Review Article

An Overview on Diagnosis and Management Approach of Systemic Lupus Erythematosus

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Abstract

The systemic lupus erythematosus (SLE) is a chronic prototypical systemic autoimmune disease with extremely varied clinical manifestations, pathogenesis, and epidemiological burden worldwide among different racial, ethnic age, and gender groups. The disease has a complex form of pathogenesis that is not fully understood as SLE has extremely varied clinical manifestations and continues to have unpredictable courses. However, the approach to SLE imposes complex modalities of management and highly experienced clinicians. Initial clinical evaluation and new classification criteria are anticipated for a better diagnostic approach. To assist internists in understanding Systemic Lupus erythematosus and the constantly evolving diagnostic criteria and recommended modalities of management, as well as observing the major risk factors. This review included clinical evidence-based guidelines conducted and analyzed by the PubMed search and only English articles, documents, and evidence-based clinical trials were included. The terms were applied within the title or abstract title ((“SLE "[Mesh] AND “Lupus” Mesh] AND “Criteria"[Mesh]AND “Management"[Mesh]). The new criteria structure will prove useful in the diagnosis of questionable SLE patients. Approach to SLE involves complex modalities of treatment and early detection of SLE comorbidities is the cornerstone of management.

Keywords: SLE, Epidemiology, Criteria, Classification, Management

Introduction

The systemic lupus erythematosus (SLE) is a chronic prototypical systemic autoimmune disease with extremely varied clinical manifestations, pathogenesis, and epidemiological burden worldwide among different racial, ethnic age, and gender groups [1, 2]. The complex etiology and clinical variations of SLE make it a difficult disease to grasp in clinical practice [3]. Classification criteria is an essential diagnostic approach for defining SLE unpredictable courses. Furthermore, the approach to SLE elaborates complex modalities of treatment that requires experienced clinicians [4]. This review will improve the understanding of Systemic Lupus erythematosus for internists and provide the constantly evolving diagnostic criteria and recommended modalities of managing the disease, as well as observing the risk factors and morbidity and mortality rates.

Materials and Methods

This review included clinical evidence-based guidelines conducted and analyzed by the PubMed search and only English articles, documents, and evidence-based clinical trials were included. The terms were applied within the title or abstract title ((“SLE "[Mesh] AND “Lupus” Mesh] AND “Criteria"[Mesh] AND “Management"[Mesh])). In regards to the inclusion criteria, the articles were selected based on the inclusion of one of the following topics: systemic lupus erythematosus, approach, evaluation, diagnosis, and management. Exclusion criteria were all other articles that did not have one of these topics as their primary endpoint.

Review

Epidemiology

A recent 2018 study had accurately described a worldwide prevalence and incidence of SLE. California Lupus

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Surveillance Project and the Manhattan Lupus Surveillance program reported a higher incidence of lupus in women regardless of any racial background. However, both studies estimated a greater incidence and prevalence of SLE in Asians and Hispanics in comparison with Caucasians [1]. SLE is found to be more prevalent in African and Native-American populations and they also experience high mortality rates. Moreover, on a recent data presented by Michigan Lupus Epidemiology and Surveillance Registry Arab-Americans have a higher incidence than non-Arab Caucasians and African Americans. However, the epidemiology about SLE in the Middle East appears to be insufficient due to lack of further research in this matter [1, 5].

Pathogenesis

SLE has a complex form of pathogenesis that is not fully understood. According to a 2015 study, genetic factors have an enormous impact on the pathogenicity of SLE and other autoimmune disorders. SLE was estimated with a first-degree relative risk of 5.87% but with high heritability rates of 43.9% [6, 7]. Environmental factors linked to exogenous and indigenous mechanisms also have a potential association with SLE pathogenicity. Several Exogenous factors linked to SLE pathogenicity such as solvents, UV radiation, pesticides. Moreover, intrinsic factors include the patient's reproductive history in females mostly and latent infections as Epstein Barr virus infection [3]. The effect of these environmental factors leads to activation of the innate immune cells and self-reactive lymphocytes [8]. Drugs induced lupus erythematosus are reported in rare cases [9].

Diagnosis

Systemic lupus erythematosus progress and severity depend on the course of the disease and major systemic involvement, including most commonly the skin, renal, musculoskeletal cardiopulmonary, hematologic reproductive, and neuropsychiatric systems [10, 11]. Systemic lupus erythematosus has extremely varied clinical manifestations and continues to have unpredictable courses. Once SLE is suspected initial clinical evaluation and diagnostic criteria **(Table 1)**. In 2012, ACR (American College of Rheumatology) classification criteria performed better results in terms of sensitivity rather than specificity while SLICC (Systemic Lupus International Collaborating Clinics) classification criteria anticipated better results in terms of specificity. However, in 2017 a new perspective has been revised and presented a jointly supported ACR/EULAR (European League Against Rheumatism) criteria with a percentage of (93-97%) specificity and (96-98%) in terms of sensitivity [12, 13].

In 2019, EULAR/ACR has been adapted as a new classification criterion. EULAR is built on previous classification criteria adding non-infectious fever as a new item in the early stages of SLE and ANA (antinuclear antibodies) as an essential criterion. Moreover, EULAR introduced a more logical approach to identify SLE with sufficient 10 points; reaching 6 points is significant for maintaining EULAR classification [14]. On the other hand, ACR structure for classification depends on detecting any 4 of the 11 ACR criteria, while SLICC structure depends mainly on histological compatibility with lupus nephritis and abnormal ANA titers of anti-dsDNA or any 4 of the 17 features that must include at least one immunological symptom [11, 14].

Table 1. Diagnosis of SLE in three classifications Involving SLICC, ACR and new EULAR/ACR 2019 Criteria [11, 14]

Systems	SLICC	ACR	EULAR/ACR 2019
Skin	Subacute or acute cutaneous lupus	Malar(Butterfly) facial rash	Acute cutaneous lupus [6] Subacute lupus [4] Discoid lupus [4]
Immunologic	-ANA Positive results, antiphospholipid antibodies or anti-Sm, anti-dsDNA, low complement (C3, C4, CH50), - direct Coombs test (Hemolytic anemia) - Chronic cutaneous lupus - Oral and nasal ulcers - Non-scarring alopecia	-ANA Positive results -Elevated antiphospholipid antibodies or anti-Sm, anti-dsDNA - Discoid rash - Oral and nasal ulcers - Photosensitivity	- ANA entry criterion - low complements: C3 or C4 [3] C3 and C4 [4] -antiphospholipid [2] -Anti-dsDNA and Anti-Sm [6] - Coombs+ hemolytic anemia [4] - Non-scarring alopecia [2] - oral and nasal ulcers [2]
Musculoskeletal	Synovitis in 2 or more joints(effusion or swelling)morning stiffness for 30minutes	Arthritis in 2 or more joints	Arthritis [6]
Renal	Urinary Creatinine >500mg or red cell casts/24hours	Persistent proteinuria or red cell cast	-Proteinuria [4] -Lupus nephritis Classes: - II/V [8] - III/IV [10]
Hematologic	Leukopenia <4000 cell/mm^{3}more than once or lymphopenia <1500cell/mm^3 Hemolytic anemia, Thrombocytopenia< 100,000 cells/mm^3	Leukopenia <4000 cell/mm^3 and lymphopenia <1500cell/mm^3 Hemolytic anemia, Thrombocytopenia< 100,000 cells/mm^3	-Leukopenia [3] -Thrombocytopenia[4]

Neuropsychiatric	Mononeuritis complex, psychosis. Seizures, cranial or peripheral neuropathy, myelitis	Psychosis or seizures	-Delirium [2] -Psychosis [3] -Seizures [5]
Cardiopulmonary	Serositis (involves pleurisy, pericardial and pleural effusion and pericarditis)	Pleurisy and pericarditis	-Effusion [5] -Pericarditis [6]

However, detection of SLE does not rely upon fulfilling classification criteria itself, but rather depends on the physician performance and his approach to an SLE patient [13].

Management

The approach to SLE involves complex modalities of treatment that requires experienced clinicians from different specialties [4]. In general, early detection of SLE comorbidities is the cornerstone of management. SLE comorbidities are highly associated with modifiable life-threatening risks especially in patients with cardiovascular (with a higher prevalence of 28-40%) and renal involvement. About 50% of patients are presented with renal injury (Lupus nephritis) notably in elderly individuals and 15% are presented with homocysteinemia, both are considered risk factors for myocardial infarction and thrombosis in patients with lupus [11, 15].

As an internist, patients with SLE should receive intense educational guidance and support sessions as SLE therapeutic measures are sometimes non-pharmacological. Changing lifestyle activities to avoid future complications is essential. Recommend regular exercise to avoid generalized fatigability and improve cognitive dysfunction that accompanies fibromyalgia. It is recommended to educate patients about cardiovascular and renal complications as well as possible opportunistic infections such as pneumonia. Refer to Rheumatologist for further checkup [11, 15].

Conclusion

The systemic lupus erythematosus (SLE) is a chronic prototypical systemic autoimmune disease with extremely varied clinical manifestations. The new criteria structure will prove useful in the diagnosis of questionable SLE patients. Approach to SLE involves complex modalities of treatment and early detection of SLE comorbidities is the cornerstone of management. The internist needs to coordinate closely with a rheumatologist to improve the quality of care for the SLE patient.

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