is variable and nonspecific, which can often make diagnosis difficult. The diagnosis of SLE is determined by the presenting clinical conditions in conjunction with serologic laboratory test results. The SLE classification criteria outlined by the American College of Rheumatology (ACR) in 1982 were initially introduced to standardize diagnostic criteria for research purposes. These criteria became a useful diagnostic framework for use in clinical practice and were revised in 1997 and 2012. The 2012 revision by the Systemic Lupus International Collaborating Clinics group requires that either 4 of 17 criteria (including at least 1 positive immunologic serology result and 1 clinical criterion) be met or that a biopsy-confirmed finding of lupus nephritis (LN) and 1 positive immunologic serology result be present for a diagnosis of SLE. The European League Against Rheumatism (EULAR) and the ACR recently tested and approved updated classification criteria for the SLE scoring tool. When validated against the ACR 1997 and the Systemic Lupus International Collaborating Clinics 2012 classification systems, the EULAR/ACR 2019 system had comparable sensitivity (0.96; 95% CI, 0.95-0.98) and better specificity (0.93; 95% CI, 0.91-0.95) for diagnosing SLE. The EULAR/ACR 2019 classification criteria are shown in Table 1. Improvements to the diagnostic algorithm for this complex autoimmune disorder have facilitated accurate diagnosis and timely, appropriate treatment.

Types and Clinical Patterns

Different types of this disease have been described as neonatal lupus erythematosus, discoid lupus erythematosus, drug-induced lupus erythematosus (DIL), and SLE with multisystem manifestations. Neonatal lupus is a rare condition that is associated with antibodies from the mother, and discoid lupus manifests with cutaneous lesions. This article focuses primarily on the most common type, SLE, yet clinicians should be aware of DIL as a potential diagnosis. These lupus types are chronic conditions with the exception of the DIL type, which subsides after cessation of drug exposure. Hydralazine, procainamide, isoniazid, and minocycline are the drugs most commonly associated with this adverse effect, which is typically associated with cumulative and higher drug doses. Typical clinical presentations of DIL include fever, rash, arthralgia, and myalgia. Serum antibody results are notable for a positive ANA titer but negative anti-dsDNA and anti-Smith antibody titers. The presence of classic autoimmune disorder constitutional symptoms with a positive ANA titer and negative SLE-specific antibody titers should prompt a comprehensive medication history covering the previous 6 months. The prognosis for DIL is good, with resolution of clinical symptoms and autoantibody levels over weeks to months. A comprehensive medication history can clarify the cause and prognosis for patients with new-onset clinical presentations of lupus erythematosus.

Disease activity of SLE is defined in terms of magnitude and timing of the clinical and laboratory test manifestations of the chronic inflammatory disease process. A clinically significant, measurable increase in SLE-associated disease activity in 1 or more organ systems or laboratory findings is the definition of a flare. The increased inflammation, autoantibody production, and number of immune complexes exceeds the remission threshold maintained by the patient’s SLE.
Flares are categorized as mild, moderate, or severe, and these exacerbations warrant consideration of a change to the patient’s treatment plan. Laboratory results that predict a flare of SLE include an increase in anti-dsDNA antibody titer and a decrease in complement levels, especially C3 and C4. Three patterns of SLE disease activity have

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**Table 1: EULAR/ACR Classification Criteria for Systemic Lupus Erythematosus**

1. ANA titer ≥1:80 (serum indirect immunofluorescence assay on human epithelial type 2 cells)
   - Positive titer: evaluate additional criteria
   - Negative titer: do not classify as SLE

2. **Clinical and immunologic domains and criteria**
   - Do not count criteria that have a more likely explanation than SLE
   - Criteria only required to have at least 1 occurrence and not simultaneously
   - Count the highest score within a domain if more than 1 present
   - SLE classification requires at least 1 clinical criterion and score ≥10

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<td>Anti-dsDNA antibody or anti-Smith antibody</td>
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*Classify as SLE if 1) ANA criteria met and 2) criteria total score ≥10*

**Total score:**

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Abbreviations: ACR, American College of Rheumatology; ANA, antinuclear antibody; dsDNA, double-stranded DNA; EULAR, European League Against Rheumatism; SL-E, systemic lupus erythematosus.

* Adapted with permission from Aringer et al.*
been described: relapsing-remitting (intermittent flares followed by periods of remission), chronic active, and long quiescent (quiescent for over 1 year). A pattern is considered persistent if it continues for 3 years. The relapsing-remitting pattern is the most prevalent, the chronic active pattern is the second most prevalent, and the long quiescent pattern is the least frequent, with a prevalence of 10% among patients with SLE.

Many SLE flares do not have identifiable triggers. Ultraviolet light, infections (viral and bacterial), smoking, drugs, estrogen levels, and psychoemotional stress are clinical triggers for both new-onset SLE and lupus flares. Flares may also occur during or after a dose taper or withdrawal of immunosuppressant drugs. Close monitoring for flare signs and symptoms during drug regimen changes with prompt intervention can minimize the tissue and organ damage.

A number of tools have been tested and used to measure SLE disease activity and monitor flare patterns. The SLE Disease Activity Index 2000 (SLEDAI-2K) instrument is commonly used to score disease activity and identify patterns over time. This validated and reliable tool has 24 scored clinical and laboratory test variables. Most patients have a cumulative score of less than 20 (range, 0-105). Each SLEDAI-2K criterion has a weighted score ranging from 1 to 8, and the cumulative score categorizes the degree of disease activity and allows evaluation of disease progression over time. The heterogeneity of SLE clinical manifestations, disease activity fluctuations, and different disease patterns highlight the complexity of diagnosing and managing this autoimmune disorder. The British Isles Lupus Assessment Group disease activity index and the Safety of Estrogens in Lupus Erythematosus National Assessment–SLEDAI Flare Index are other commonly used disease activity measurement instruments.

Case Presentation Continued

D.B. remained in college and continued to take prednisone (20 mg daily) for her SLE. Eight months after her initial diagnosis she presented with viral symptoms and received a diagnosis of influenza and another pericarditis flare. Fortunately, she did not require an interventional procedure, but she required another pulse dose of methylprednisolone followed by a steroid dose taper. To minimize the complications associated with steroids, including infection, her treatment regimen was changed to a steroid-sparing combination therapy with daily hydroxychloroquine, low-dose prednisone (5 mg), and colchicine. The chronic active pattern of her SLE led to emergency department visits, hospitalizations, and treatment changes for flares presenting as esophagitis, pleuritis, and repeat pericarditis over 2 years. Fortunately, D.B. did not require ICU care during her hospitalizations because of her access to a health care center with rheumatology specialists, her prompt diagnoses, and her appropriate flare treatment. After graduating from college, D.B. relocated to the West Coast for a career opportunity.

A year after relocating, D.B. went to the emergency department with abdominal bloating and pain, swollen and painful elbow joints, bilateral grade 2 peripheral edema up to her knees, and a 15-lb weight gain. Her SLE maintenance medications included daily low-dose prednisone, hydroxychloroquine, mycophenolate mofetil, and ibuprofen for chronic arthralgia. She presented with a heart rate of 93/min, blood pressure of 153/93 mm Hg (mean blood pressure, 108 mm Hg), respiratory rate of 20/min, and no fever. Significant laboratory blood test results were a white blood cell count of 3200/μL, hemoglobin level of 8 g/dL, creatinine level of 1.26 mg/dL, albumin level of 2.6 g/dL, C-reactive protein level of 22 mg/dL, positive anti-dsDNA antibody level of 1691 IU/mL, and low complement levels (C3, 50 mg/dL; C4, 8 mg/dL). Her urinalysis results included a moderate amount of hemoglobin and a protein level of greater than 500 mg/dL. Her creatinine clearance was 85 mL/min/1.73 m². Abdominal imaging showed no acute disorders, and she was admitted for management of her SLE flare and further workup of acute kidney injury. Class IV LN was diagnosed on the basis of D.B.’s renal biopsy histology results along with her clinical presentation. Class IV LN represents histologic damage related to immune complex deposits and endocapillary proliferation involving more than 50% of glomeruli.

The treatment plan for D.B.’s SLE flare and LN included pulse-dose methylprednisolone followed by a slow steroid dose taper over 6 weeks; cyclophosphamide infusion induction followed by doses every 2 weeks for 6 weeks; discontinuation of mycophenolate mofetil while she was taking cyclophosphamide;
discontinuation of ibuprofen because of potential adverse renal effects; and continuation of antihypertensive medications.

**Immunologic Laboratory Tests**

The serum laboratory test that identifies the presence of an autoimmune disease is a positive ANA titer. These autoantibodies target substances in the cell nucleus, leading to accumulation of antigen-antibody immune complexes and resultant cell and tissue damage associated with autoimmune disorders. Further serum testing for SLE-associated autoantibodies is required along with evaluation of clinical presentation criteria to confirm the SLE diagnosis. The presence of anti-dsDNA antibodies helps differentiate SLE from other autoimmune disorders, has a high specificity for diagnosing SLE, and is an indicator of disease activity. Other immunologic test results associated with SLE include low complement levels (C3, C4, or CH50), SLE-specific antibodies (anti-dsDNA or anti-Smith antibodies), and antiphospholipid antibodies (anticardiolipin antibodies, anti-β₂ glycoprotein I antibodies, or lupus anticoagulant). The patient’s current immunological laboratory results should be reviewed along with past results to differentiate SLE disease activity from other conditions that also have an associated inflammatory response.

**Clinical Presentations**

The classic clinical presentation of SLE includes the constitutional symptoms of fatigue, fever, rash, weight loss, arthralgia, and myalgia. The widespread inflammation and tissue damage caused by SLE can present as single or multiple organ system dysfunction over the trajectory of this chronic disease. This section reviews SLE-associated cardiac, renal, neuropsychiatric, and infectious complications because they are the most prevalent, may require critical care, and are associated with higher mortality. See Table 2 for a more comprehensive list of conditions associated with new-onset SLE or flare episodes.

Cardiovascular events are among the most common clinical manifestations of SLE. Pericarditis is the most common cardiac manifestation of SLE, with an incidence of 25% among patients presenting with symptoms and up to 50% when asymptomatic cases detected on echocardiography are included. Signs and symptoms of pericarditis include tachycardia, a friction rub upon auscultation, pleuritic or chest pain that may resolve with repositioning (sitting forward), and ST-segment elevations.

<table>
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<tr>
<th>Table 2: Clinical Conditions Associated With New-Onset Systemic Lupus Erythematosus or Flare Episodes</th>
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across all leads except for V₁ and aVR on 12-lead electrocardiography. Low C₄ complement levels and elevated SLE-specific antibodies indicate SLE-associated pericarditis.³⁴³⁵ Pulse-dose glucocorticoids are recommended for the severe complications of constrictive pericarditis and cardiac tamponade associated with SLE-related pericarditis.⁵³ Progression to constrictive pericarditis and cardiac tamponade requiring critical care intervention is less common, but patients should be monitored for this possibility after a pericarditis diagnosis.⁵⁶ Viral infection is the leading cause of pericarditis in immunocompetent patients and its first-line treatment is nonsteroidal anti-inflammatory drug administration, which differs from the treatment for pericarditis caused by SLE.⁴⁹ The decision to manage pericardial effusion with pericardiocentesis is based on the patient’s hemodynamic and symptom status regardless of the cause. Myocarditis, valvular disease, atherosclerotic disease, and coronary artery disease are other cardiovascular manifestations, with coronary artery disease a leading cause of later mortality in patients with SLE.⁴⁴⁶⁵

Up to 60% of patients with SLE also have LN, and up to 20% develop end-stage renal disease.⁴⁴⁵⁹ Clinical manifestations of LN include hypertension, proteinuria, microscopic hematuria, hypoalbuminemia, edema, weight gain, and signs of renal insufficiency.⁵⁰ The diagnosis of LN is confirmed with renal biopsy findings and is classified (classes I through VI) according to histopathologic findings.⁵² Biopsy findings in lupus reveal interstitial immune complex deposits, mesangial proliferation, and proliferative glomerular nephritis. Treatment with pulse-dose steroids and an additional immunosuppressive agent such as mycophenolate mofetil, a calcineurin inhibitor, or cyclophosphamide is indicated for class III and class IV LN.⁶⁰⁶¹ Blood pressure management with angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers as well as daily hydroxychloroquine are recommended since they are associated with a reduced risk of LN flares.⁶⁰⁶¹ Urine protein levels of less than 0.3 g/d indicate complete remission from a LN flare.⁴⁵ Early detection and prompt intervention can minimize damage to the kidneys.

Manifestations of neurologic and psychiatric conditions associated with SLE are categorized as neuropsychiatric conditions. A large multinational cohort study found a 52% occurrence rate of SLE-associated neuropsychiatric events, with 27% of patients having more than 1 event.⁴⁷ Neuropsychiatric clinical presentations include headaches, seizures, transverse myelitis, peripheral neuropathy, hemorrhagic and thrombotic stroke, transient and multifocal ischemia, cognitive dysfunction, anxiety, and depression.⁴¹⁴⁷⁴⁸⁶² The relative risk of a neuropsychiatric event during the first 2 years after SLE diagnosis is 6.16 (95% CI, 4.96-7.66), and these events are associated with increased mortality.⁴⁷ Patients with SLE are at high risk for infection because of the immunosuppression associated with the disease, the treatment regimen of corticosteroids, and the various types and doses of immunosuppressant and cytotoxic agents required for increases in disease activity. Management of serious infections is the leading reason for hospital admission for people with SLE, who have hospitalization rates 12 times higher than those who do not have SLE.⁶³ The most common infection-related diagnoses on hospital admission are pneumonia, sepsis, urinary tract infection, skin or soft-tissue infections, and opportunistic infections with organisms like varicella-zoster virus.⁴² Infectious complications are associated with viral, bacterial, or parasitic pathogens; new-onset SLE is most commonly associated with viral infections.⁶⁵ The viral pathogens most frequently identified with SLE are Epstein-Barr virus, cytomegalovirus, varicella-zoster virus, and parvovirus B19.⁶⁵ Patients with infectious complications of SLE are at high risk of progression to sepsis, septic shock, and multiple organ dysfunction without early detection and prompt intervention to identify the source of infection and provide supportive care.

**Pregnancy and SLE**

Pregnancy can trigger new-onset SLE or a flare for patients with chronic disease. Multiple organ system flares occur in up to 45% of patients with SLE and include life-threatening maternal and perinatal complications.⁶⁴⁶⁵ Recognition of a SLE flare during pregnancy is challenging because the signs and symptoms of a flare mimic manifestations of other pregnancy-related conditions. Pregnancy-related conditions to rule out before attributing the signs to SLE include preeclampsia/eclampsia; abruptio placenta; antiphospholipid syndrome; and the hemolysis, elevated
liver enzyme, and low platelet count syndrome. Thrombocytopenia, pericarditis, proteinuria, hypertension, and diffuse alveolar hemorrhage are the most common manifestations of SLE flares during pregnancy. Admission to the ICU because of complications associated with SLE flares requires management of blood pressure, coagulopathy, hemorrhage, seizures, and infection. The interdisciplinary ICU team must differentiate pregnancy-related critical conditions from SLE-related conditions to determine the treatment plan, including the decision for prompt delivery to optimize maternal and neonatal outcomes. Maternal and perinatal complications associated with SLE are premature birth, intrauterine growth restriction, stillbirth, preeclampsia, LN, and maternal death. Rates of maternal and perinatal morbidity and mortality are higher in patients with new-onset SLE than in those with chronic active SLE. Counseling about pregnancy and contraception is required for women with SLE because of the high-risk complications associated with these hormone-related triggers. Management of immunosuppression regimens for SLE during pregnancy is beyond the scope of this article but requires collaboration between rheumatology and obstetric departments for this high-risk population.

Management
The goals of SLE management are to achieve the lowest level of disease activity and flares, reduce the chronic activity of SLE, and minimize the frequency and severity of organ damage associated with the disease or the adverse effects of the treatment regimen. Clinical practice recommendations for treating patients with SLE are not straightforward because of the heterogeneity of the disease types and clinical manifestations. International and national professional societies and study groups continue to publish evidence-based clinical practice guidelines for the management of SLE as innovations and research progress. The 2019 EULAR practice guidelines for the management of SLE outline medication management recommendations that are both general and specific to clinical manifestations.

The 2019 EULAR general recommendations focus on preventing SLE flares, with strategies to optimize medication adherence including patient education, monitoring for treatment efficacy, and early detection and management of treatment-associated adverse effects. Disease activity scoring systems for SLE, such as the SLEDAI-2K, help with tracking disease activity over time and evaluating patients after treatment regimen changes. Standard hygiene and social distancing practices related to infection prevention, along with ongoing surveillance for signs and symptoms of infection, are also important educational content for patients and their families.

Although vaccines are a standard prevention intervention for the general population, concerns about vaccine use in patients with SLE include reduced efficacy related to the impaired immune response and the potential risk of triggering a flare. The EULAR has endorsed evidence-based recommendations for vaccine administration according to the patient’s disease activity status and vaccine type. A large nationwide cohort study of effects of the influenza vaccine in patients with SLE was conducted in Taiwan. Compared with the nonvaccinated cohort of patients with SLE, patients who received the influenza vaccine had significantly lower rates of hospital and ICU admission, less need for renal replacement therapy, and a lower mortality rate (hazard ratio, 0.41; 95% CI, 0.22-0.61).

Numerous medication regimens are used to treat SLE flares according to the organ systems involved and severity of the flare. An antimalarial agent is recommended for all patients with SLE because these agents can reduce the risk of flares and are steroid-sparing interventions that can reduce the daily steroid dose. Hydroxychloroquine is the most commonly used antimalarial agent for SLE and requires monitoring for retinal toxicity with long-term use. The mechanism of action of hydroxychloroquine is not fully understood, but its flare reduction effect and few adverse effects make it a first-line therapy for SLE.

Glucocorticoids are potent anti-inflammatory agents that are first-line therapy for SLE because they provide rapid relief for the exacerbated inflammatory immune response. Most patients with SLE take long-term low-dose glucocorticoids to keep disease activity low and prevent flares. The temporary adverse effects of glucocorticoids that resolve with dose tapering include hyperglycemia, hypertension, and neuropsychiatric symptoms ranging from mild confusion to psychotic behaviors. Coronary artery disease, stroke, osteoporosis-related
fractures, and avascular necrosis are the most common adverse effects of chronic glucocorticoid use.\textsuperscript{73} Tapering the glucocorticoid dose to the lowest dose necessary to suppress disease activity is a primary goal for SLE treatment to minimize the risk of these adverse effects. The cumulative glucocorticoid dose over time, duration of use, and frequency of pulse doses are associated with organ damage in patients with SLE.\textsuperscript{74} The recommended daily target dose of prednisone is 7.5 mg/d or lower because the risk of adverse effects increases with higher doses. A daily intravenous pulse dose (250-1000 mg) of methylprednisolone for 3 days followed by a slow taper back to the target daily prednisone dose is recommended for moderate or severe disease activity.\textsuperscript{70} The higher 1000-mg dose of methylprednisolone is the pulse dose recommended for acute life-threatening SLE-related cardiac, neuropsychiatric, and renal clinical manifestations.\textsuperscript{61,74} Close monitoring for signs of increased disease activity during glucocorticoid dose tapers that follow pulse-dose interventions is recommended. Slowing and prolonging the dose taper for disease activity manifestations during a taper is based on expert opinion because of the current lack of high-grade evidence.\textsuperscript{76}

A number of second-line immunosuppressant agents are used in conjunction with pulse-dose glucocorticoids for additional immunomodulatory effects and to facilitate a more rapid steroid taper. The most commonly used and recommended second-line immunosuppressant agents include methotrexate, azathioprine, mycophenolate mofetil, tacrolimus, cyclosporine, and cyclophosphamide.\textsuperscript{78} Although these agents have different mechanisms of action, they are powerful immunosuppressants that render patients at higher risk for infectious complications during their course of administration.

Biologic therapies are a more recent addition to the menu of treatment options for SLE. Belimumab is the first approved monoclonal antibody agent that targets and inhibits B-cell activity that is recommended for refractory nonrenal clinical manifestations of SLE.\textsuperscript{77} Rituximab has mixed efficacy results but is recommended for some SLE flares refractory to first- and second-line therapies.\textsuperscript{51,75} Other investigational biologic therapies are currently being studied for efficacy and safety in patients with SLE.\textsuperscript{70} The 2019 EULAR guidelines for management of SLE outline the recommended treatment regimens for specific organ system clinical manifestations in further detail.\textsuperscript{70}

The impact of SLE and the disease trajectory on patients’ lives extends beyond the clinical manifestations and medication regimens. An international quality-of-life survey of people with lupus administered by the World Lupus Federation had 4000 respondents from 75 countries.\textsuperscript{73} The results showed a significant negative impact of lupus on physical activities of daily living (eg, stair climbing and household chores) along with limitations on caring for children or family members. Respondents indicated that their lupus symptoms interfered with their social activities with families and friends, which negatively impacted their quality of life. The reported negative impact on quality of life and physical mobility was greater in people with SLE than in those with other types of lupus. Ideally an interdisciplinary team management model with rheumatology providers, advanced practice nurses, social workers, case managers, psychologists, and occupational and rehabilitation therapists would strategize solutions to address the quality-of-life concerns of those living with this chronic disease.

### SLE and ICU Care

Like D.B., who presented with pericarditis-associated cardiac tamponade requiring ICU care, some patients present with a life-threatening condition that leads to their SLE diagnosis. Noninfectious causes of ICU admission for patients with SLE include cardiogenic shock, pericardial effusion, diffuse alveolar hemorrhage, gastrointestinal bleeding, seizures, and intracranial hemorrhage.\textsuperscript{40,41,79} Infection and sepsis are the leading ICU admission diagnoses for patients with SLE.\textsuperscript{2} Patients with sepsis and septic shock have longer ICU stays and higher morbidity and mortality rates than do SLE patients with noninfectious ICU admission diagnoses.\textsuperscript{41} Pneumonia, diffuse alveolar hemorrhage, seizures, and complications of pericarditis are the most common causes for ICU admission.\textsuperscript{7,40} Respiratory failure and acute respiratory distress syndrome are sequelae of pneumonia, the most common infectious complication of SLE.\textsuperscript{41} The complex diagnostic workup and treatment of SLE patients with critical illness associated with flare activity or another complication of the disease is challenging in the ICU and requires close
collaboration between critical care clinicians and rheumatology specialists.

Patients with SLE may require ICU care for either SLE-related complications or non-
SLE-related conditions. The plan of care for these patients should include a thorough review of their SLE flare and medication history and monitoring for new signs of disease activity. Another consideration for patients taking glu-
corticoids is the potential for drug-induced adrenal insufficiency, which can occur when the glucocorticoid dose is not adequate during the stress response to an acute illness, during a glucocorticoid dose taper, or after glucocorticoids are stopped abruptly.80 The nonspecific signs and symptoms of adrenal insufficiency are fatigue, anorexia, nausea, vomiting, abdominal pain, postural hypoten-
sion, and hyponatremia. Adrenal crisis is the more severe manifestation of adrenal insuffi-
ciency and causes fever, hypotension, and dis-
tributive shock.80 Patients with SLE admitted to the ICU require initial and ongoing evalu-
ation for complications of their disease and for adverse effects of their treatment regimen.

Case Presentation Summary

Two months after D.B. started the more potent immunosuppressive treatment regimen for her new LN diagnosis, her disease activity subsided and her renal function improved (cre-
tinine level, 0.87 mg/dL). She took a mild diuretic medication for 2 months and continued taking an antihypertensive medication after her LN diagnosis. She was followed closely by her primary rheumatologist, with monitoring for flares and complications during her slow steroid dose taper and SLE treatment regimen change, and by her nephrologist. D.B. continued to work and joined a lupus support group in her community.

Conclusion

Despite advances in SLE treatment regimens, patients with this chronic illness are at high risk for life-threatening complications that require hospitalization and critical care. The complex clinical presentations of SLE make it difficult to differentiate between a SLE-associated disease flare and a complication of the disease or treatment regimen. This article provides an overview of the types and patterns of lupus, the clinical presentations, the diagnostic criteria, and management strategies that can help critical care nurses provide optimal care to their patients with SLE. Further research to identify strategies that affect the quality of life for patients liv-
ing with SLE and to discover effective treat-
ments that have minimal adverse effects is warranted to improve the outcomes of patients with this chronic condition.

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