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Management of neuropsychiatric lupus

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Nervous system disease in systemic lupus erythematosus (SLE) is manifested by a wide variety of clinical manifestations. Despite the development of a universal classification for neuropsychiatric (NP) lupus in 1999, there continues to be considerable variability in the reported prevalence of NP syndromes between different lupus cohorts. Due to the lack of specificity of individual NP manifestations, non-SLE causes such as complications of therapy and co-morbidities must be considered in advance of attributing the event to one or more primary immunopathogenic mechanisms. These include intracranial microangiopathy, autoantibodies to neuronal and non-neuronal antigens, and the generation of proinflammatory cytokines and mediators. The diagnosis of NP-SLE remains largely one of exclusion and is approached in individual patients by thorough clinical evaluation, supported when necessary by autoantibody profiles, diagnostic imaging, electrophysiologic studies and objective assessment of cognitive performance. Given the diversity in clinical manifestations, the management is tailored to the specific needs of individual patients. In the absence of controlled studies, the use of symptomatic therapies, immunosuppressives, anticoagulants and non-pharmacologic interventions is supported by case series and clinical experience.

Key words: autoantibodies; cognitive function; lupus; nervous system; neuropsychiatric; treatment.

Involvement of the nervous system by systemic lupus erythematousus (SLE) has been recognized for over 100 years and includes a wide variety of neurologic (N) and psychiatric (P) manifestations. Despite recent advances in our understanding of this

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particular subset of lupus, the presentation of neuropsychiatric (NP) disease in individual SLE patients continues to pose diagnostic and therapeutic challenges for rheumatologists. These difficulties arise in part due to the lack of specificity of the majority of the NP manifestations, uncertainty regarding the pathogenic mechanisms and a paucity of data to support therapeutic strategies. This chapter summarizes the most recent information on this intriguing aspect of SLE, with emphasis on diagnosis and management.

CLASSIFICATION OF NP-SLE

The American College of Rheumatology (ACR) classification criteria for SLE include the NP manifestations, seizures and psychosis. However, it is widely acknowledged that a much broader range of NP disease manifestations occurs in SLE patients. Virtually all studies indicate that most NP events reflect involvement of the central nervous system compared to involvement of either the peripheral or autonomic nervous systems. A particular NP event might be due to either a diffuse disease process (e.g. psychosis and depression) or focal process (e.g. stroke and transverse myelitis), depending on the anatomic location of pathology. Although several classifications have been developed for NP-SLE[1–3], most have lacked definitions for individual manifestations and uniformity in the approach to investigation and diagnosis. In 1999, the ACR research committee produced a standard nomenclature and diagnostic criteria for 19 NP syndromes that are known to occur in SLE patients (Table 1).[4] For each of the 19 NP syndromes, potential etiologies other than SLE were identified for either exclusion, or recognized as an 'association', acknowledging that in some clinical presentations definitive attribution is not possible. The identification of other non-lupus causes for NP events in SLE patients is of critical importance and has not been adequately addressed in previous classification systems. Guidelines for reporting NP events were also developed by the ACR research committee and specific diagnostic tests were recommended for each syndrome. Although these criteria were developed primarily to facilitate research studies of NP-SLE, they also provide a practical guide to the assessment of individual SLE patients with NP disease.

Table 1. Neuropsychiatric syndromes in SLE as defined by the American college of rheumatology nomenclature (adapted from Ref. 4).

Central nervous system	Peripheral nervous system
Aseptic meningitis	Guillain–Barré syndrome
Cerebrovascular disease	Autonomic neuropathy
Demyelinating syndrome	Mononeuropathy
Headache	Myasthenia gravis
Movement disorder	Cranial neuropathy
Myelopathy	Plexopathy
Seizure disorders	Polyneuropathy
Acute confusional state	
Anxiety disorder	
Cognitive dysfunction	
Mood disorder	
Psychosis	