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Neurological Complications in Patients with Systemic Lupus Erythematosus

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Abstract

Purpose of Review Systemic lupus erythematosus (SLE) is commonly associated with neurological manifestations. Rapid recognition and treatment of these complications may improve outcomes. In this article, we review the neurological conditions associated with SLE, their diagnosis and management strategies.

Recent Findings Recent meta-analysis showed that patients with neuropsychiatric manifestations of SLE were more likely to have positive antiphospholipid, antiribosomal P, and antineuronal antibodies. Another meta-analysis showed an association between SLE and antiphospholipid antibodies with cognitive impairment. Two large retrospective studies have shown that the peripheral nervous system is commonly involved in SLE frequently alongside the central nervous system.

Summary Neurological manifestations occur in most of SLE patients. Antiphospholipid antibodies are common in patients with SLE and increase the odds of neurological complications. Management typically involved a combination of treatments directed toward the neurological complication and therapies directed toward SLE itself. The efficacy of these treatment protocols, however, has not been rigorously studied and deserves further investigation.

Keywords Systemic lupus erythematosus · Acute ischemic stroke · Intracerebral hemorrhage · Cerebral venous sinus thrombosis · Demyelination · Multiple sclerosis · Peripheral neuropathy

Introduction

Systemic lupus erythematosus (SLE) is a chronic connective tissue disease that affects multiple organ systems. The prevalence is reported to be 130/100,000 and is more common among African Americans and women [1, 2]. Neurological manifestations are common in SLE and often reported in the literature along with the psychiatric manifestation under the combined term of neuropsychiatric SLE. The reported prevalence of neurological manifestations of SLE ranges between 14 and 95% and is more common in children than adults [1, 3–5]. This variation could be attributed to using different criteria to define SLE and the neurological complications in the literature. Furthermore, neurological manifestations can occur in the absence of serologically active SLE and can be the presenting symptoms in 39–50% of cases. The American College of Rheumatology proposed nomenclature system for the neuropsychiatric syndromes associated with SLE, which has been widely used ever since [6•]. The involvement of the nervous system is associated with worse outcomes and mortality rates ranging from 2 to 45%. In this article, we review the neurological conditions commonly associated with SLE, their diagnosis and management strategies, summarized in Table 1.

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Central Nervous System Complications

Acute Ischemic Stroke

The risk for ischemic stroke is higher in patient with SLE. Stroke affects 3–20% of patients with SLE and usually occurs within the first 5 years of the diagnosis. [7–10] Of note, there

Table 1 Most common neurological manifestations of systemic lupus erythematosus

Neurological complication	Prevalence in SLE	Diagnosis	Treatment
Acute ischemic stroke	3–20%	Clinical presentation with sudden onset of neurological symptoms and brain MRI	Acute: intravenous thrombolysis and mechanical thrombectomy. Prevention: depending on the etiology may include antiplatelets, anticoagulation, and immunosuppression
Cerebral venous sinus thrombosis	0.4–6.6%	Acute or subacute onset of headache, encephalopathy, seizures, vision changes, and other focal neurological symptoms. Brain MRI, Brain MR, or CT venogram.	Anticoagulation (lifelong if a predisposing factor was found otherwise 6 months) Mechanical thrombectomy
PRES	0.4–1.8%	Headache, seizure, and encephalopathy. Vasogenic edema in the posterior circulation on brain MRI	Treat causative factor (e.g., HTN) and supportive care
CNS demyelination	0.3–2.7%	Acute to subacute onset of neurological symptoms depending on the location of the lesion. The spinal cord and optic nerves are commonly involved. Differentiating from other demyelinating disorders is challenging	Corticosteroids and immunosuppressants
Chorea and movement disorders	1.2–2%	Clinically and brain MRI to rule out other etiologies	Antidopaminergic agents
Seizures	2.1–11.6%	Clinically and electroencephalography	Antiseizure medications
Headaches	24–72%	Made clinically. Look for headache red flags to determine if further work up needed.	Depending on the headache type
Cognitive impairment and dementia	17–90%	Diagnosis made clinically with the help of cognitive assessment tests. Ruling out other etiologies may require brain imaging and CSF analysis.	No specific treatment available, supportive care.
Peripheral neuropathy	3.4–7.5%	Clinical, nerve conductive studies, rule out common etiologies.	Steroids and immunosuppression for SLE-related neuropathy, and correction of any other potential cause.
Mononeuritis multiplex	1.2%	Clinical, nerve conductive studies, biopsy	Consider corticosteroids and immunosuppression
Inflammatory demyelinating polyneuropathies	< 1%	Clinical presentation, nerve conduction studies, and CSF analysis	IVIG or plasma exchange. Consider steroids and immunosuppression for SLE

is higher risk for all stroke subtypes in patients with SLE. [8] Several mechanisms are implicated in the pathogenesis of stroke in the setting of SLE including hypercoagulable state due to antiphospholipid antibodies, cardioembolism from marantic endocarditis, enhanced atherosclerosis, and cerebral vasculitis, summarized in Table 2.

Antiphospholipid syndrome (APS) is an autoimmune disease associated with increased risk for thrombotic venous and arterial events involving multiple organs. [11•] APS is commonly associated with SLE, and about 20–30% of patients with SLE have moderate-to-high-risk antiphospholipid antibody profiles that are associated with increased risk for thrombotic events. [11•, 12] When APS occurs without SLE, it is called primary antiphospholipid syndrome. [11•] The pathophysiological mechanisms by which APS causes thromboembolism include binding to β_2-glycoprotein 1 leading to upregulating of prothrombotic cellular adhesion molecules, reducing the activity of protein C, and activating the complement [11•, 13, 14]. It is thought that platelet activation, in addition to the interaction between antiphospholipid antibodies and the endothelium, play a key role in the pathogenesis of APS. [11•]

Table 2 Syndromes and conditions associated with systemic lupus erythematosus and ischemic stroke

Name of the syndrome	Prevalence in SLE	Neurological manifestations	Diagnosis	Treatment
APS	20–30% (< 1% of general population)	Stroke or TIA DVT/PE or CVST Cognitive impairment Peripheral neuropathy Chorea	The revised Sapporo criteria. Clinical criteria and positive laboratory testing on two or more occasions 12 weeks apart.	No antithrombotics for primary stroke prevention ASA alone for secondary stroke prevention Warfarin alone or Warfarin+ASA on case-by-case
Libman-Sachs endocarditis	10%	Stroke or TIA	Echocardiogram	Anticoagulation
Sneddon syndrome	Very rare	Stroke, livedo reticularis racemosa	Clinically based on skin findings and strokes	Supportive, antiplatelet therapy for stroke prevention. May consider anticoagulation if associated with APS
CNS vasculitis	< 1%	Subacute headaches, encephalopathy, focal symptoms, seizures	Bilateral infarcts and meningeal enhancement on brain MRI, inflammatory markers in the CSF, vasculopathic changes in the medium and small vessels on CTA, MRA or DSA, and brain biopsy	Corticosteroids and cyclophosphamide

The diagnosis of APS is made based on clinical presentation and laboratory findings. The revised Sapporo criteria have been used to make the diagnosis, which includes a combination of clinical criteria with positive laboratory testing on two or more occasions 12 weeks apart [15]. APS is further categorized into different profiles depending on the serum levels of lupus anticoagulant antibodies, cardiolipin antibodies, and anti-β_2-glycoprotein 1 antibodies [11•]. The risk for first time thromboembolic event in patients with high-risk profile is estimated at 5% per year. [16] Routine testing for APS is not recommended for all stroke patients [17]. Of note, Sneddon syndrome has been commonly reported in patients with APS [18]. Sneddon syndrome most commonly presents with livedo racemosa and recurrent cerebrovascular strokes [18].

Although aspirin has been used, there is currently no evidence to support primary stroke prevention in patients with APS. [11•, 19] Secondary stroke prevention in the setting of APS also remains controversial. According to the 13th international congress of antiphospholipid antibodies, consensus could not be reached on the best secondary prevention for arterial events. [20] Options for secondary prevention include warfarin with INR goal of > 3, warfarin with INR 2–3 in addition to antiplatelet, warfarin with INR 2–3 alone, or an antiplatelet medication alone [20]. AHA guidelines for stroke prevention recommend considering anticoagulation depending on the perception for the risk for recurrent stroke [17]. The Antiphospholipid Antibodies and Stroke Study (APASS) that included 1770 patients showed no difference in stroke recurrence rates between patients taking aspirin alone and patients taking warfarin for secondary stroke prevention. [21] Higher INR target was tested and was not superior to the 2–3 goal. [22] Direct oral anticoagulants (DOACs) can be considered only if patient cannot take warfarin. [23] For example, warfarin is contraindicated during pregnancy, and it is known to have numerous drug interactions due to its effect on cytochrome P450 enzymes. Furthermore, maintaining therapeutic levels of INR may be challenging as it requires several diet restrictions and often influenced by infections and antibiotic treatment. Given the uncertainty of stroke prevention in the setting of APS, our practice is to treat patients with first time ischemic arterial stroke or TIA in the setting of APS with aspirin initially and leave warfarin with INR 2–3 for aspirin failures as shown by recurrence of events.

Libman-Sacks endocarditis can be associated with SLE and APS and is characterized by the formation of non-infective thrombotic and inflammatory vegetations on the valvular leaflets, typically on the mitral valve. Libman-Sacks is found in about 10% of patients with SLE [24]. This condition is associated with increased risk for cerebrovascular embolization, about third of the patients with Libman-Sacks endocarditis had cerebral infarcts when screened with brain magnetic resonance imaging (MRI). [25] Anticoagulation, in addition to treating the underlying cause, is usually recommended for secondary stroke prevention in patients with Libman-Sacks endocarditis. [26]

Central nervous system (CNS) vasculitis is another mechanism of ischemic stroke in the setting of SLE. CNS vasculitis is rare and is found in < 1% of patient with SLE [27, 28]. Diagnosing CNS vasculitis remains challenging and is made based on a combination of suspicious findings of bilateral infarcts and meningeal enhancement on brain MRI, cerebrospinal fluid (CSF) abnormalities, inflammatory markers, and vasculopathic changes in the medium and small vessels on digital subtraction angiography (DSA) [27]. Brain biopsy remains the gold standard confirmatory test. Once diagnosed, CNS vasculitis is treated with immunosuppressants using a combination of cyclophosphamide and/or corticosteroids [29].

Atherosclerosis is associated with SLE, although the exact pathophysiology remains unknown. In the Systemic Lupus International Collaborating Clinics cohort, 1.8% of patients had atherosclerotic events (both cardiovascular and cerebrovascular). [30] Patients with SLE who have atherosclerotic disease tend to be older men [30].

Cerebral Venous Sinus Thrombosis

Cerebral venous sinus thrombosis (CVST) has been reported in 0.4–6.6% of SLE patients. [31, 32] Most often associated with APS and active SLE disease. [31] The diagnosis of CVST is made clinically with supportive imaging findings. Patients most commonly present with headache alone but could also have focal neurological symptoms, seizures, and altered mental status. Several imaging modalities could be used for the diagnosis including MRI brain and MR or CT venograms.

CVST is treated with anticoagulation with heparin or low-molecular-weight heparin followed by warfarin with a target INR goal of 2–3 [11•]. Treatment of active SLE with immunosuppression is recommended although the effect on the CVST has not been tested in a clinical trial. [31] Direct oral anticoagulants have not been formally studied in the setting of CVST and are not used as a first line therapy, but they can be considered when enoxaparin and warfarin cannot be given or failed. Rivaroxaban for example failed to reach non-inferiority when compared to warfarin for preventing venous thromboembolism in patients with APS. [33] Mechanical thrombectomy can be tried in severe cases of CVST to reduce clot burden and reduce intracranial pressure, but it is considered experimental. The presence of venous ischemic infarction, intracerebral hemorrhage, or seizures is associated with worse prognosis. [34]

Posterior Reversible Encephalopathy Syndrome

Posterior reversible encephalopathy syndrome (PRES) has been reported in 0.4–1.8% of patients with SLE. [35–37] PRES has been associated with female gender, active SLE, renal involvement, and hypertension [37, 38]. Patients with

SLE who develop PRES have higher mortality rates [35, 37]. PRES presents clinically as encephalopathy, headache, seizures, visual changes, and ischemic and hemorrhagic stroke. Brain MRI shows vasogenic edema mainly in the posterior circulation territory [39]. The exact pathophysiology of PRES in SLE remains unknown but though to be related to dysfunction in flow autoregulation and increased blood-brain barrier permeability [39, 40].

Treatment for PRES consists of supportive care and removing the offending etiology. When patients presenting with active SLE and PRES, it might be reasonable to use immunosuppression to control SLE; in one study, all patients were treated with 3 days of high dose corticosteroids for severe SLE associated with PRES. [36] However, several case reports on patients presenting with PRES after treatment with immunosuppressant such as mycophenolate have been found in the literature. [41, 42]

CNS Demyelination

Demyelination of the CNS has been reported in 0.3–2.7% of SLE patients. [29, 43, 44] SLE-related demyelination can have a monophasic or multiphasic presentation and could resemble other primary demyelinating disorders [45]. In fact, there is an overlap between SLE, multiple sclerosis (MS) and it is often challenging to differentiate between the two conditions. Epidemiologically, they both preferentially affect women of childbearing age. Furthermore, patients with autoimmunity can have more than one disorder simultaneously. In clinical practice, presenting with demyelinating lesions without symptoms of SLE commonly raises the suspicion for MS. Diagnosis of MS requires dispersion in space and time; however, most patients initially present with a clinically isolated syndrome. There is no single clinical feature, test or imaging modality, that can reliably differentiate between SLE-related demyelination and MS, and diagnosis is made based on a combination of all three modalities.

Clinical symptoms of SLE-related demyelination could be indistinguishable from MS. If present, associated symptoms of APS or other systemic symptoms of SLE could favor the diagnosis of SLE-related demyelination. Specifically, renal involvement, livedo reticularis, rash, arthritis, myalgia, headache, and meningismus were considered features that should raise the suspicion for SLE diagnosis not MS. [46] MRI brain is essential diagnostic tool and could show multiple lesions with Dawson's fingers in periventricular distribution, a typical feature of MS. The presence of oligoclonal bands in the CSF favors MS. Although high antinuclear antibody (ANA) titers favor diagnosis of SLE, it has been reported that ANA can be present in 3–80% of MS patients. [47] Similarly, detecting positive anti-phospholipid antibodies favors SLE; however, these antibodies have been detected in 2–44% of patients with MS. [47, 48]

In a systemic review of SLE patients presenting with demyelinating disease, 50% of the patients had features that fulfilled the diagnostic criteria for neuromyelitis optica spectrum disorder (NMOSD). [44] NMO antibodies were detected in 0.9% of patients with SLE. [49] In one study, NMO antibodies were positive in 27% patients with demyelinating SLE while anti-myelin oligodendrocyte glycoprotein (MOG) antibodies were detected in 18% of these patients. [50]

Differentiating SLE-related demyelination from MS, NMOSD, and other types of demyelination is crucial to form a successful treatment strategy. Immunosuppression is the treatment of choice for demyelinating conditions. Although there has been no randomized clinical trials, initial short period of high dose steroids followed by immunosuppressant medication commonly used to treat SLE-related CNS demyelination [51].

Transverse Myelitis

Transverse myelitis has been reported in 1–1.5% of SLE patients. [29, 43] It presents as an inflammatory lesion within the spinal cord that can occur prior to the diagnosis of SLE or years after. [52] Transverse myelitis has a strong association with APS. [53] Clinical symptoms vary based on the longitudinal and transverse location of the lesion. The involvement of spinal cord is not specific for SLE as it is also common in MS, NMO, and other demyelinating disorders.

The pathophysiology of transverse myelitis and demyelination in SLE remains unclear but thought to be related to the underlying physiology of the disease. The neurological damage is possibly caused by a combination of inflammatory cells, autoantibodies, chemokines, oxidative stress, vasculopathy, and ischemic changes. [54] Furthermore, antiphospholipid antibodies can directly damage the myelinated cells. [55]

The best treatment for patients with transverse myelitis in the setting of SLE is uncertain, but typically combines the management of SLE with the management of acute transverse myelitis. In the acute setting, the treatment of transverse myelitis aims at stopping the inflammatory process and minimize the damage to the spinal cord, which may require immunosuppression with high dose steroids and/or cyclophosphamide. [45, 54, 56] Other treatment options have been tried with variable success including plasma exchange and IVIG. [54, 57] Maintenance immunosuppression can be later achieved with azathioprine, methotrexate, mycophenolate, or cyclophosphamide with or without steroids. [54, 57]

Isolated Optic Neuritis

Patients present with central scotoma, decreased visual acuity, and orbital pain optic neuritis and it can lead to blindness [58] and has been reported in 1% of SLE patients [59]. It could be unilateral or bilateral. Most commonly optic neuritis in SLE is

caused by ischemia, but it can also be related to demyelination or axonal loss [59]. Diagnosis is made clinically and supported by finding optic nerve enhancement on MRI. Treatment with high-dose corticosteroids is associated with better outcomes. [59]

Progressive Multifocal Leukoencephalopathy

Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease that is caused by the reactivation of the JC virus in immunosuppressed patients. SLE patients are often treated with immunosuppression and thus are at risk for this condition. PML has been reported in 1.0–2.4/100,000 cases of SLE and has been associated with a poor prognosis [60]. While diagnosis is made based on the radiographic manifestations and identifying JC virus or its antibodies in the serum and CSF, definitive diagnosis requires brain biopsy. [60, 61] There is currently no effective therapy for PML; discontinuation of immunosuppression and supportive care are currently the treatment of choice. [60–62]

Chorea and Often Movement Disorders

Chorea is an ongoing sequence of discrete random involuntary overlapping movements. Chorea is a known manifestation of SLE that has been reported in 1.2–2% of patients and is commonly associated with APS [63, 64]. It may occur after diagnosis of SLE or may be the presenting symptom. [64, 65] Most patients experience a single episode of chorea that subsides within days to months [66]. A study followed 32 patients with chorea and SLE or APS for an average of 12 years and noted that the chorea relapsed in 8 patients [67].

The pathological mechanism remains unknown, but may be related to direct binding of auto-antibodies to lipid-rich areas of the basal ganglia leading to neuronal depolarization and sometimes neuronal injury [63]. Diagnosis of chorea is made clinically. The MRI of the brain is usually unremarkable in the setting of SLE- or APS-related chorea but should be performed to rule out other etiologies. Treatment with antidopaminergic agents. Immunosuppression, anticoagulation, and plasmapheresis can be used to treat SLE and/or APS and have variable degree of success in treating the chorea [66].

Seizures

Seizures have been reported in 2.1–11.6% of SLE patients and with higher rates in children. [68–70] Seizures maybe the presenting symptom of SLE or can occur after the diagnosis is made [71]. Most commonly seizures have a generalized tonic-clonic semiology but could also have a focal presentation [71]. Multiple mechanisms could be implicated in the pathogenesis of seizures in the setting of SLE. Seizures could be secondary to SLE complications such as CVST or PRES as described above. Seizures could also be caused by microinfarcts, meningeal hemosiderosis, or direct neurotoxicity from autoantibodies. [72]

SLE patients presenting with seizures are more likely to have positive antiphospholipid antibodies and anti-ribosomal P antibodies. [69, 73] Treatment includes traditional antiseizure medication in addition to the management of SLE and its complications such as CVST or PRES if present.

Idiopathic Intracranial Hypertension

Patients present with positional headache, papilledema, and visual changes including scotomas and sixth nerve palsy. Idiopathic intracranial hypertension (IIH) has been reported in 0.7–1.5% of SLE patients. [74, 75] The pathogenesis of IIH in SLE remains unknown; one series showed that six patients out of eight had positive anti-Ro antibodies and proposed a role for this antibodies in the pathogenesis of IIH [74]. Acetazolamide is used for IIH to help decrease CSF production. Ventriculoperitoneal shunting may be needed for severe cases. [59] The role of corticosteroids for IIH in the setting of SLE remains controversial. [74]

Aseptic Meningitis

Aseptic meningitis has been reported in 0.2% of SLE patients. [68] It usually occurs early in the course of the disease but can happen any time. [76] Aseptic meningitis presents with fever, headache, and CSF lymphocytic or polymorphonuclear pleocytosis with negative microbiology. Several reports have associated the use of non-steroidal anti-inflammatory drugs (NSAIDs) especially ibuprofen with aseptic meningitis [76].

Headaches

The prevalence of headache in SLE varies widely in the literature ranging from 24 to 72% with no clear association with disease activity [77, 78]. It is unclear if the prevalence of headache in SLE is higher than that in the general population [77]. Migraines and tension headaches are the most common, followed by cluster headaches [77, 79]. The prevalence of primary headaches is comparable to the general population except for chronic headaches which are more common in SLE [79]. Headache is a common manifestation of SLE complications that involve increased ICP or meningeal inflammation, such as CVST, PRES, aseptic meningitis, or IIH as described above.

Lupus headache is a term used to describe a severe headache that is directly attributed to SLE with no secondary cause [77]. The concept of lupus headache is controversial, and the pathogenic mechanism is unclear. [77]

Dementia

Cognitive impairment has been reported in 17–90% of SLE patients. [55, 80•] Although less common, higher rate of dementia has been associated with SLE [80•, 81]. APS specifically has been associated with higher risks of cognitive dysfunction. [55] The exact pathological mechanism of cognitive dysfunction in the setting of SLE remains unclear. Cumulative effects of CNS involvement through autoimmune demyelination, microvascular thrombosis, and volumetric brain loss could play a role. [82] APS-related microvascular thrombosis and immune-mediated pathways may be implicated. [55] Furthermore, antiphospholipid antibodies can cause endothelial injury at the level of blood-brain barrier and directly bind neurons and astrocytes. [55]

Treatment remains supportive care as no specific treatment for dementia in the setting of SLE is currently available. Memantine did not show any benefit in a clinical trial of 51 SLE patients. [83]

Peripheral Nervous System Complications

Peripheral Neuropathy

Polyneuropathy has been reported in 3.4–7.5% of SLE patients [84•, 85]. Sensory-motor and sensory polyneuropathies were the most common forms [84•, 85]. These neuropathies could be axonal, demyelinating, or mixed [85]. Polyneuropathy could be attributed directly to SLE or related to other common concomitant etiologies such as diabetes mellitus, vitamin deficiencies, or toxic medications [85]. SLE-related neuropathy has been reported in 1% of patients with SLE [86]. SLE-related neuropathy is often associated with CNS involvement [86]. SLE-related polyneuropathy occurs earlier in the course of the disease and is associated with higher disease activity when compared to non-SLE-related polyneuropathy [85]. Treatment with corticosteroids and immunosuppression should be considered in SLE-related neuropathy, in addition to the correction of any other potential causes if found. [85]

Mononeuritis Multiplex

Mononeuritis multiplex has been reported in 1.2% of patients with SLE [85]. When found in SLE patients, it is often thought to be related directly to SLE and rarely other causes are found [85]. Clinically, patients present with sensory-motor or pure sensory deficits [87]. Lower extremities are more commonly involved [87]. Pathologically, the most common mechanism is vasculitis, while thrombosis and lymphocytic inflammation were noted in some cases [87]. Prompt diagnosis and treatment with immunosuppressants are recommended [87].

Cranial Neuropathies

Cranial neuropathy has been reported in 1.7–2.4% of SLE patients [84•, 85]. Multiple or single cranial nerves could be involved [84•]. Most common cranial nerves involved are III, V, VI, and VII [85].

Inflammatory Demyelinating Polyneuropathies

Acute inflammatory demyelinating polyneuropathy (AIDP) and chronic inflammatory demyelinating polyneuropathy (CIDP) are rare and have been reported in 0.8% of patients with SLE [85]. Diagnosis is made based on clinical presentation, nerve conduction studies, and CSF analysis. Severe SLE has been associated with more aggressive form of CIDP [88]. Patients with CIDP and AIDP are treated with IVIG or plasma exchange. Treatment in the setting of SLE has not been studied; many cases in the literature have been treated with steroids and immunosuppression in addition to IVIG or plasma exchange [88].

Myasthenia Gravis

Myasthenia gravis (MG) is rare and has been reported in 0.1–0.2% of patients with SLE [84•, 86]. Commonly, MG is diagnosed before SLE but could also be diagnosed after [89]. In patients who had MG diagnosed first, thymectomy was thought to precipitate the development of SLE [89]. Diagnosis is typically made clinically with the presence of ocular symptoms and/or fatigable weakness and confirmed using nerve conduction studies and acetylcholine receptor antibody detection.

Autonomic Neuropathy

Reported in 40–100 in 100,000 of patients with SLE. [84•, 86] No relation to disease duration or activity has been noted [90]. Most common clinical manifestations include dry/running nose, diarrhea/constipation, warm/cold extremities, sweating disturbances, and impotence [90].

Necrotizing Autoimmune Myopathy

Necrotizing autoimmune myopathy (NAM) is rare. SLE has been reported in 21% of patients with NAM, while the rest of the cases are associated with statin use or anti-signal recognition particle (SRP) antibodies. [91, 92] Most patients with SLE-related NAM do not have myositis-specific antibodies [91]. Clinically, patients often present with symmetric proximal muscle weakness that develops over the course of weeks to months [91]. Diagnosis is made based on clinical presentation, elevated serum CK often more than 5000 u/ml, and

electromyographic testing; muscle MRI could be useful [91]. Treatment with immunosuppressants and steroids [91, 92].

Conclusions

- Neurological manifestations are common in SLE patients.
- APS is commonly associated with SLE; its presence increases the likelihood of neurological complications.
- SLE is associated with acute ischemic stroke. Several mechanisms are implicated including increased thrombosis due to APS, embolization from Libman-Sacks endocarditis, CNS vasculitis, and higher prevalence of atherosclerosis.
- Demyelination of the central nervous system could be secondary to SLE. Demyelination could also be related to MS and NMOSD both of which overlap with SLE. Differentiating among those three conditions is challenging and may have major implications on the choice of treatment.
- Most patients with SLE develop headache during the disease course. SLE can cause headaches by multiple mechanisms such as CVST, PRES, aseptic meningitis, and IIH. It might be the only manifestation of these serious complications.
- Peripheral nervous system involvement is common and could be attributed directly to SLE in some cases. Immunosuppressants and corticosteroids often needed for treatment.

Compliance with Ethical Standards

Conflict of Interest Amir Shaban, MD[1]; Enrique C. Leira each declare no potential conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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